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Nanoemulgel-Based Herbal Drug Delivery System of *Boswellia serrata* and *Withania somnifera* for Effective Osteoarthritis Relief

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ABSTRACT:
The present study aimed to formulate and evaluate a herbal nanoemulgel containing BOSWELLIA SERRATA and WITHANIA SOMNIFERA extracts for topical management of osteoarthritis. Herbal extracts were prepared by Soxhlet extraction using ethanol and subjected to preliminary phytochemical screening, extractive value determination, and ash value analysis. The nanoemulgel formulations (F1–F4) were prepared using Tween 80 as surfactant, PEG 400 as co-surfactant, ethanol as co-solvent, and Carbopol 940 as gelling agent. The prepared formulations were evaluated for physicochemical properties including pH, viscosity, droplet size, polydispersity index (PDI), zeta potential, spreadability, gel strength, adhesiveness, drug content, encapsulation efficiency, and in-vitro drug release behaviour. Phytochemical screening confirmed the presence of alkaloids, flavonoids, phenols, tannins, terpenoids, and glycosides in both extracts. All nanoemulgel formulations showed acceptable physicochemical properties suitable for topical application. Among all formulations, F2 exhibited optimized characteristics with pH 6.1, viscosity 1985 cP, droplet size 132 nm, PDI 0.17, and zeta potential of -31.4 mV, indicating superior stability and homogeneity. Encapsulation efficiency of F2 was found to be 97.6% for BOSWELLIA SERRATA and 95.8% for ZINGIBER OFFICINALE. In-vitro drug release study demonstrated sustained release over 24 hours, with maximum cumulative release of 94.2% observed for formulation F2. Drug release kinetic analysis revealed best fitting with the Korsmeyer–Peppas model, indicating diffusion-controlled release mechanism. The developed herbal nanoemulgel demonstrated promising characteristics for enhanced topical delivery, prolonged drug release, and improved therapeutic potential in osteoarthritis management.

INTRODUCTION:

Osteoarthritis (OA) is a chronic degenerative joint disorder characterized by progressive cartilage degradation, inflammation, pain, stiffness, and restricted joint mobility. It is one of the most common musculoskeletal diseases affecting the elderly population worldwide and significantly reduces quality of life. The pathogenesis of osteoarthritis involves destruction of articular cartilage, synovial inflammation, oxidative stress, and alteration of subchondral bone structure. Conventional management of osteoarthritis mainly includes non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and analgesics, which provide symptomatic relief but are often associated with adverse effects such as gastrointestinal irritation, cardiovascular complications, renal toxicity, and poor patient compliance during long-term therapy. Therefore, there is a growing interest in the development of safer and more effective alternative therapies for the management of osteoarthritis. Herbal medicines have gained considerable scientific attention due to their therapeutic efficacy, lower toxicity, and multi-target pharmacological actions. Among various medicinal plants, *Boswellia serrata* (Turmeric) and *Withania somnifera* (Ginger) have been

widely investigated for their potent anti-inflammatory and antioxidant activities [1]. *Boswellia serrata* contains curcuminoids, particularly curcumin, which inhibits inflammatory mediators such as cyclooxygenase (COX), lipoxygenase (LOX), tumor necrosis factor-α (TNF-α), and nuclear factor-kappa B (NF-κB). Similarly, *Withania somnifera* contains active constituents such as gingerols and shogaols that possess significant anti-inflammatory, analgesic, and antioxidant properties. The synergistic combination of these herbal extracts may provide enhanced therapeutic benefits in osteoarthritis by reducing inflammation, oxidative stress, and pain. Despite their promising pharmacological activities, the therapeutic effectiveness of herbal constituents is often limited due to poor aqueous solubility, instability, low bioavailability, and inadequate skin permeation. Topical drug delivery systems offer several advantages in osteoarthritis treatment by providing localized drug action, reducing systemic side effects, improving patient compliance, and maintaining sustained therapeutic concentration at the site of application [2]. However, conventional topical formulations may exhibit poor penetration through the stratum corneum barrier, limiting drug absorption. Nanoemulsion-based drug delivery systems have emerged as advanced carriers capable of improving the solubility, stability, and permeation of active pharmaceutical ingredients due to their nano-sized droplets and large surface area. Nanoemulsions also enhance dermal and transdermal drug delivery by increasing drug diffusion across biological membranes. Incorporation of nanoemulsion into a gel matrix forms nanoemulgel, which combines the advantages of nanoemulsion and gel systems, including enhanced drug penetration, improved spreadability, better viscosity, prolonged residence time, and patient acceptability. Nanoemulgels are considered promising carriers for topical administration of herbal drugs in inflammatory disorders [3]. Therefore, the present study was aimed to formulate and evaluate a herbal nanoemulgel containing *Boswellia serrata* and *Withania somnifera* extracts for topical management of osteoarthritis. The prepared formulations were evaluated for physicochemical properties, stability parameters, encapsulation efficiency, and in-vitro drug release behaviour in order to identify an optimized formulation with enhanced topical performance and sustained therapeutic potential.

MATERIALS AND METHODS:

Materials:

BOSWELLIA SERRATA extract and WITHANIA SOMNIFERA extract were selected as herbal active pharmaceutical ingredients due to their reported anti-inflammatory, antioxidant, and analgesic activities. Tween 80 was used as surfactant, polyethylene glycol 400 (PEG 400) as co-surfactant, ethanol as co-solvent, Carbopol 940 as gelling agent, and triethanolamine (TEA) as neutralizing agent. Distilled water was used for preparation of formulations. All chemicals and reagents used in the study were of analytical grade and procured from authenticated chemical suppliers.

Collection, Processing and Extraction of Plant Material:

Fresh rhizomes of BOSWELLIA SERRATA and WITHANIA SOMNIFERA were collected from local herbal sources and authenticated by a botanist. The collected plant materials were washed thoroughly with distilled water to remove dirt and foreign matter and then shade dried at room temperature to prevent degradation of thermolabile constituents. The dried rhizomes were pulverized separately into coarse powder using a mechanical grinder and stored in airtight containers until extraction. The powdered plant materials were subjected to Soxhlet extraction using ethanol as extraction solvent. About 100 g of powdered material was packed in a thimble and extracted continuously until the solvent in the siphon tube became colourless. The obtained extracts were concentrated by evaporating the solvent using a rotary evaporator and dried under reduced pressure. The dried extracts were stored in airtight containers at refrigerated conditions for further studies [4-5].

Preliminary Phytochemical Screening:

Test for Alkaloids:

About 5 mL of extract solution was treated with Mayer's reagent. Formation of cream coloured precipitate indicated the presence of alkaloids.

Test for Flavonoids:

The extract was treated with dilute ammonia solution followed by concentrated sulfuric acid. Appearance of yellow colour confirmed the presence of flavonoids.

Test for Phenols:

A few drops of ferric chloride solution were added to the extract solution. Development of bluish green colour indicated the presence of phenolic compounds.

Test for Tannins:
The extract was mixed with ferric chloride solution. Formation of dark green or blue-black colour confirmed the presence of tannins.
Test for Terpenoids:
The extract was mixed with chloroform and concentrated sulfuric acid was added carefully along the sides of the test tube. Formation of reddish-brown interface indicated the presence of terpenoids.
Test for Saponins:
The extract was shaken vigorously with distilled water. Formation of persistent froth indicated the presence of saponins.
Test for Glycosides:
The extract was treated with glacial acetic acid and ferric chloride followed by addition of concentrated sulfuric acid. Formation of brown ring indicated the presence of glycosides.

Determination of Extractive Values
Extractive values were determined using water, ethanol, and methanol as solvents to evaluate the extraction efficiency of different solvents. About 5 g of powdered plant material was macerated separately with 100 mL of solvent for 24 hours with intermittent shaking. The mixtures were filtered and evaporated to dryness. The dried residues were weighed and percentage extractive values were calculated [6].
Determination of Ash Values
Ash values were determined to assess the purity and inorganic content of crude drugs. About 2 g of powdered drug was accurately weighed and incinerated in a silica crucible at 500–600°C until carbon-free ash was obtained. The ash was cooled and weighed to determine total ash value. Acid-insoluble ash and water-soluble ash values were determined according to standard pharmacognostic methods [7].

Formulation Design of Nanoemulgel
Table 1. Composition of Nanoemulgel Formulations (F1–F4)

Ingredient	F1 (% w/w)	F2 (% w/w)	F3 (% w/w)	F4 (% w/w)
Boswellia serrata Extract	1	1	1	1
Withania somnifera Extract	1	1	1	1
Tween 80	14	10	12	15
PEG 400	4	5	4	3
Ethanol	5	8	6	5
Carbopol 940	1	1	1	1
Triethanolamine	0.5	0.5	0.5	0.5
Distilled Water q.s. to 100 g	73.5	73.5	75.5	73.5

Preparation of Nanoemulsion:
Accurately weighed quantities of BOSWELLIA SERRATA and WITHANIA SOMNIFERA extracts were dissolved in ethanol. Tween 80 and PEG 400 were added and mixed under continuous stirring. Distilled water was added dropwise with continuous homogenization using high-speed homogenizer at 30,000 rpm for 15 minutes to obtain uniform nanoemulsion. The prepared nanoemulsion was subjected to ultrasonication for 5 minutes to reduce droplet size and improve stability [8-10].

Preparation of Gel Base:
Carbopol 940 was dispersed slowly in distilled water with continuous stirring and allowed to hydrate for 30 minutes. Triethanolamine was added dropwise to neutralize the dispersion and obtain transparent gel with suitable viscosity [11].

Preparation of Nanoemulgel
The prepared nanoemulsion was incorporated gradually into the Carbopol gel base under gentle stirring to avoid air entrapment. Mixing was continued until a homogeneous nanoemulgel was obtained. The prepared formulations were transferred into airtight containers and stored at room temperature for further evaluation [12-13].

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Evaluation of Nanoemulgel Formulations:

pH Determination:

The pH of nanoemulgel formulations was measured using a calibrated digital pH meter at room temperature.

Viscosity Study:

Viscosity of formulations was determined using Brookfield viscometer at controlled temperature conditions [14].

Droplet Size, PDI and Zeta Potential:

Droplet size, polydispersity index (PDI), and zeta potential were measured using dynamic light scattering (DLS) technique after suitable dilution of formulations.

Spreadability:

Spreadability was evaluated by placing nanoemulgel between two glass plates under applied weight and measuring spreading diameter.

Gel Strength and Adhesiveness:

Gel strength and adhesiveness were evaluated using texture analysis method by measuring force required for gel deformation and adhesion [15].

Drug Content and Encapsulation Efficiency:

Drug content was determined by dissolving nanoemulgel in suitable solvent followed by UV spectrophotometric analysis at respective λmax values. Encapsulation efficiency was calculated using standard formula.

In-vitro Drug Release Study:

In-vitro drug release study was performed using Franz diffusion cell containing phosphate buffer pH 7.4 as receptor medium maintained at 32 ± 1°C. Samples were withdrawn at predetermined intervals and analyzed spectrophotometrically. The cumulative percentage drug release was calculated and kinetic models including zero-order, first-order, Higuchi, and Korsmeyer–Peppas were applied to determine release mechanism [16].

RESULTS AND DISCUSSION:

Phytochemical Screening of Extracts:

Preliminary phytochemical screening of BOSWELLIA SERRATA and WITHANIA SOMNIFERA extracts confirmed the presence of several important bioactive constituents including alkaloids, flavonoids, tannins, phenols, terpenoids, glycosides, and saponins. The presence of these phytoconstituents supports the therapeutic potential of both herbal drugs in the management of inflammatory disorders such as osteoarthritis. Flavonoids and phenolic compounds are known for their antioxidant activity, while terpenoids and alkaloids contribute to anti-inflammatory and analgesic effects. The phytochemical screening results are presented in **Table 2** and illustrated in **Figure 1**.

Figure 1. Preliminary Phytochemical Screening of Herbal Extracts

Table 2. Phytochemical Screening of Boswellia Serrata and Withania Somnifera Extracts

Phytochemical	Curcuma longa	Zingiber officinale
Alkaloids	Present	Present
Flavonoids	Present	Present
Phenols	Present	Present
Tannins	Present	Present

Terpenoids	Present	Present
Saponins	Present	Absent
Glycosides	Present	Present

Extractive Values:

Extractive values were determined using water, ethanol, and methanol as solvents to evaluate the extraction efficiency of different solvents. Methanol showed the highest extractive value for both plant materials, indicating its superior ability to extract active phytoconstituents. Ethanol also demonstrated good extraction efficiency, whereas aqueous extraction showed comparatively lower yield. The extractive values are summarized in **Table 3** and represented graphically in **Figure 2**.

Figure 2. Comparative Extractive Values of Herbal Extracts

Table 3. Extractive Values of Herbal Extracts

Solvent	Boswellia serrata (%)	Withania somnifera (%)
Water	13	11
Ethanol	19	18
Methanol	22	20

Ash Values:

Ash values were determined as quality control parameters to evaluate the inorganic content and purity of crude drugs. BOSWELLIA SERRATA showed total ash value of 7.9%, acid-insoluble ash value of 1.1%, and water-soluble ash value of 4.2%, while WITHANIA SOMNIFERA showed slightly higher ash values. The low acid-insoluble ash values indicated minimal contamination with earthy materials and silica. The ash value results are presented in **Table 4**.

Table 4. Ash Values of Herbal Extracts

Ash Type	Boswellia serrata (%)	Withania somnifera (%)
Total Ash	7.9	8.6
Acid Insoluble Ash	1.1	1.3
Water Soluble Ash	4.2	5.1

Evaluation of Nanoemulgel Formulations:

The prepared nanoemulgel formulations were evaluated for pH, viscosity, droplet size, zeta potential, PDI, spreadability, gel strength, adhesiveness, drug content, and encapsulation efficiency. The results are summarized in **Table 5**.

Table 5. Physicochemical Evaluation of Nanoemulgel Formulations

Parameter	F1	F2	F3	F4
pH	5.8	6.1	5.9	5.7
Viscosity (cP)	1650	1985	1850	1720
Zeta Potential (mV)	-26.5	-31.4	-29.2	-24.6
PDI	0.24	0.17	0.20	0.28
Droplet Size (nm)	168	132	145	174

Spreadability (cm^2/sec)	4.2	3.9	4.0	4.4
Gel Strength (g)	45.1	51.6	47.2	43.8
Adhesiveness (g·s)	7.8	9.1	8.3	7.2
Drug Content Boswellia serrata (mg)	9.44	9.81	9.62	9.35
Encapsulation Efficiency Boswellia serrata (%)	94.8	97.6	96.1	93.9
Drug Content Withania somnifera (mg)	9.28	9.58	9.40	9.22
Encapsulation Efficiency Withania somnifera (%)	92.5	95.8	94.1	91.7

pH Determination:
The pH of all nanoemulgel formulations ranged between 5.7 and 6.1, which is within the acceptable skin-compatible range. This indicates suitability of formulations for topical application without causing skin irritation.

Viscosity Study:
Viscosity values ranged from 1650 cP to 1985 cP. Formulation F2 exhibited highest viscosity, suggesting stronger gel consistency and improved retention at the site of application.

Droplet Size, PDI and Zeta Potential:
All formulations showed droplet size within nano range (<200 nm), indicating successful nanoemulsion formation. F2 exhibited the smallest droplet size (132 nm) and lowest PDI (0.17), indicating narrow droplet distribution and superior homogeneity. Higher negative zeta potential value observed for F2 (-31.4 mV) suggested greater physical stability due to electrostatic repulsion among droplets.

Spreadability, Gel Strength and Adhesiveness:
Spreadability values indicated easy application of nanoemulgel on skin surface. F2 showed slightly lower spreadability due to higher viscosity but demonstrated highest gel strength and adhesiveness, which may improve residence time and therapeutic efficacy.

Encapsulation Efficiency
High encapsulation efficiency values were observed for all formulations. F2 showed maximum encapsulation efficiency for both herbal extracts, indicating effective incorporation of active constituents within nanoemulsion droplets.

In-vitro Drug Release Study
In-vitro drug release study was carried out using Franz diffusion cell to evaluate sustained release behaviour of nanoemulgel formulations. All formulations exhibited gradual and controlled drug release over 24 hours. Formulation F2 demonstrated highest cumulative drug release of 94.2% due to smaller droplet size and better diffusion characteristics. The cumulative drug release results are shown in **Table 6** and represented graphically in **Figure 3**.

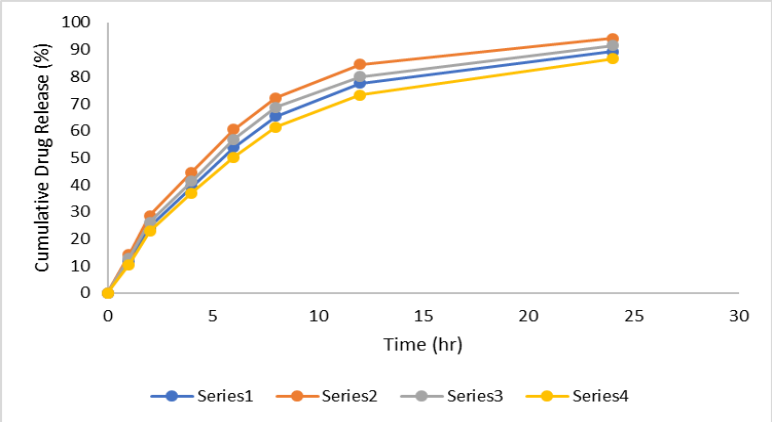

Figure 3. In-vitro Cumulative Drug Release Profile of Nanoemulgel Formulations

Table 6. Cumulative Drug Release (%) of Nanoemulgel Formulations

Time (h)	F1	F2	F3	F4
0	0	0	0	0
1	11.8	14.2	12.9	10.5
2	24.5	28.6	26.1	22.8
4	39.2	44.7	41.3	36.9
6	53.8	60.5	56.9	50.2
8	65.4	72.1	68.7	61.4
12	77.5	84.6	80.1	73.3
24	89.3	94.2	91.5	86.7

Drug Release Kinetics:

The release data were fitted into different kinetic models including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The Korsmeyer–Peppas model showed highest correlation coefficient values for all formulations, indicating diffusion-controlled drug release mechanism. The release kinetics data are summarized in **Table 7**.

Table 7. Drug Release Kinetics Model Fitting

Formulation	Zero Order (R^2)	First Order (R^2)	Higuchi (R^2)	Korsmeyer–Peppas (R^2)	n Value
F1	0.928	0.915	0.968	0.981	0.44
F2	0.941	0.923	0.975	0.989	0.47
F3	0.936	0.918	0.971	0.984	0.46
F4	0.924	0.910	0.964	0.978	0.42

CONCLUSION:

The present study successfully formulated and evaluated a herbal nanoemulgel containing BOSWELLIA SERRATA and WITHANIA SOMNIFERA extracts for topical management of osteoarthritis. Phytochemical screening confirmed the presence of important bioactive constituents responsible for anti-inflammatory and antioxidant activities. The prepared nanoemulgel formulations exhibited satisfactory physicochemical characteristics including suitable pH, viscosity, droplet size, zeta potential, spreadability, gel strength, and encapsulation efficiency, indicating good stability and suitability for topical application. Among all formulations, F2 was identified as the optimized formulation due to its smallest droplet size, lowest PDI, highest zeta potential, superior encapsulation efficiency, and maximum cumulative drug release. The in-vitro drug release study demonstrated sustained release behaviour over 24 hours, while kinetic analysis confirmed diffusion-controlled drug release mechanism following the Korsmeyer–Peppas model. Overall, the developed herbal nanoemulgel showed promising potential as an effective topical delivery system for osteoarthritis treatment by enhancing drug permeation, prolonging drug release, and improving therapeutic efficacy with reduced systemic side effects. The study suggests that nanoemulgel-based herbal formulations may serve as a safe and effective alternative approach for the management of inflammatory joint disorders.

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