



DESIGN AND DEVELOPMENT OF A DUAL COMPONENT CONTROLLED-RELEASE TABLET OF DIOSMIN AND *EUPHORBIA PROSTRATA* EXTRACT.

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Abstract: Hemorrhoids are one of the most common anorectal disorders, causing pain, bleeding, prolapse, itching, and significant discomfort that adversely affects patients' quality of life. Conventional therapies often require frequent dosing and may provide only temporary symptomatic relief. The present study focuses on the development and evaluation of a controlled-release tablet containing Diosmin and Euphorbia prostrata extract for the effective management of hemorrhoids. Diosmin, a well-established flavonoid, exhibits venotonic, vasoprotective, anti-inflammatory, and antioxidant properties, while *Euphorbia prostrata* possesses hemostatic, anti-inflammatory, wound-healing, and astringent activities that complement the therapeutic action of Diosmin. A controlled-release matrix tablet was formulated using suitable polymers to achieve sustained drug release, reduce dosing frequency, and improve patient compliance. The prepared formulations were evaluated for pre-compression and post-compression parameters, including flow properties, hardness, friability, weight variation, drug content, and in vitro dissolution studies. The optimized formulation demonstrated acceptable pharmaceutical characteristics and sustained drug release over the desired period, following appropriate release kinetics. The study concludes that the controlled-release combination tablet of Diosmin and *Euphorbia prostrata* represents a promising therapeutic approach for the effective and prolonged management of hemorrhoids, with the potential to enhance efficacy, reduce recurrence, and improve patient adherence.

Keywords: Hemorrhoids; Controlled-release tablet; Diosmin; *Euphorbia prostrata*; Matrix tablet; Venotonic activity; Anti-inflammatory activity; Herbal formulation; In vitro dissolution.

INTRODUCTION

Hemorrhoids are among the most common anorectal disorders encountered in clinical practice and represent a significant cause of morbidity worldwide. Although frequently considered a benign and self-limiting condition, symptomatic hemorrhoidal disease can markedly impair quality of life due to bleeding, prolapse, pain, pruritus, and perianal discomfort. Hemorrhoids are defined as the pathological enlargement and distal displacement of the normal anal cushions, which are vascular structures composed of arteriovenous channels, connective tissue, and smooth muscle fibers located within the anal canal [1].

Anatomically, hemorrhoids are classified as internal or external based on their origin relative to the dentate (pectinate) line. Internal hemorrhoids arise above the dentate line and are covered by columnar epithelium, which lacks somatic pain fibers; therefore, they typically present with painless rectal bleeding [2]. External hemorrhoids originate below the dentate line and are covered by anoderm, which is richly innervated, making them potentially painful, particularly when thrombosed. Mixed hemorrhoids may involve components of both types [3].

Controlled release (CR) tablets are specialized oral solid dosage forms formulated to release the active pharmaceutical ingredient (API) at a predetermined and controlled rate for a prolonged period of time. The primary objective of controlled release systems is to maintain consistent plasma drug concentrations within the therapeutic window while minimizing fluctuations associated with conventional immediate-release formulations. By sustaining drug release, CR tablets reduce dosing frequency, improve patient compliance, and enhance therapeutic efficacy, particularly in chronic disease management [4].

Controlled release systems are particularly beneficial for drugs with short biological half-lives, narrow therapeutic indices, or those intended for long-term therapy such as antihypertensives, antidiabetics, analgesics, and antidepressants [5].

The design of controlled release tablets requires careful consideration of the physicochemical and pharmacokinetic properties of the drug. Ideal candidates for CR formulations typically possess moderate half-lives (2–8 hours), good aqueous solubility, high potency, and uniform absorption throughout the gastrointestinal tract [6].

Diosmin is a semisynthetic flavonoid derived from hesperidin, a natural compound found in citrus fruits. It is classified as a venotonic and vasoprotective agent and is widely used in the management of venous disorders [7]. Diosmin is primarily prescribed for conditions associated with impaired venous circulation, particularly chronic venous insufficiency (CVI), varicose veins, and hemorrhoids. By improving vascular tone and protecting blood vessels, it plays an important role in treating diseases related to weak or dilated veins [8].

The primary mechanism of action of diosmin involves increasing venous tone by prolonging the vasoconstrictor effect of norepinephrine on the vein walls. This reduces venous distensibility and venous stasis, thereby enhancing venous return to the heart [9].

Chemical Information

Generic name: Diosmin

Chemical name (IUPAC): 3',5,7-Trihydroxy-4'-methoxyflavone-7-rhamnoglucoside (flavone glycoside form)

Melting point: 270–280 °C

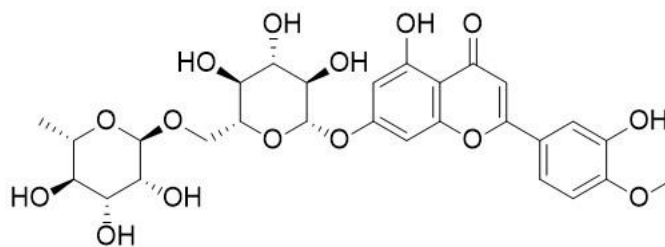
Therapeutic class: Venotonic agent, vasoprotective

Pharmacological class: Bioflavonoid (flavone glycoside)

Category: Not classified as DMARD/NSAID/sterol/etc.; typically falls under venoactive phytochemical agents used in vascular disorders [10].

Molecular formula: C₂₈H₃₂O₁₅

Molecular weight: 608.54 g/mol

Chemical structure:**Fig Diosmin**

Euphorbia prostrata is a small, fast-spreading, prostrate herb belonging to the family Euphorbiaceae [11]. It is widely distributed across tropical and subtropical regions of the world, including India, Southeast Asia, parts of Africa, and the Americas. Commonly found along roadsides, in gardens, lawns, and disturbed soils, *Euphorbia prostrata* is often regarded as a weed due to its rapid growth and adaptability [12].

Botanically, *Euphorbia prostrata* is a low-growing, mat-forming annual herb. It has reddish, hairy stems that spread flat along the ground, and small, opposite leaves that are elliptical or oblong in shape, often bearing a purplish spot at the center [13].

The plant is rich in bioactive compounds, including flavonoids (such as quercetin and rutin), tannins, triterpenoids, phenolic acids, and essential oils. These phytochemicals are responsible for a range of pharmacological properties attributed to the plant [14].

Modern pharmacological studies have validated many of these traditional uses. Research has demonstrated that *Euphorbia prostrata* exhibits anti-inflammatory, hemostatic (stops bleeding), antimicrobial, antioxidant, and astringent activities. It has been particularly noted for its effectiveness in treating hemorrhoids, and several herbals [15].

**Fig. *Euphorbia prostrata* [16]**

Table 1. Taxonomical Classification

S. No.	Taxonomic Rank	Classification
1	Kingdom	Plantae
2	Subkingdom	Tracheobionta (Vascular plants)
3	Superdivision	Spermatophyta (Seed plants)
4	Division	Magnoliophyta (Angiosperms)
5	Class	Magnoliopsida (Dicotyledons)
6	Subclass	Rosidae
7	Order	Malpighiales
8	Family	Euphorbiaceae
9	Genus	Euphorbia
10	Species	<i>Euphorbia prostrata</i> Aiton

EXTRACTION OF PLANT EXTRACT (SOXHLET EXTRACTION):**Procedure:**

Step-I: Preparation of Plant Material-Collect the plant and wash thoroughly with the water. Shade dries for the weeks and then grind into coarse powder (4.560 g).

Step- II: Loading the Sample-Weigh specific quantity of powdered plant and packed into the thimble (60g in each thimble). Placed the thimble in Soxhlet extractor, attached the extractor to the round bottom flask containing solvent.

Step-III: Extraction Process-Gently heat the solvent in the round-bottom flask. The solvent evaporates and moves upward through the Soxhlet apparatus. It then condenses in the condenser and drips onto the thimble containing the plant material. Once the chamber fills up, the solvent siphons back into the round-bottom flask with the extracted compounds. This repeated cycle of evaporation, condensation, and siphoning continues for several time until the solvent in the siphon turns nearly colourless, showing that the extraction process is complete.

Step-IV: Extract Recovery-Once the extraction process is finished, the round bottom flask is removed from the assembly and extracted compounds are collected. The solvent is removed to obtain concentrated extract and stored in desiccator [17].

PHYTOCHEMICAL SCREENING

Preliminary phytochemical screening of the *Euphorbia prostrata* extract was carried out using standard qualitative methods to detect major secondary metabolites. *Euphorbia prostrata* is widely used in the management of hemorrhoids because of its anti-inflammatory, antioxidant, analgesic, venotonic, and wound-healing properties. Alkaloids, flavonoids, tannins, glycosides, terpenoids, and phytosterols were identified using Dragendorff's, alkaline reagent, ferric chloride, Keller–Killiani, Salkowski, and Liebermann–Burchard tests, respectively. The presence of these phytoconstituents was confirmed by the characteristic colour change or precipitate produced during the respective qualitative tests, indicating the therapeutic potential of the extract for hemorrhoidal treatment [19].

CHARACTERIZATION OF DIOSMIN

Hydroxychloroquine was evaluated for its physical appearance, melting point, solubility profile, and identification characteristics according to pharmacopeial standards.

DESIGNING OF FORMULATION:

Wet granulation method: Accurately weighed quantities of Diosmin, Euphorbia prostrata extract, Ethyl Cellulose, lactose and Microcrystalline Cellulose (MCC) were passed through sieve No. 40 and mixed uniformly in a mortar for 10–15 minutes with Polysorbate 80. Polyvinylpyrrolidone (PVP K30) was dissolved in a suitable quantity of purified water to prepare the binder solution. The binder solution was gradually added to the powder blend with continuous mixing until a coherent wet mass was obtained.

The wet mass was passed through sieve No. 16 to produce granules and dried in a hot air oven at 50–60°C until the desired moisture content was achieved. The dried granules were then passed through sieve No. 20 to obtain uniform-sized granules. Finally, magnesium stearate was added as lubricant, respectively, and blended thoroughly with the granules.

EVALUATION PARAMETERS OF POWDER BLEND:

The blend of powders was evaluated for the following parameters:

Angle of Repose:

The fixed funnel method was used to calculate the angle of repose. The granules were permitted to pass through a funnel that was set on a level surface at a specific height. The angle of repose was computed using the following formula after the height (h) and radius (r) of the powder heap were measured [19].

$$\theta = \tan^{-1} (h/r)$$

Where: h = height of pile, r = radius of pile

Bulk Density:

A precisely measured amount of granules was added to the measuring cylinder, and the initial volume was recorded [20].

Bulk Density = Mass of powder / Bulk volume

Tapped Density:

The granule-filled measuring cylinder was mechanically tapped until a consistent volume was achieved, at which point the final tapped volume was noted [21].

Tapped Density = Mass of powder / Tapped volume

Carr's Compressibility Index:

Granules were precisely weighed and then put into a dry, clean measuring cylinder. Bulk volume was defined as the initial volume that the granules occupied. After that, the cylinder was mechanically tapped a certain number of times to achieve a consistent volume; the resulting volume was recorded as the tapped volume. Carr's compressibility index was computed using bulk density and tapped density [18].

Carr's Index = $\frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$

Formulation of Tablet:

The controlled-release tablets containing Diosmin and Euphorbia prostrata extract were prepared by the wet granulation method according to the composition shown in Table 1. Each formulation contained 300 mg of Diosmin and 50, 75 mg of Euphorbia prostrata extract respectively, while the concentrations of Ethyl Cellulose were varied to optimize the drug-release profile. Diosmin, euphorbia prostrata, Ethyl Cellulose and Microcrystalline Cellulose (MCC) were accurately weighed, passed through sieve No. 40, and blended thoroughly to obtain a uniform powder mixture. Polyvinylpyrrolidone K30 (PVP K30) was used as a binder to prepare the wet mass also add Polysorbate 80 as a wetting agent for extract, which was subsequently granulated through sieve No. 16 and dried in a hot air oven at 50–60°C. The dried granules were resized through sieve No. 20 and lubricated with magnesium stearate. The lubricated granules were then compressed into tablets using a rotary tablet compression machine fitted with a 9.7 mm punch and die set. A total of four formulations (F1–F4) were prepared and evaluated for their physicochemical characteristics and controlled-release performance.

Table no.1 Composition of Unit Dose of Tablet

S. No.	Component	Function	F1	F2	F3	F4
1	Diosmin	API	300	300	300	300
2	Euphorbia prostrata	API	50	75	50	75
3	Ethyl Cellulose	Controlled Release Polymer	120	160	90	200
4	MCC	Filler / Bulking Agent	90	75	70	80
5	Lactose	Diluent	15	15	10	15
6	Polyvinyl Pyrrolidone (PVP)	Binder	10	10	10	10
7	Magnesium Stearate	Lubricant	5	5	5	5
8	Polysorbate 80 (Tween 80)	Wetting Agent	10	10	15	15

POST-COMPRESSION EVALUATION OF TABLETS

The quality and effectiveness of the manufactured herbal tablets were assessed by post-compression evaluation experiments.

Physical Appearance: The general appearance of tablet was studies visually in shape, color, texture and odor.

Thickness Test: A Vernier caliper was used to measure the tablet thickness. The average thickness was determined using tablets that were chosen at random [22].

Hardness Test: A Monsanto hardness tester was used to measure the tablets' hardness. The average hardness of randomly chosen tablets was measured in kg/cm².

Friability Test: The Roche friabilator was used to conduct the friability test. The friabilator was used to rotate pre-weighed tablets at 25 RPM for four minutes. After the test was finished, the tablets were dedusted and reweighed [23].

Friability (%) = $\frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \times 100$

Weight Variation Test: A digital balance was used to weigh each of the twenty tablets that were chosen at random. In accordance with pharmacopoeial norms, the average weight was computed and contrasted with the weights of individual tablets [24].

Disintegration Test: USP disintegration equipment was used to conduct the disintegration test. The time it took for the tablets to completely disintegrate was noted after they were put in a basket rack assembly with distilled water kept at $37 \pm 2^\circ\text{C}$ [25].

Dissolution study: Using USP dissolution equipment with an appropriate dissolution medium kept at $37 \pm 0.5^\circ\text{C}$, an in vitro dissolution investigation was conducted. Samples were taken out at prearranged intervals and subjected to spectrophotometric analysis [22].

Drug Release (%) = $\frac{\text{Amount of drug released}}{\text{Total amount of drug}} \times 100$

RESULTS AND DISCUSSION

Characterization of Diosmin:

Physical Appearance:

Table No.2 Physical properties of Diosmin

Parameter	Description
Texture	Fine, free-flowing crystalline powder
Color	Pale yellow to light yellow
Taste	Slightly bitter
Odor	Odorless or practically odorless
appearance	Fine crystalline powder

Melting Point:

Melting Point of Diosmin was found to be 277 by using Digital Melting/Boiling point apparatus.



Fig. 1 Melting Point of Diosmin

Solubility Profile

Diosmin exhibits the following solubility characteristics:

Table 3 Solubility Profile of Diosmin

Solvent	Solubility
Water	Practically insoluble (very low; typically, <0.05 mg/mL at room temperature, depending on conditions)
Ethanol	Slightly soluble
Methanol	Slightly to moderately soluble
Dimethyl sulfoxide (DMSO)	Freely soluble
Dimethylformamide (DMF)	Soluble
Acetone	Slightly soluble
Chloroform	Practically insoluble
Ether	Practically insoluble

UV Spectroscopy:

Ultraviolet spectroscopic analysis of Diosmin was performed in the wavelength range of 200–800 nm. Diosmin exhibits characteristic absorption maxima at approximately 268 nm in suitable solvent (i.e DMSO).

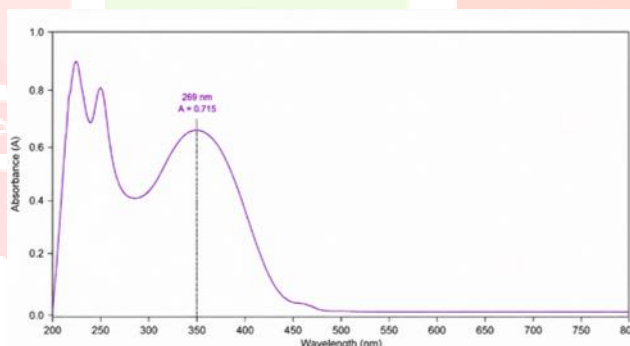


Fig. 2 Absorbance of Diosmin in UV Spectrophotometer

HPLC:

HPLC analysis of Diosmin was carried out using UV detection at 268 nm. The chromatogram showed a sharp and well-defined peak at a retention time of approximately 3.5 min, corresponding to Diosmin. The absence of significant interfering peaks near the drug retention time indicated good specificity of the method. The observed retention time and peak characteristics confirmed the identity of Diosmin and demonstrated the suitability of the drug sample for further formulation studies.

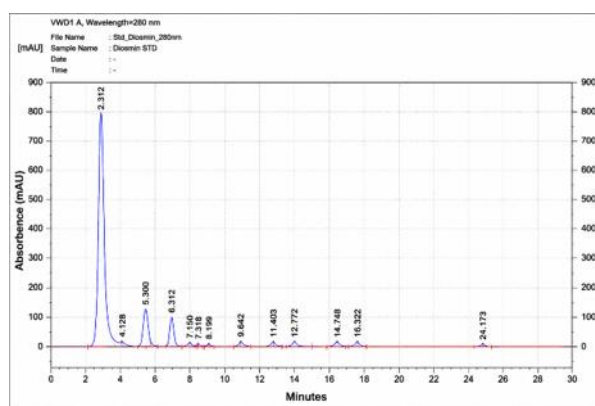


Fig. 3 HPLC analysis of HCQ

PERCENTAGE YIELD

The percentage yield of *Euphorbia prostrata* extract was determined after the extraction process. From 250 g of dried stem powder, 28.5 g of dried extract was obtained, resulting in a percentage yield of 11.4% w/w.

The yield was calculated using the ratio of the weight of dried extract to the weight of dried powder and was found to be satisfactory for further formulation and evaluation studies.

PHYTOCHEMICAL SCREENING

Table 4 Qualitative analysis of *Euphorbia prostrata* in Ethanol

{+} = positive, {-} = negative

Sr. no.	Phytochemicals	Results
1.	Alkaloids	+
2.	Flavanoids	+
3.	Tanins	+
4.	Treprenoids	+
5.	Phytosteroles	+
6.	Glycosides	+

PRE-COMPRESSION PARAMETERS OF TABLET

The pre-compression parameters of the prepared herbal tablet granules were evaluated to determine their flow and compression characteristics, and the results are presented in Table 6.7. The angle of repose ranged from $27.95 \pm 0.29^\circ$ to $31.44 \pm 0.38^\circ$, indicating good to excellent flow properties. Formulation F3 exhibited the lowest angle of repose ($27.95 \pm 0.29^\circ$), suggesting superior flowability, whereas F4 showed the highest value ($31.44 \pm 0.38^\circ$), which remained within acceptable limits for tablet compression. The bulk density of the granules ranged from 0.51 ± 0.02 to 0.60 ± 0.03 g/mL, while the tapped density varied between 0.63 ± 0.02 and 0.74 ± 0.03 g/mL, demonstrating satisfactory packing characteristics. The Carr's Compressibility Index ranged from $17.39 \pm 1.20\%$ to $20.00 \pm 1.50\%$, indicating fair to good compressibility of the granules. The Hausner ratio was found to be between 1.21 ± 0.03 and 1.25 ± 0.02 , confirming acceptable flow properties. Overall, the pre-compression evaluation demonstrated that all formulations possessed satisfactory flowability and compressibility suitable for tablet compression, with F4 exhibiting the best compressibility characteristics due to its lowest Carr's Index and Hausner ratio, making it the most suitable formulation for further tablet development.

Table 5 Results of Pre-compression Parameters of Tablet

Parameter	F1	F2	F3	F4
Angle of Repose (°)	28.62 ± 0.34	30.18 ± 0.41	27.95 ± 0.29	31.44 ± 0.38
Bulk Density (g/mL)	0.52 ± 0.02	0.57 ± 0.03	0.51 ± 0.02	0.60 ± 0.03
Tapped Density (g/mL)	0.65 ± 0.03	0.69 ± 0.02	0.63 ± 0.02	0.74 ± 0.03
Carr's Index (%)	20.00 ± 1.50	18.92 ± 1.40	19.05 ± 1.10	17.39 ± 1.20
Hausner Ratio	1.25 ± 0.02	1.23 ± 0.02	1.24 ± 0.02	1.21 ± 0.03

Mean ± SD, where n = 3

EVALUATION OF PREPARED TABLET

The prepared controlled-release tablets were evaluated for various post-compression parameters, including appearance, diameter, thickness, weight variation, hardness, friability, and disintegration time. The results are presented in Table 6. All formulations were uniform in appearance, smooth in texture, and free from visible defects such as cracks, chipping, or discoloration. The diameter of all tablet formulations was found to be approximately 9.00 mm, demonstrating uniform die filling and consistent compression during tablet manufacture. The tablet thickness ranged from 5.12 ± 0.02 mm to 5.28 ± 0.04 mm, indicating only minor variations among the formulations. The average tablet weight varied from 597.8 ± 4.5 mg to 601.3 ± 3.8 mg, and all formulations complied with the pharmacopeial limit for weight variation ($\pm 5\%$) applicable to tablets weighing more than 250 mg. The low standard deviation values confirmed uniform die filling and good manufacturing consistency.

Tablet hardness ranged from 9.18 ± 0.16 to 13.24 ± 0.14 kg/cm², indicating adequate mechanical strength to withstand handling, packaging, and transportation. Formulation F4 exhibited the highest hardness, whereas F1 showed the lowest. The friability values ranged from $0.61 \pm 0.02\%$ to $0.78 \pm 0.03\%$, which were well below the pharmacopeial limit of 1%, confirming satisfactory resistance to abrasion and tablet durability.

The disintegration time of the controlled-release tablets ranged from 2.48 ± 0.05 h to 4.68 ± 0.06 h. Formulation F1 showed the shortest disintegration time, whereas formulation F4 exhibited the longest. The gradual increase in disintegration time was attributed to the higher concentration of Ethyl Cellulose, which effectively maintained tablet integrity and prolonged drug release. Overall, all formulations exhibited acceptable post-compression characteristics, with Formulation F4 demonstrating the most desirable mechanical properties and sustained-release behaviour, making it the optimized formulation for further evaluation.

Table 6 Results of Post-compression Parameters of Herbal Tablets

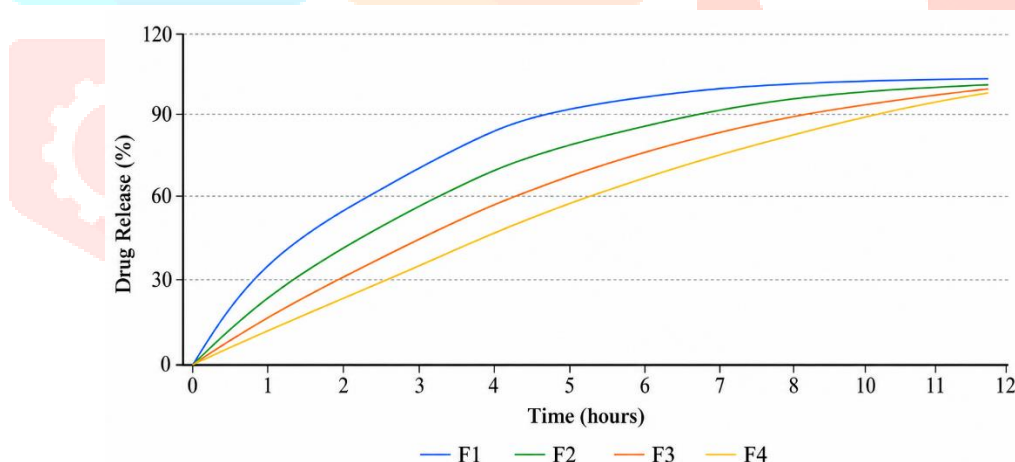
Parameter	F1	F2	F3	F4
Diameter (mm)	9.00 ± 0.01	9.00 ± 0.01	9.00 ± 0.03	9.00 ± 0.02
Thickness (mm)	5.18 ± 0.04	5.21 ± 0.03	5.28 ± 0.04	5.12 ± 0.02
Weight Variation (mg)	598.6 ± 4.2	601.3 ± 3.8	597.8 ± 4.5	600.5 ± 3.1
Hardness (kg/cm ²)	9.18 ± 0.16	11.28 ± 0.17	12.48 ± 0.18	13.24 ± 0.14
Friability (%)	0.78 ± 0.03	0.71 ± 0.02	0.68 ± 0.03	0.61 ± 0.02
Disintegration Time (h)	2.48 ± 0.05	3.12 ± 0.07	3.86 ± 0.08	4.68 ± 0.06

Table 7 In-vitro Dissolution Study of Herbal Controlled-Release Tablets

Time (h)	F1 (%release)	F2 (%release)	F3 (%release)	F4 (%release)
0	0	0	0	0
1	36 ± 1.3	31 ± 1.2	26 ± 1.1	20 ± 1.0
2	55 ± 1.5	48 ± 1.4	42 ± 1.3	34 ± 1.2
3	72 ± 1.6	63 ± 1.5	56 ± 1.4	48 ± 1.3
4	86 ± 1.5	76 ± 1.6	68 ± 1.5	61 ± 1.4
5	95 ± 1.2	86 ± 1.5	78 ± 1.6	71 ± 1.5
6	99 ± 0.8	92 ± 1.3	86 ± 1.5	80 ± 1.4
7	100 ± 0.0	96 ± 1.0	91 ± 1.2	87 ± 1.3
8	100 ± 0.0	99 ± 0.6	95 ± 1.0	92 ± 1.2
10	100 ± 0.0	100 ± 0.0	99 ± 0.8	97 ± 0.8
12	100 ± 0.0	100 ± 0.0	100 ± 0.0	99.8 ± 0.2

Dissolution Profile Graph Data

Comparison of cumulative drug release (%) from formulations F1–F4 over 12 hours. F4 shows the most sustained release profile and is selected as the optimized formulation.



Egg Albumin Denaturation

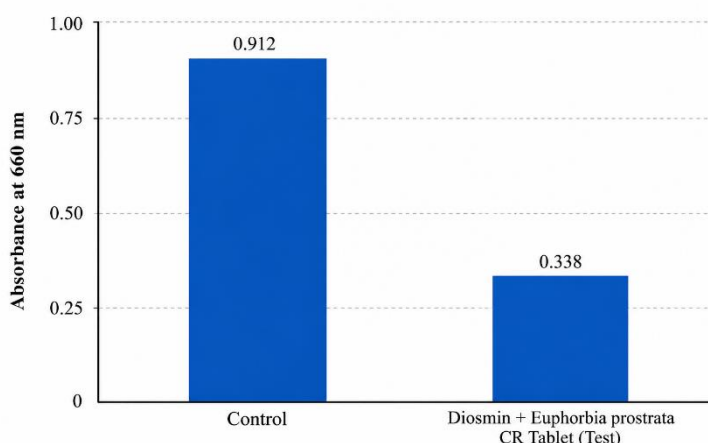
The anti-inflammatory activity of the controlled-release tablet containing Diosmin and *Euphorbia prostrata* was evaluated using the egg albumin denaturation assay. The assay is based on the ability of the formulation to inhibit heat-induced protein denaturation, which is considered one of the mechanisms involved in inflammatory processes.

The control exhibited an absorbance of 0.912, whereas the test formulation showed an absorbance of 0.338 at 660 nm. The lower absorbance of the test formulation indicates effective inhibition of protein denaturation.

The percentage inhibition was calculated using the following equation:

$$\begin{aligned}
 \% \text{ Inhibition} &= \frac{\text{Absorbance of Control} - \text{Absorbance of Test}}{\text{Absorbance of Control}} \times 100 \\
 &= \frac{0.912 - 0.338}{0.912} \times 100 = 62.94\%
 \end{aligned}$$

The controlled-release tablet containing Diosmin and *Euphorbia prostrata* exhibited 62.94% inhibition of protein denaturation, indicating significant in vitro anti-inflammatory activity. The observed reduction in absorbance compared with the control suggests that the formulation effectively stabilizes proteins against heat-induced denaturation. This activity may be attributed to the combined anti-inflammatory properties of Diosmin, a flavonoid known to inhibit inflammatory mediators, and *Euphorbia prostrata*, which contains bioactive phytoconstituents possessing antioxidant and anti-inflammatory effects. These findings demonstrate the potential of the formulated controlled-release tablet as a promising anti-inflammatory dosage form.



Graph 1 Absorbance comparison of Standard and test sample

CONCLUSION

The present study successfully achieved the design, development, and evaluation of a dual-component controlled-release tablet containing Diosmin and *Euphorbia prostrata* extract for the management of hemorrhoids. The herbal extract was successfully authenticated, extracted, and characterized, while Diosmin was evaluated using standard physicochemical and analytical methods. The prepared formulations exhibited satisfactory pre-compression and post-compression characteristics, indicating good flow properties, compressibility, and tablet quality. Among the developed formulations, the optimized formulation demonstrated the most desirable pharmaceutical performance, including sustained drug release and satisfactory physical properties. The in vitro anti-inflammatory study further confirmed the therapeutic potential of the formulation by effectively inhibiting protein denaturation. The combination of Diosmin and *Euphorbia prostrata* provides complementary venotonic, vasoprotective, anti-inflammatory, antioxidant, hemostatic, and wound-healing activities, making it a promising therapeutic approach for hemorrhoid management. Overall, the developed controlled-release tablet has the potential to improve therapeutic efficacy, reduce dosing frequency, enhance patient compliance, and provide prolonged symptom relief. Further stability studies and clinical investigations are recommended to establish its long-term safety and therapeutic effectiveness.

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