Formulation of Solid Lipid Nanoparticles Loaded Nasal Drops Containing Aegle Marmelos (Linn) Correa. Extract

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ABSTRACT

The present study was aimed to formulate solid lipid nanoparticles loaded in nasal drops containing Aegle Marmelos by cold technique to impart better antidepressant activity. It can improve penetration of drugs to the CNS and show faster pharmacological action. Nasal drops were prepared by sodium chloride and benzalkonium chloride. Nasal drug delivery systems are better at imparting the antidepressant activity. The pH of the formulation was found to be within the range of 4.5 to 6.5. The viscosity of SLN-loaded nasal drops was found to be around 05-30 cp.

Keywords: SLN-loaded nasal drop, benzalkonium chloride, sodium chloride, phosphate buffer, etc.

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INTRODUCTION:

Depression is defined as disorders of mood rather than disturbances of thought or cognition; it may range from a very mild condition, bordering on normality, to severe psychotic depression accompanied by hallucinations and delusions. Major depression is a common disorder that continues to result in considerable morbidity and mortality despite major advances in treatment.Bael (*Aegle marmelos*), a plant of Indian origin having tremendous therapeutic potential, it is belonged to family Rutaceae, it is known by the several other names in the different parts of the country and also outside of the country. The utility of bael is mention in the Indian ancient system of medicine, every part of the bael tree such as root, bark, leaf, flower, fruits, seed and even its latex are also important in several traditional system of medicine, that's why it is one of the most important plants in the India. The bael fruit is having lots of pharmacological activity, fruit of it possesses anti dyspepsia, anti diarrhea and anti dysentery. The fruit is also used as a dietary supplement, it is also used to cure intermittent fever, mental disease, hypoglycemic effect, anti fungal effect, anti microbial, analgesic, anti inflammatory, among its many properties are antipyretic, anti-dyslipidemic, immune-suppressive, anti-proliferative, wound-healing, anti-fertility, and insecticidal.Bael plant acts as a "Sink" for chemical pollutants as it absorbs poisonous gases from atmosphere and makes them inert or neutral. It is a member of plant species group known as 'Climate Purifiers', which emit a greater percentage of oxygen in sun light as compare to other plants. The tree is likewise classified as a "Fragrant" species. Aegle marmelos is one of the medicinal plants of India. The Aegle marmelos, (Bael) leaves, bark, roots and fruit have been used for over 5000 years in the Indian traditional system of medicine, the Ayurveda and in various folk medicines to treat various diseases.

MATERIALS AND METHODS:

Materials:

Aegle marmelos were obtained from the local market from Umarga. Cow ghee as Lipid Core i.e all ingradients used i.e Polaxomer 188, PEG-400, Tween-80, Triethanolamine,Benzalkonium chloride,Phosphate buffer, Sodium chloride,distilled water were pharmaceutical grade.

Table -1 Formulation table

Ingradients	F1	F2	F3
SLN dispersion	Equi to 1%	Equi to 1%	Equi to 1%
Sodium Chloride	0.85 gm	0.9 gm	0.91gm
Benzalkonium chloride	0.01 gm	0.01 gm	0.01 gm
Phosphate Buffer	Q.S	Q.S	Q.S
Distilled Water	Up to 100 ml	Up to 100 ml	Up to 100 ml

Developing *Aegle Marmelos* extracts using the maceration method

1.5 kg of fresh leaves were cleaned with water. The leaf material was then allowed to air dry for two days. In order to obtain extracts, a specific amount of dried material was macerated with ethanol by soaking 500 g of dried powdered plant in a bottle with two liters of ethanol for seventy-two hours. After that, the ethanol mixture was filtered and concentrated by utilizing a rotary evaporator to evaporate the alcohol under low pressure.

Preparation of SLN Loaded Nasal Drop

Take required quantity SLN dispersion and add sodium chloride (0.9%) and Benzalkonium chloride (0.01%) Adjust the PH to 5.5 to 6.5 using Phosphate buffer and make final volume with distilled water stir gently to obtain uniform Nasal drop formulation and then fill formulation into sterile amber coloured nasal dropper bottles, label properly and store refrigerated conditions at (4-8^{0}C).

Evaluation of Nasal Drop

1. Physical Appearance

F1			
Time (min)	**Absorbance**	**Dilution**	**% DR**
0	0.000	1	0.00
30	0.010	1	7.00
60	0.021	1	15.20
120	0.044	1	32.36
180	0.066	1	48.77
240	0.081	1	59.96
360	0.097	1	71.90
480	0.105	1	77.87
720	0.122	1	90.55

2. PH Determination
3. Volume Uniformity
4. Osmolarity/ Isotonicity
5. *In-vitro* drug release study
6. Drop Characteristics
7. Stability studies

1. Physical Appearance

Solid Lipid Nanoparticle (SLN) loaded nasal drops are generally described as liquid, white, or opaque-white, slightly viscous dispersions or suspensions, often appearing similar to a white liquid emulsion. They are designed to be homogeneous (uniform in appearance) with no visible particulate matter or agglomeration.

2. pH Determination

The pH determination of Solid Lipid Nanoparticle (SLN) loaded nasal drops is a critical quality attribute (CQA) to ensure stability, minimize irritation, and maintain efficient drug delivery. The ideal pH for nasal formulations is typically between 4.5 and 6.5, which matches the natural pH of nasal secretions.

3. Volume Uniformity

Volume uniformity refers to ensuring that each administered drop (or delivered dose) from a nasal drop formulation contains a consistent and reproducible volume, which is crucial for accurate dosing of SLN (Solid Lipid Nanoparticle) dispersions. and using dropper calibration method.

4. Viscosity Measurement

Viscosity measurement is an important evaluation parameter for Solid Lipid Nanoparticle (SLN)–loaded nasal drops, as it determines the flow behavior, spreadability/drop formation, and nasal residence time of the formulation.

5. Osmolarity/ Isotonicity

Osmolarity (or isotonicity) is an important quality control parameter for SLN (Solid Lipid Nanoparticle)–loaded nasal drops. It ensures that the formulation has a similar solute concentration as nasal fluids, preventing irritation and improving patient tolerance. Normal Nasal Osmolarity Nasal fluid is approximately isotonic with blood

Ideal range: 270–320 mOsm/kg Equivalent to 0.9% NaCl solution

***In-vitro* drug release study**

The in-vitro drug release study of SLN (Solid Lipid Nanoparticle)–loaded nasal drops is performed to evaluate the rate, extent, and pattern of drug release from the nanoparticles into a simulated nasal environment.

F2			
Time (min)	**Absorbance**	**Dilution**	**% DR**
0	0.000	1	0.00
30	0.011	1	7.74
60	0.025	1	18.19
120	0.047	1	34.60
180	0.069	1	51.01
240	0.085	1	62.95
360	0.102	1	75.63
480	0.111	1	82.34
720	0.126	1	93.53

Table no:2 % drug release nasal drop (F1)
Table no:3 % drug release nasal drop (F2)

F3			
Time (min)	**Absorbance**	**Dilution**	**% DR**
0	0.000	1	0.00
30	0.008	1	5.50
60	0.016	1	11.47
120	0.037	1	27.14
180	0.060	1	44.30
240	0.077	1	56.98
360	0.089	1	65.93
480	0.096	1	71.15
720	0.115	1	85.33

Table no:4 % drug release nasal drop (F3)

6. Drop Characteristics

Drop characteristics refer to the physical properties of individual droplets formed from SLN (Solid Lipid Nanoparticle)–loaded nasal formulations, which directly influence dose accuracy, nasal deposition, and patient comfort.

Drop Size (Volume per Drop)

Indicates volume of a single drop (µL or mL) Ideal nasal drop volume: 25–50 µL per drop

Must be uniform across all drops

7. Stability Studies

Aegle Marmelos Loaded SLN nasal drop Stability studies for ensure their physical, chemical, and microbiological integrity over time, determining shelf life and storage conditions. Key assessments include pH (4.5–6.5), viscosity, drug content uniformity, and sterility. Accelerated studies often show increased degradation at 40°C, with stability enhanced by preservatives or antioxidants

Table no: 5 Evaluation of Nasal drop formulation

Formulation code	pH	Viscosity	Osmolarity/Isotonicity
F1	5.7	6 cp	292 mOsm/kg
F2	5.9	8 cp	297 mOsm/kg
F3	6.2	10 cp	305 mOsm/kg

CONCLUSION:

Various formulation (F1, F2 and F3) were developed by using a Sodium Chloride and phosphate buffer. To Formulate Solid lipid nanoparticles Loaded Nasal drop containing *Aegle marmelos* extract were evaluated for the physiochemical parameters such as drug content, pH, viscosity, *in vitro* drug diffusion. Viscosity studies of various formulations revealed that formulation F2 was better to compare to others. From among all the developed formulation, F2 shows better drug diffusion, did good Rheological properties. pH of the F2 formulation is sufficient enough to improve the penetration of drug to CNS and show faster pharmacological action Thus, SLN Loaded nasal drop can be successfully prepared using sodium chloride as Isotonicity/Osmolarity suitable for Nasal application Hence formulation F2 should be further developed for scale-up to industrial production.

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CONFLICT OF INTEREST:

The authors declare that there is no any conflict of interest.

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