IJPHT Journal
Papers Having Good Impact

International Journal of Pharmacy and Herbal Technology- ISSN NO: 2583-8962 (Online)

Date of Acceptance:08th Apr,2024 Date of Publication: 16th Apr,2024

EXPLORING THE POTENTIAL OF SOLID LIPID NANOPARTICLES-BASED LOTION CONTAINING VITEX NEGUNDO OIL: A REVIEW OF CONCEPTUAL FRAMEWORK AND FUTURE DIRECTIONS

Jyoti S. Kolapkar, Sandip B. Ahire, Niketan N. Khairnar, Vinod A. Bairagi
K.B.H.S.S Trust's Institute of Pharmacy, Malegaon. Maharashtra
Corresponding author Mail ID: jyotikolapkar04@gmail.com

ABSTRACT:

Chronic pain and inflammation represent significant challenges in healthcare, necessitating the exploration of innovative therapeutic approaches. This review explores the potential of solid lipid nanoparticles (SLNs) for delivering Vitex negundo oil, an herbal remedy, in managing pain and inflammation. Despite limited prior research, SLNs offer promise in enhancing bioavailability and efficacy. The review outlines mechanistic insights and synergistic effects, proposing future research directions. Key considerations include formulation optimization, safety evaluation, and regulatory pathways for clinical translation, emphasizing the need for further exploration of SLN-based Vitex negundo oil formulations in pain and inflammation management.

KEYWORDS: *Solid lipid nanoparticles, Vitex negundo oil, pain management, inflammation, herbal formulation, conceptual framework, future directions.*

INTRODUCTION

Inflammation, Pain, and rheumatism are still significant issues in the present era. Inflammation is a sophisticated immunological response to vascular tissue injury or pathogen-induced infection, clinically manifested as redness, swelling, pain, discomfort, warmth, and loss of function. [1,2] Lipid-based Nanosystems have emerged as a potentially useful class of nanocarrier in recent years for incorporating a wide range of active chemicals. Solid lipid nanoparticles (SLNs) offer excellent physical and colloidal stability and great biocompatibility. We can create formulations with the required physicochemical attributes and biological properties by carefully designing the carrier structure through component selection and preparation procedures.

Solid Lipid Nanoparticles

Solid lipid nanoparticles (SLNs) were Invented in the 1990s as a nanomedicine alternative to conventional carriers, utilizing solid lipids instead of liquid ones. Having a size range of 10-1000 nm, the active pharmaceutical ingredients (API) are immersed or encapsulated in lipids. As shown in the Figure 1. SLNs exhibit oil-in-water emulsion-like dispersions. Unlike emulsions, SLNs utilize solid lipids at room temperature, allowing for the encapsulation of both hydrophobic and hydrophilic compounds. Addressing challenges like rapid metabolism, plasma concentration fluctuations, low absorption, and water solubility. Recent years emphasize that advancing novel drugs alone is insufficient; strategic drug delivery techniques are imperative in pharmacy advancement. [3,4]

Benefits of Topical Drug Delivery

1. Preventing First Pass Metabolism:
2. Convenient and Easy Application:
3. Mitigation of Risks in Absorption Conditions:
4. Efficacy at Lower Dosages:
5. Ease of Medication Termination:
6. Wider Application Area:
7. Targeted Drug Delivery:
9. Utilization of Short Half-life Drugs:
11. Improved Patient Compliance:
12. Suitability for Self-medication:

Drawbacks of Topical Drug Delivery

1. Contact dermatitis or Skin irritation
2. Poor Permeability of Some Drugs
3. Potential for Allergenic Reactions
4. Limited Applicability to Low Plasma Concentration Drugs
5. Enzymatic Denaturation in Epidermis
6. Challenges with Larger Particle Size Drugs. [5]

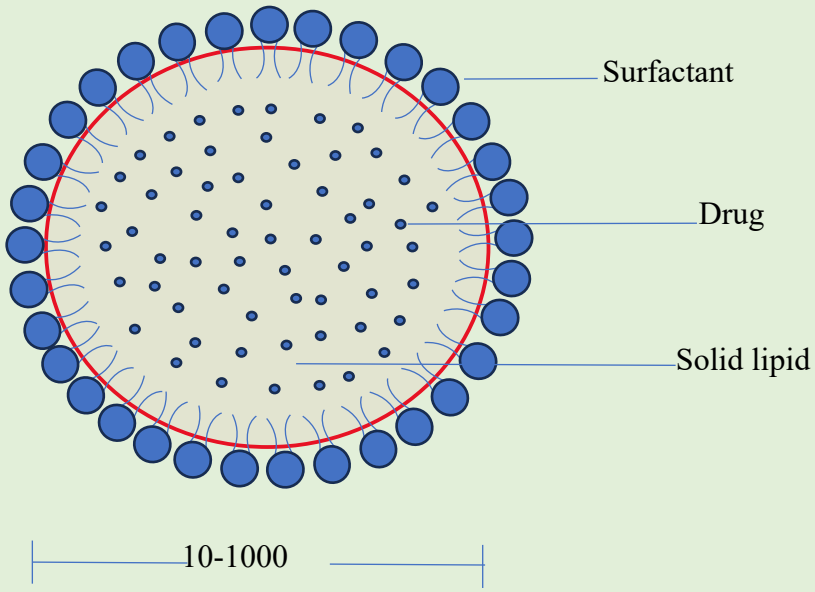

Fig. No. 1. Schematic figure of solid lipid Nanoparticle

The Evolution and Synergy of Natural and Modern Therapeutics in Pharmaceutical Practices

Natural product

Natural products have been used for centuries in medicinal practices, with around 75% of the global population relying on traditional herbal medications. Traditional systems like Ayurveda and Chinese medicine emphasize the use of herbal remedies. While developing nations like India and China have a significant reliance on herbal medicines, Western countries have moved away from these practices. Many modern drugs have their origins in natural products, with pharmacological classes like atropine, morphine, and quinine being derived from natural prototypes. There is a growing interest in herbal compounds globally, with annual sales exceeding $0.1 trillion in the US. Herbal medicines often contain a variety of chemicals that work together to influence biological processes. Examples like Aloe vera and Vitex Negundo demonstrate analgesic and anti-

inflammatory properties and can be used alongside conventional medications to potentially reduce side effects. Nirgundi, the Sanskrit term for V. negundo, denotes that which guards the body against illness. This herb finds mention in all Ayurvedic Samhitas, highlighting its prominence in traditional pharmaceutical literature. The integration of natural and modern therapeutics showcases the potential synergy between the two approaches in pharmaceutical practices, offering diverse treatment options for various health issues. [6-9]

Vitex Negundo:

Taxonomical classification:

Table1. Botanical name: Vitex negundo

Taxonomy	Vitex Negundo
Kingdom	Plantae
Order	Lamiales
Family	Verbenaceae
Genus	Vitex Linn.
Species	Panjghust (vitex negundo Linn), (Chastetree)
Division	Magnoliophyta (Flowering plants)
Super division	Spermatophyte (Seed plants)

Ancient Indians identified two types of nirgundi: Sindhuvar (white flowers) (shwetapushpi), and Pushpanilika, -Blue Flowers (nirgundi). In Ayurveda various properties of V.N. are mentioned, Rasa (Tikta, Katu), Guna (Ruksha, Laghu), Vipaka (Vipaka Doshakarma), Virya (Usha), Doshakarma (Kapha). [10,11]

Vitex Negundo oil:

Fig. No. 2. Vitex Negundo oil

- **Solubility:** organic solvents such as Ethanol, ethyl acetate, or alcohol, Insoluble in water
- **Category:** Antimicrobial activity, Anti-inflammatory, Antirheumatic
- **Appearance:** light yellow or brown-yellow clear
- **Odor:** characteristic

Inflammation, a complex response to physiological and pathological changes, involves leukocyte activation, migration to the injury site, and release of Cytokines, Nitrogen, and oxidative species that are reactive. Oil of nirgundi, containing Luteolin, mitigates inflammation by slowing down tissue oxidative stress and Luteolin inhibiting Interleukin-NF synthesis. Kappa B aids in the lowering of Cyclooxygenase (COX). [12] Vitex negundo Linn. essential oil exhibits potent anti-inflammatory properties, making it a promising candidate for pharmaceutical applications. Its efficacy extends to treating arthritis, rheumatic diseases, and inflammatory conditions in the musculoskeletal system, highlighting its potential as a natural anti-inflammatory agent. [13]

Table2. Composition of Vitex Negundo oil and its properties: [14,15]

Key components	Properties
Linalool (terpene alcohol)	Antioxidant, Sedative, and Anti-Inflammatory
Beta-caryophyllene (Sesquiterpene)	Anti-inflammatory, Analgesic
Sabinene (Monoterpene)	Anti-inflammatory, Antioxidant,
1,8-Cineole (Eucalyptol) (Monoterpene)	Anti-inflammatory, Analgesic and Bronchodilator
α -Pinene (Monoterpene)	Anti-inflammatory, Antimicrobial and Bronchodilator
α -terpinene (Monoterpene)	Antioxidant and Anti-inflammatory
Terpinen-4-ol (Monoterpene alcohol)	Antimicrobial and Anti-inflammatory

MATERIAL:

1. Drug: Vitex negundo oil, Methyl Salicylate (Topical analgesic)
2. Surfactants: e.g., Tween 80, Span-20,60(Emulsifier), Poloxamer-188 and 407.
3. Co-Surfactant: e.g., Propylene Glycol, Polyethylene Glycol-200 and PG-400, 600, Ethanol.
4. Solvent: e.g., Distil Water, Ethanol, Methanol, Acetone, Acetonitrile
5. Oil Phase: e.g., Eucalyptus oil (Fragrance and soothing properties, Penetration enhancer), Dimethicone, Cetyl alcohol, Isopropyl Palmitate
6. Emulsifier/Surfactant: e.g., Glyceryl Monostearate, Lecithin, PEG 100 Stearate
7. Thickeners: e.g., Carbomer, Stearic Acid, Cetyl Alcohol, Triethanolamine (pH adjuster).
8. Enhancing Agent: e.g., Menthol (Cooling sensation).
9. Moisturizing Agent: e.g., Lanoline.
10. Preservative: Methylparaben, Propylparaben etc.

METHOD OF PREPARATION

1. High-pressure homogenization
1.1 Hot homogenization and
1.2 Cold homogenization

2. Ultrasonication/high-speed homogenization
2.1 Bath ultrasonication
2.2 Probe ultrasonication
3. Solvent evaporation
4. Solvent emulsification-diffusion
5. The Supercritical fluid approach
6. Membrane Contactor method
7. Microemulsion-based approach
8. Coacervation technique
9. Spray drying
10. Double emulsion method
11. Precipitation
12. Film-ultrasound dispersion etc. [15, 18]

Preparation of (SLN) Solid Lipid nanoparticles using ultrasonic-nano emulsification method with slight modifications.
SLN Formulation:
1. Weigh the lipid phase (glyceryl monostearate and Cetyl palmitate).
2. Heat above 85°C (Above the M.P. of lipid) and add VN oil.
3. Disperse surfactants (Tween 80, lecithin) in water.
4. Add the water phase to the lipid phase at 50°C with stirring.
5. Ultrasonic treatment (100 W, 3-15 min).
6. Disperse pre-nano emulsions in cold water.
7. Filter through 0.45 µm membrane and store at 4°C.
Lotion Formulation: SLN can be used in a variety of formulations, including lotion. A lotion is an emulsion-based topical Formulation that is often used as a medicinal or cosmetic product. An SLN lotion can also deliver active, nature-identical chemicals.
1. Melt oil phase ingredients.
2. Dissolve glycerine in heated water.
3. Add the oil phase to the water phase with homogenization.
4. Incorporate SLNs (Methyl Salicylate and Camphor).
5. Increase homogenization speed.

Advantages: Low-cost, extremely efficient technique that does not employ toxic organic solvents. The solid lipid-matrix material was chosen to be glyceryl monostearate (GMS), which is biocompatible, non-toxic, and generally regarded as safe (GRAS). [3,20]

CHARACTERIZATION OF SOLID LIPID NANOPARTICLES:
1. Particle size
solid lipid nanoparticle size analysis was carried out according to the major SLN Particle size characteristics by using a digital microscope. PixelPro was the program utilized. The microscope has been thoroughly cleaned. A stage micrometer was used to calibrate the microscope. On a clean glass slide, a drop of Solid lipid Nanoparticle dispersion was applied. This slide was set up on stage. The microscope was set up correctly to view the SLNs. On a clean glass slide, a drop of Solid lipid Nanoparticle dispersion was applied. This slide was set up on stage. The microscope was properly adjusted to see the SLNs. The image was recorded. PixelPro

Software was utilized to calculate the nanoparticle size. Three separate measurements of the particle size were made.

2. Entrapment efficiency

The ratio of actual to expected drug content can be used to compute entrapment efficiency. A cooling centrifuge technique was used to determine it. To begin, the Vitex negundo Oil was poured into vials after being dissolved in ethanol. It was spun in a centrifuge. The clear liquid above (supernatant) was dissolved in distilled water with ethanol to a volume of 10 ml. An ultraviolet UV spectrophotometer "Jasco V-730, Japan" was used to measure absorbance. The concentration was determined based on the absorption values. This is the VNO's starting weight. The cooling centrifuge vials were filled with the SLN dispersion (which included VNO). After that, the dispersion was centrifuged for one hour at 9000 rpm. After being collected, the supernatant was diluted to 10 mL with ethanol. After recording the absorbance, the concentration was computed.

Formula for Calculation,

$$\text{Percent Entrapment, efficiency} = \frac{\text{Actual drug loading}}{\text{Therotical drug loading}} \times 100$$

Physicochemical property

The color, Odor, pH, and solubility of SLN in an aqueous media were used to describe the physicochemical properties of SLN dispersions.

FTIR spectra of SLN

The analysis for SLN was performed by Jasco FT/IR- 4600 Fourier Transform Infrared spectrophotometer. Individual samples were sorted using potassium bromide and observed spectroscopically between 4000- 400 cm^{-1}.

In vitro drug release

Artificial cellophane with a 12,000 molecular weight membrane with a 12,000 molecular weight was used for drug release investigations. A vertical Franz diffusion cell was employed in the experiment. A pH 6.8 phosphate buffer was produced. The formulated buffer was poured into the mark in the diffused cell. It's known as a receptor compartment. A cellophane membrane was inserted between two portions of the cell after being dipped in hot water. The donor compartment is the top half of the cell. The receptor compartment's temperature was kept constant at $37\pm5°C$, and it was constantly agitated with a magnetic stirrer. In the (facing) donor compartment, a 10 mg SLN dispersion was put on the cellophane membrane. 1 ml of the receptor compartment sample was extracted and diluted with ethanol to a volume of 10 ml. The concentration was calculated using UV analysis. Similarly, the sample was taken out its concentration was determined by UV analysis every hour. The table shows the findings of particle size, drug loading, and release. Analysis was carried out three Times. The research lasted 8 hours.

Zeta Potential

A zeta sizer was used to conduct zeta potential research. In the test tube, one milliliter of the dispersion was made soluble in purified water. The solution was double-distilled since it was discovered to be exceedingly opaque. For another 10 minutes, ultrasonication was used to avoid agglomeration. The solution was appropriately poured into a glass cuvette. and the zeta potential has been assessed.

pH Determination

Assessment of pH was conducted using a pH meter. Dissolve Solid Lipid Nanoparticles (SLN) corresponding to one gram into 100 ml of Purified water and allow it to stand for 2 hours. Subsequently, immerse the rods in standard buffers to ascertain the pH. Following this calibration, immerse the rods in a triplicate fashion into a solution containing SLNs for further analysis.

Stability study

In the stability investigation, the refined formulation undergoes storage at both 5°C and 45°C for 90 days. Post this period, the formulations are subjected to assessment in terms of particle size, encapsulation efficiency, Drug release, and characteristics.

Characterization Studies of Lotion

Physical evaluations of the lotion were performed for homogeneity, appearance, and color

Physical Appearance

The Lotion was examined for its appearance (color, Odor) nature.

pH

A pH meter was used to assess this. In 100 ml of distilled water, one gm of lotion was dissolved. It had been set aside for two hours. The rod was immersed in a lotion solution.

The viscosity of the Lotion

Viscosity analysis was performed employing a Brookfield viscometer assessing the lotion's viscosity at ambient temperature. Measurements were taken specifically at five, ten, twenty, fifty, and hundred revolutions per minute (rpm).

Density

1. Weigh empty containers with an analytical balance.

2. Measure the known volume of lotion in a graduated cylinder.

3. Weigh the container with lotion on an analytical balance.

4. Calculate lotion density: Density = Mass / Volume.

5. Repeat steps with water for comparison.

6. Calculate specific gravity: Specific Gravity = Density of Lotion / Density of Water.

7. Consider accurate measurements, minimize air bubbles, and account for temperature variations.

Spread-ability

Glass slides (Chromatography plates) were meticulously prepared for the assessment of spread-ability. 1gm. lotion was accurately weighed, and applied to the glass slide, followed by placing another glass slide over it. A standardized weight of 100 g was positioned on top. The diameter of the dispersed lotion was systematically calculated, and the procedure was repeated in triplicate for robust analysis.

Stability study

The Formulated lotion is kept at 5°C to 45°C for 90 days for the stability testing. The compositions were examined for physical characteristics, viscosity, and spreadability 90 days later.[1,19-21]

CONCLUSION

SLN-based lotion with Vitex negundo oil offers a novel approach to pain relief. Future work should optimize formulations and ensure safety for clinical use, potentially providing a safer alternative for managing pain and inflammation.

RESULT

Study shows that SLN carriers may be utilized to deliver bioactive plant components such as essential oils effectively. Solid lipid nanoparticles (SLNs) loaded with Vitex negundo oil may show promise for pain and inflammation management. A carefully designed formulation, incorporating surfactants, co-surfactants, oils, and enhancing agents, may enhance stability and delivery. Eucalyptus oil aids absorption, while Methyl Salicylate adds analgesic properties. Because of the high demand for pure natural components in the food and pharmaceutical sectors, these natural phytochemicals have been widely employed all over the world. One downside of employing these carriers may be the rapid release of plant bioactive chemicals loaded in SLN nanoparticles in systemic circumstances and the internal milieu of the body with varying pH.

REFERENCES:

1. Chaudhari, P. M.; Bind, V. M. Topical Solid Lipid Nanoparticles Based Ge l of Lavender Essential Oil for Anti-Inflammatory Activity. Asian J. Pharm. Clin. Res. 2019, 12 (11), 175–182.
2. Banik, B.; Das, S.; Das, M. K. Medicinal Plants with Potent Anti-Inflammatory and Antiarthritic Properties Found in Eastern Parts of the Himalayas: An Ethnomedicinal Review. Pharmacogn. Rev. 2020, 14 (28), 121–137.
3. Pucek-Kaczmarek, A. Influence of Process Design on the Preparation of Solid Lipid Nanoparticles by an Ultrasonic-Nano Emulsification Method. Processes 2021 July 22, 9 (8), 1265.
4. Mukherjee, S.; Ray, S.; Thakur, R. S. Solid Lipid Nanoparticles: A Modern Formulation Approach in Drug Delivery System. Indian J. Pharm. Sci. 2009 July, 71 (4), 349–358.
5. Toche, V.; Deshmukh, A.; Rabade, A. Topical Gels as Drug Delivery System-A Comprehensive Review. Int. J. Anal. Exp. Modal Anal. 2021, 13 (4), 664–681.
6. Abdulkhaleq, L. A.; Assi, M. A.; Abdullah, R.; Zamri-Saad, M.; Taufiq-Yap, Y. H.; Hezmee, M. N. M. The Crucial Roles of Inflammatory Mediators in Inflammation: A Review. Vet. World 2018, 11 (5), 627–635.
7. Tandon, V. R.; Gupta, R. K. Vitex negundo Linn (VN) Leaf Extract as an Adjuvant Therapy to Standard Anti-Inflammatory Drugs. Indian J. Med. Res. 2006, 124 (4)(OCT.), 447–450
8. Vikrant, A.; Arya, M. A Review on Anti-Inflammatory Plant Barks. Int. J. PharmTech Res. 2011, 3 (2), 899–908.
9. Meena, A. K.; Perumal, A.; Kumar, N.; Singh, R.; Ilavarasan, R.; Srikanth, N. et al. Studies on Physicochemical, Phytochemicals, Chromatographic Profiling & and Estimation, and in-Silico Study of Negundoside in Roots & and Small Branches of Vitex negundo Plant. Phytomed. Plus 2022 February 1, 2 (1), 100205.

10. Ladda, P.; Magum, C. Vitex negundo Linn.: Ethnobotany, Phytochemistry, and Pharmacology – A Review. J. Adv. Pharm. Biol. Chem. 2012, 1 (1), 111–120.
11. Ladda, P.; Magum, C. Vitex negundo Linn.: Ethnobotany, Phytochemistry, and Pharmacology – A Review. J. Adv. Pharm. Biol. Chem. 2012, 1 (1), 111–120.
12. Ingram, S.; Diotallevi, M. Reactive Oxygen Species: Rapid Fire in Inflammation. Biochemist 2017, 39 (4), 30–33.
13. Rajguru, J. R.; Shirsat, M. K.; Navale, S. D. Development of the Formulation and Evaluation of the Anti-Inflammatory Activity of Vitex negundo Gel and Latex. Int. J. Pharm. Qual. Assur. 2023, 14 (1), 159–164.
14. Poonphatanapricha, T.; Katanyutanon, S.; Jitapunkul, K.; Lawtrakul, L.; Toochinda, P. The Preservation and Enantiomeric Selection of Linalool by Nanoencapsulation Using Cyclodextrins. Sci. Pharm. 2021 September 3, 89 (3), 42.
15. Nogueira, C.; Lemos-Senna, E.; da Silva Vieira, E.; Sampaio, T. B.; Mallmann, M. P.; Oliveira, M. S.; Bernardi, L. S.; Oliveira, P. R. β-Caryophyllene Cationic Nanoemulsion for Intranasal Delivery and Treatment of Epilepsy: Development and In Vivo Evaluation of the Anticonvulsant Activity. J. Nanopart. Res. 2023 January, 25 (1), 19.
16. Khairnar, S. V.; Pagare, P.; Thakre, A.; Nambiar, A. R.; Junnuthula, V.; Abraham, M. C.; Kolimi, P.; Nyavanandi, D.; Dyawanapelly, S. Review on the Scale-Up Methods for the Preparation of Solid Lipid Nanoparticles. Pharmaceutics 2022 September 6, 14 (9), 1886.
17. Battaglia, L.; Gallarate, M.; Panciani, P. P.; Ugazio, E.; Sapino, S.; Peira, E.; Chirio, D. Techniques for the Preparation of Solid Lipid Nano and Microparticles. Appl. Nanotechnol. Drug Deliv. 2014 July 25, 1, 51–75.
18. Parhi, R.; Suresh, P. Preparation and Characterization of Solid Lipid Nanoparticles-A Review. Curr. Drug Discov. Technol. 2012 March 1, 9 (1), 2–16.
19. Nugraha, M. W.; Iswandana, R.; Jufri, M. Preparation, Characterization, and Formulation of Solid Lipid Nanoparticles Lotion from Mulberry Roots (Morus Alba L.). Int. J. Appl. Pharm. 2020 March, 12, 182–186.
20. Üner, M. Characterization and Imaging of Solid Lipid Nanoparticles and Nanostructured Lipid Carriers. InHandbook of Nanoparticles 2016, (pp. 117–141); Springer.
21. Khurana, G.; Sharma, V. V.; Arora, D. QbD-Driven Development and Characterization of Solid Lipid Nanoparticles (SLNs)–Based Nanogel of Luliconazole for the Effective Management of Dermal Fungal Infection. J. Pharm. Innov. 2023 December, 18 (4), 2249–2264.