RESEARCH PAPER

# PEG BASED NANOCARRIER FOR THE DELIVERY OF BUTEA MONOSPERMA NANPEMULSION IN THE MANAGEMENT OF TRIGEMINAL NEURALGIA

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**Abstract**
Trigeminal neuralgia (TN) is a chronic neuropathic pain disorder characterized by recurrent, severe facial pain that significantly impairs quality of life. Conventional pharmacological agents, while effective, are often associated with dose-dependent side effects, reduced patient compliance, and poor long-term efficacy. Phytoconstituents with multimodal actions are gaining attention as safer alternatives. *Butea monosperma*, a medicinal plant known for its anti-inflammatory, antioxidant, and neuroprotective properties, has shown promise in alleviating neuropathic pain. However, its therapeutic application is hindered by poor solubility, low systemic bioavailability, and rapid metabolism. Nanocarrier-based drug delivery systems offer a viable strategy to overcome these limitations. Polyethylene glycol (PEG), a biocompatible and non-immunogenic polymer, provides advantages such as enhanced solubility, prolonged circulation time, and controlled release of encapsulated drugs. Development of a PEG-based nanocarrier for *Butea monosperma* aims to optimize its pharmacokinetics, ensure sustained therapeutic action, and minimize systemic toxicity in TN management. This novel approach integrates the therapeutic potential of phytomedicine with the precision of nanotechnology, offering a promising, patient-friendly, and effective alternative for the long-term management of trigeminal neuralgia.

Keywords: Trigeminal neuralgia, Butea monosperma, nanocarrier, PEG
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## INTRODUCTION:

The International Association for the Study of Pain (IASP) in 2020 defined pain as "an unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage". The International Association for the Study of Pain (IASP) in November 2010 defined neuropathic pain as "pain initiated or caused by a primary lesion or dysfunction of the peripheral or central nervous system". The manifestation of neuropathic pain clinically varies from dysaesthesia (altered sensation) to allodynia (exaggerated painful response to a painless stimulus). Neuropathic pain also manifests as episodic, paroxysmal pain with a severe, painful expression. The International Association of Pain defines Trigeminal neuralgia as a sudden, usually unilateral, severe, brief stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve (Zakrzewska et al. 2017). The pain is more severe in onset and gradual in duration, triggered while washing the face, speaking, touching, brushing, and even by a puff of wind. It is also known as Fothergill disease or suicidal disease, which affects the patient's quality of life as well as their day-to-day activities(Sjaastad and Bakketeig 2007). There is a deterioration in the quality of life. The pain lasts for 10 seconds to 1 minute only, and the pain doesn't cross the midline of the face.

Demographic data from worldwide in the 1990s shows an annual incidence of 5.7 per 100,000 women and 2.5 per 100,000 men affected by TN every year (Katusic et al. 1991). A general practice-based survey on neurological diseases stated the incidence to be 8 per 10,000 people per year (MacDonald et al. 2000)). A lifetime prevalence of 0.3% in Germany has been reported(Mueller et al. 2011). There is no epidemiological data available from India.

Chronic Pain Grade Scale (CPGS) is a widely accepted, comprises questions to quantify the pain as well as QoL. In my study, we are measuring QOL and VAS score.

Since neurovascular conflict of the nerve has been stated as one of the reasons, there are different grading systems used depending on the specific nerve or area of the brain involved. The grading system ranges from I to IV. Grade I: Neurovascular contact without deformation of the trigeminal nerve. Grade II: Deformation of the trigeminal nerve without displacement or displacement of the nerve without brain stem deformity. Grade III: Displacement of the trigeminal nerve with brain stem deformity. Grade IV:

Displacement of the trigeminal nerve with brain stem deformity and deformation of the fourth ventricle (A. Rai et al, 2015).

The management protocol may vary in the management of TN. First-line therapy should be carbamazepine (CBZ; 200–1200 mg/day) or oxcarbazepine (OXC; 600–1800 mg/day) according to current evidence-based treatment guidelines(Gronseth et al. 2008). Although it has the property of calcium channel inhibition, it has a common side effect of bone marrow suppression and causing agranulocytosis and drowsiness. Agranulocytosis is more dangerous when the total neutrophil count decreases to 100 cells/mm3. Dosage ranges from 100mg-1200mg per day. Due to the most common side effects of carbamazepine, such as agranulocytosis, there is a need for an alternative to minimize the side effects of carbamazepine.

*Butea monosperma* is commonly known as 'flame of the forest', and belongs to the family Leguminosae. Commonly called palash, Bengal kino, and palash (Thiyagarajan et al, 2010). It is commonly seen in India and srilanka. Previously, it was tested in rats for its neuroprotective action and proven to hav*e a* neuroprotective effect. All parts of plants, such as flowers, bark, and leaves, possess medicinal properties. Apart from that, the flowers of *Butea monosperma* possess neuroprotective properties, as well as antioxidant and calcium channel inhibitory actions. Butea monosperma is used as a traditional medicine as an ointment, as an antiseptic, and a lotion for sepsis.

MATERIALS AND METHODS:

**2.1.1. Materials**

Tween 80 was obtained from LOBA Chemie Private Limited, Mumbai, India. Eucalyptus oil was collected from a natural-based products shop in Chennai, India. *Butea monosperma* flowers were collected from a garden at ECR Chennai-Pondicherry Highway, India.

**2.1.2. Plant material**

Butea monosperma plants are purchased from a nursery garden located at Chennai, India. The flowers and leaves are removed from the plant and it was thoroughly washed with water. A known number of leaves and flowers were dried in an oven at 40 °C for 24 h. After drying, rhizomes are pulverized in a grinder.

**2.2. Pulverization**

The leaves and flowers were removed from the plants and thoroughly washed in tap water. A known number of leaves and flowers were dried in an oven for 24 h at 40° C. The dried leaves and flowers were pulverized in a grinder, and the final weight was recorded. The powder of leaves and flowers was stored separately in a Scott bottle at room temperature for further usage.

**2.3.1. Extraction and sample preparation**

Dried flowers were dissolved separately in distilled water, methanol, and hexane with a ratio of 1:20 (g/mL). The extract was treated with a 40°C horizontal bath shaker at a middle shaking speed for 3 h. Afterwards, the content was filtered using No.1 Whatman filter paper. The solvent was evaporated from the filtrate through a rotary evaporator at 40 °C for 40 min. For preparing a 100 mg/mL of extract stock solution, a known amount of dried extract was dissolved in DMSO. The mixture was treated with ultrasonication for 30 min in order to achieve full dissolution. The membrane residue was used to remove the undissolved residues.

2.3.2 **PREPARATION OF NANOEMULSION:**

The Soxhlet device was used to carry out the extraction procedure. Here, bioactive components were extracted aqueously from a dried sample (10 g). Rotary evaporation was used to evaporate the extract and collect the powder. The nano-emulsions were prepared by dispersing 10 mg of powder into water and subsequently 60 mL of eucalyptus oil and 30 mL of Tween 80, to create an oil-in-water emulsion. The reaction mixture was sonicated for 60 min, and successful milky white formation indicates nano-emulsion formation.

2.3.3. **PREPARATION OF NANOCARRIER**

Preparation of PVA:

Total volume 20ml

10ml distilled water

0.8 g sodium alginate

0.2ml PVA was added and heated for 2 hours at 70 °C, and then 10ml of Butea monosperma nanoemulsion and ultrasonicated for 30min. Spread the preparations in a Petri dish, and keep in the hot air oven at 120 degrees overnight. After getting the samples dried, allow the samples to the characterisation.

**3. Results:**

**3.1. Particle size distribution**

The particle size distribution (Fig. 1a) is used to depict the particle size at which the nanoemulsion is dimensionally stable.

3.2. Zeta potential:

The zeta potential value rises when the particle size is at 31nm; the normal value of less than -30 up to +30 the value is unstable. The zetapotential (Fig. 1 b) is used to determine whether the nanoemulsion prepared is dimensionally stable or not. But the nano emulsion of *Butea monosperma* is -32.9, which shows that the nano emulsion is dimensionally stable.

3.3. FTIR

Fourier Transform Infrared spectroscopy (FTIR) obtains an infrared spectrum of a substance, revealing information about its chemical composition and structure. FTIR spectroscopy is widely used in various fields for analysing organic and inorganic compounds. Figure 2 depicts that OH ions are emitted initially,

followed by NH3 ions, showing that the sample dimensionally emits organic compounds.

3.4. TGA

Thermo-Gravimetric analysis (TGA) is a thermal analysis technique in which a sample's mass is tracked as its temperature varies over time. In addition to chemical events like chemisorptions, thermal breakdown, and solid-gas reactions (e.g., oxidation or reduction), this measurement offers information on physical phenomena like phase transitions, absorption, adsorption, and desorption (Rimal and Srivastava 2024). Figure 3 depicts that water molecules are excreted from the prepared sample initially, followed by nanoemulsion and aloe vera are excreted till 550 degrees centigrade. shows that the prepared gel was resistant to heat till 550 degrees centigrade.

3.5. Antimicrobial property

**Antimicrobial resistance** (**AMR** or **AR**) occurs when microbes evolve mechanisms that protect them from antimicrobials, which are drugs used to treat infections. Antimicrobial activity is useful in seeing if the prepared sample is resistant to microbial organisms. Figure 4 depicts that the prepared sample shows a very good zone of inhibition of the microbes, which shows that the prepared gel has antimicrobial activity. The test was performed in Staphylococcus aureus (S.aureus) and Escherichia coli (E.coli). One emulsion prep with plant extract loaded with hydrogel- Good zone of inhibition against E. Coli and Staphylococcus indicates it has an anti-microbial nature. Another without plant extract loaded with hydrogel- A small zone of inhibition observed, which may be due to the anti-microbial effect of eucalyptus.

4. DISCUSSION:

This study aims to formulate a PEG-Alginate-based nanocarrier for the delivery of Butea monosperma nanoemulsion in the management of trigeminal neuralgia. In the present study, we prepared an extract from BM flowers (BME) and investigated the active principles. Butea monosperma flowers have 4 polyphenol components, namely Butrin, isobutrin, isocoreopsin, and butein have 9, 10, 6, and 4 hydroxyl groups, respectively, resulting in their great ability to donate hydrogen atoms and support the unpaired electron. Isobutrin and butrin, with a high number of hydroxyl groups, showed potent antioxidant activity even at 1 µg/ml, possibly due to their high hydrogen-donating ability, which may nullify the effect of unpaired electrons. These results are consistent with previously reported results (Lavhale and Mishra 2007).

BM extracts have been reported to exhibit activity against a spectrum of wound-relevant bacteria; Aloe vera contributes additional antimicrobial and barrier-supportive effects. In infected or high-bioburden wounds, the combination may suppress local bacterial load while dampening inflammation and accelerating granulation, potentially explaining any faster wound contraction or epithelialization metrics observed in our study (Sahu and Padhy 2013).

In the present study, FTIR, TGA, antimicrobial activity, particle size distribution, zetapotential, SEM image analysis, and cytotoxic activity are studied. TN pain is driven by ectopic neural discharges, peripheral sensitization, and neuroinflammation. A BM nanoemulgel could act via: local anti-inflammatory effects by reducing cytokine/mediator-driven sensitization; antioxidant activity—limiting oxidative stress that sustains neuropathic signaling; direct modulation of nociceptor excitability through plant alkaloids/flavonoids; and improved drug residence and penetration from the gel matrix to reach perineural tissues. These mechanisms are speculative but consistent with the known pharmacology of BM extracts and the known benefits of topical anti-inflammatory/analgesic formulations (Zahra et al. 2024).

The limitations of the current study are that head-to-head reports of BM-specific nanoemulsions are sparse. Consequently, while our data suggest a benefit, broader generalization should be cautious. Long-term chemical stability of signature BM flavonoids within the nanoemulgel, preservative efficacy in the Aloe matrix, and inter-batch variability in plant extracts warrant continued surveillance.

The future scope of the current study involves performing the human trials to elaborate on the usage of the topical nanogel in the management of trigeminal neuralgia along with carbamazepine.

Conclusion:

Butea monosperma nanoemulsion with PEG-alginate-based gel aids a promising effect as an adjunctive therapy in the management of trigeminal neuralgia when applied topically. The topical route of application is the prescribed one in the management as well, because it specifically targets the trigger zone and helps in the reduction of the pain intensity. As there is a smaller number of studies and evidence, there is a need for more studies to evaluate the pharmacological actions and mechanism of the prepared nanoemulsion as well.

6. References:

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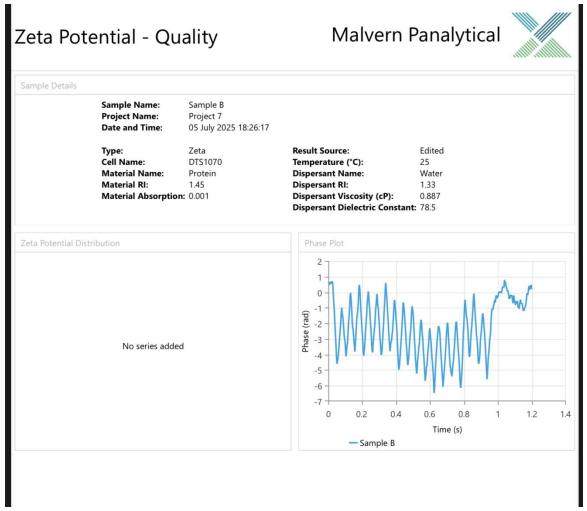
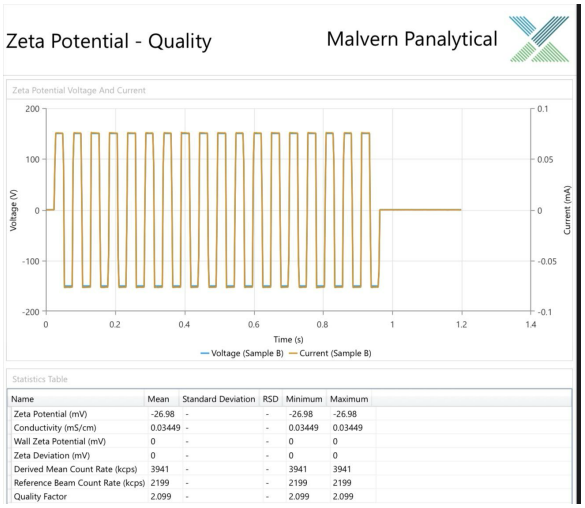
7. IMAGES FOR PEG BASED NANOCARRIER

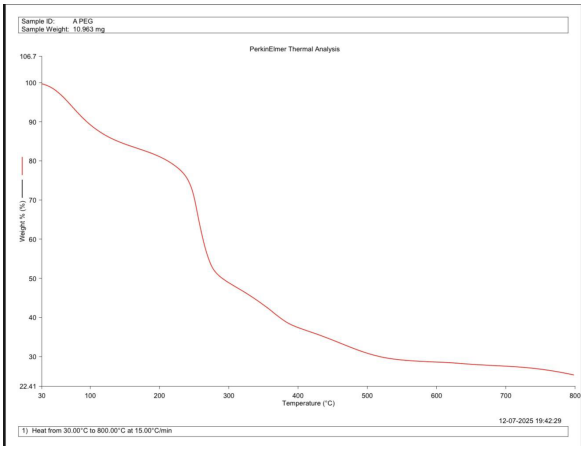
1a. Particle size distribution



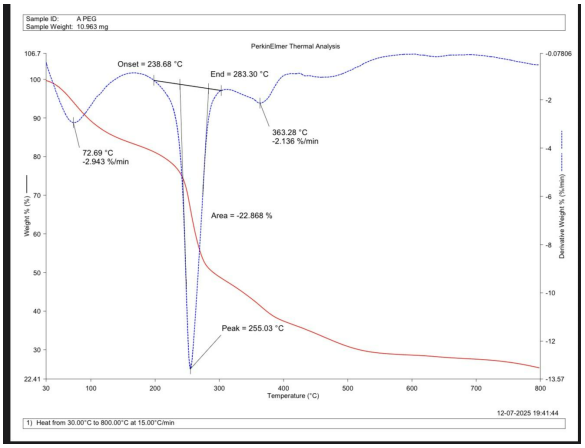

1b. Zeta potential




2. FTIR




3. TGA




4. ANTI-MICROBIAL PROPERTY


S. aureus - 12/07
PEG/TET
PEG
E. coli - 12/07
PEG/TET
PEG