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ALOEVERA-BASED NANO-CARRIER FOR THE DELIVERY OF BUTEA MONOSPERMA IN THE MANAGEMENT OF TRIGEMINAL NEURALGIA

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ABSTRACT
Trigeminal neuralgia (TN) is a debilitating neuropathic pain disorder characterized by recurrent episodes of severe, unilateral facial pain. Current pharmacological treatments, though effective in symptom relief, are often associated with adverse effects and limited long-term efficacy. Phytoconstituents with anti-inflammatory, antioxidant, and neuroprotective potential are emerging as promising alternatives for TN management. Butea monosperma, traditionally recognized for its analgesic and anti-inflammatory activities, offers therapeutic value but its clinical application is restricted due to poor solubility, low bioavailability, and rapid systemic metabolism. To overcome these limitations, nanotechnology-based drug delivery systems provide a novel approach. Aloe vera, a natural biopolymer with inherent antioxidant, anti-inflammatory, and mucoadhesive properties, serves as an excellent nanocarrier matrix, enhancing stability, sustained release, and targeted delivery of phytocompounds. The proposed Aloe vera–based nanocarrier system for Butea monosperma aims to improve drug encapsulation efficiency, prolong therapeutic action, and minimize systemic side effects in TN management. This approach not only harnesses the synergistic effects of Aloe vera and Butea monosperma but also establishes a biocompatible and sustainable platform for phytomedicine-based neural pain therapy. Such a strategy could open avenues for developing safe, effective, and patient-friendly alternatives to conventional TN therapies.

KEYWORDS: Butea monosperma, Aloevera,

1. INTRODUCTION

SThe 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. Trigeminal Neuralgia (TN) is an episodic paroxysmal neuropathic pain typically affecting the orofacial region.

The trigeminal nerve is the 5th cranial nerve in the face region, which is divided into 3 branches as ophthalmic(V1), maxillary(V2), and mandibular(V3) divisions. Apart from that, the maxillary branch comprises the largest branch of the trigeminal nerve. 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 by activities such as 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.

According to a study by Maragathavalli et al., the incidence of trigeminal neuralgia was 83.3%, while the incidence of other orofacial neuralgia was 16.7%. Most of the study participants were between the ages of 41 and 70. According to Incidence Trigeminal Neuralgia University Hospital Setting -A Retrospective Analysis (n.d.), men (54.1%) outnumbered women (45.8%) in the study population. In a study on the prevalence of trigeminal neuralgia in a private institution, Maheswari et al. discovered that there is a minor preference for females over males and that most affected people are between the ages of 30 and 60. For the treatment of trigeminal neuralgia, these patients are typically prescribed carbamazepine and mecobalamin (Murugesan, T N, and Ramalingam 2024). Arvind et al. conducted a study on nerve involvement and distribution of pain in trigeminal neuralgia and found that the most common site of involvement is the right side rather than the left side, and it is most common in the male population (Priyanka, Arvind, and Priyanka 2020).

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 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. It is commonly seen in India and srilanka. Previously, it was tested in rats for its neuroprotective action and proven to have 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.

Aloe vera is a succulent plant belonging to the Liliaceae family, widely recognized for its medicinal and therapeutic values since ancient times. It contains a rich blend of bioactive compounds, including vitamins, minerals, enzymes, amino acids, and polysaccharides, which contribute to its diverse pharmacological properties. Aloe vera exhibits anti-inflammatory, antimicrobial, antioxidant, wound-healing, and immunomodulatory effects, making it highly valuable in both traditional and modern medicine (R et al. 2023).

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

The plants known as Butea monosperma are bought from a nursery garden in Chennai, India. The plant was stripped of its leaves and blooms and given a good water wash. A predetermined quantity of leaves and blossoms was dried for 24 hours at 40 °C in an oven. The preparation was dried and then ground 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. Extraction and sample preparation

After removing the plants' leaves and blossoms, they were carefully cleaned with tap water. A predetermined quantity of leaves and blossoms was dried for 24 hours at 40° C in an oven. The final weight was noted after the dried leaves and blossoms were ground up in a grinder. For later use, the leaf and flower powder were kept apart in a Scott bottle at room temperature.

2.4. Preparation of nanoemulsion

The extraction process was performed using a Soxhlet apparatus. Here, a 10 g dried sample was used for the aqueous extraction of bioactive compounds. The extract was evaporated, and the powder was collected by using rotary evaporation. In order to prepare nano nanoemulsion, 10 mg of powder was added to 10 mL of water. To which 60 mL of palm oil and 30 mL of Tween 20 were added to prepare an oil-in-water emulsion. Then, the mixture was ultrasonicated for 60 min using an ultrasonics processor. The formation of a milky white coloured solution indicates the formation of an emulsion. The nanoemulsion formulation was further characterized by using various techniques. The size distribution of the droplet was identified by the dynamic light scattering method. The stability of the emulsion was determined by using a Zetasizer.

2.5. METHODOLOGY

Tween 20 was purchased from Loba Chemie Private Limited, located in Mumbai, India. Eucalyptus oil was purchased from a natural-based plant company, Chennai, India. Extract of Butea monosperma was collected from a naturally available herbal centre located at Madurai, India.

2.6. Addition of aloe vera polymer to nanoemulsion

Total volume 20ml

Apparatus Required

10ml distilled water
5ml of aloe vera gel
5ml Butea monosperma nanoemulsion

10ml of distilled water, 5ml of aloe vera gel, and 5ml of nanoemulsion were added, and ultrasonication was done using an ultrasonicator for 30 minutes. 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 undergo the characterisation.

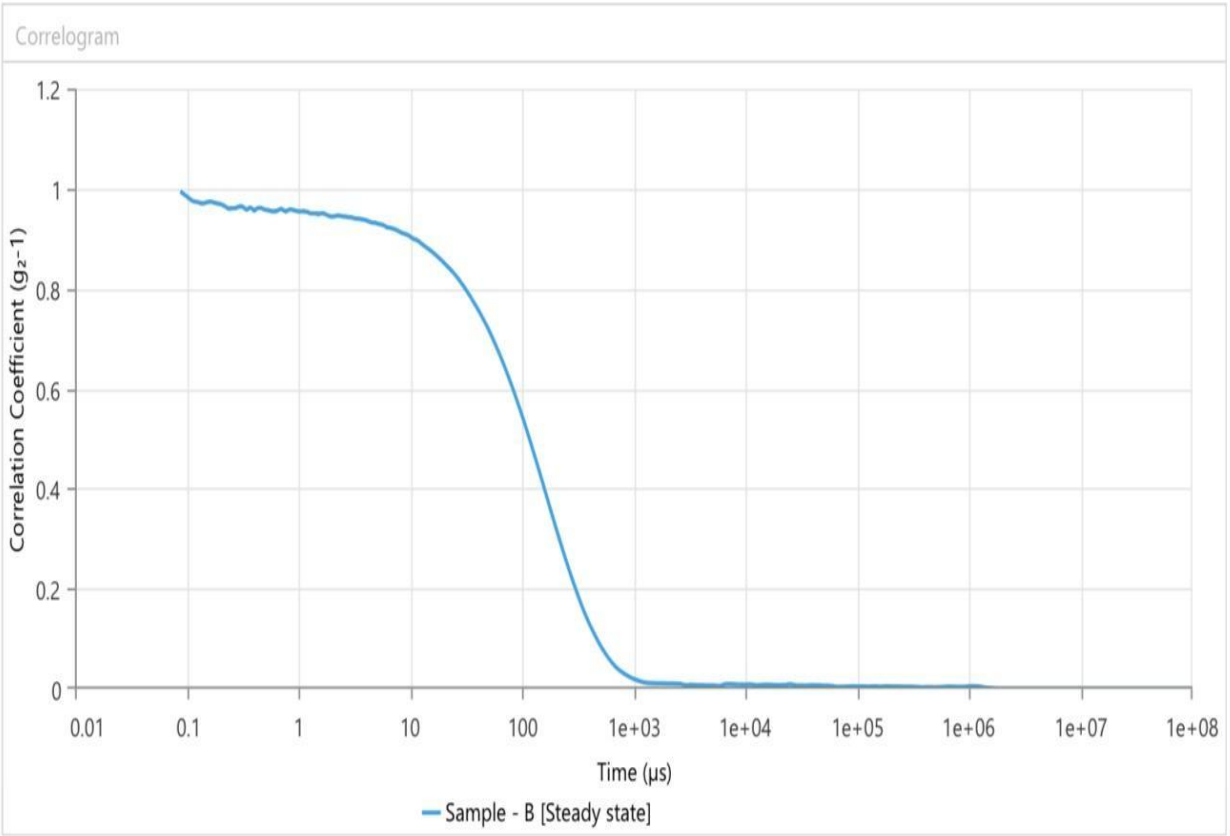
3. RESULTS

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.

PSD by Intensity - Statistics

Malvern Panalytical



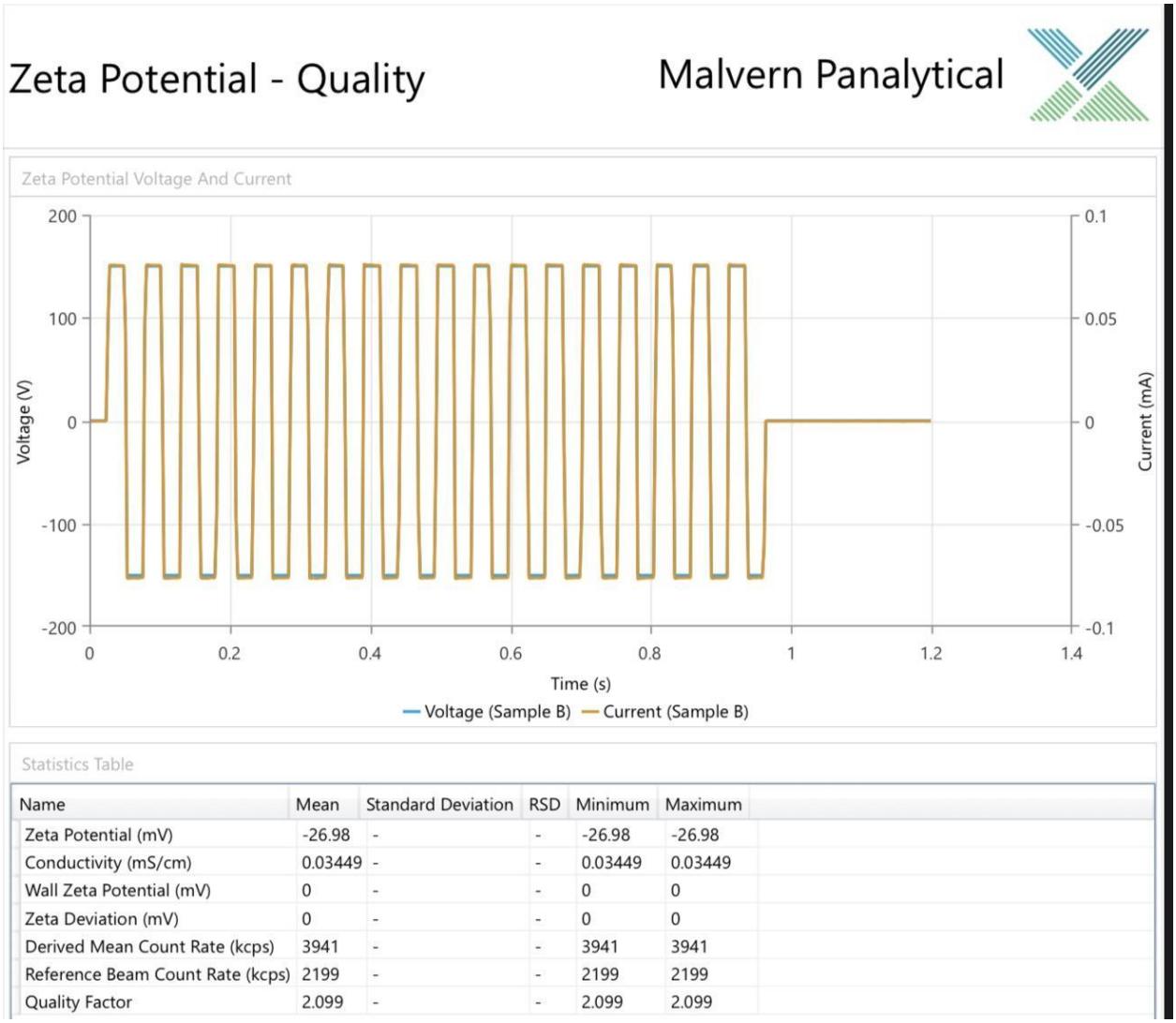
Statistics Table

Name	Mean	Standard Deviation	RSD	Minimum	Maximum
Z-Average (nm)	117.5	-	-	117.5	117.5
Polydispersity Index (PI)	0.217	-	-	0.217	0.217
Intercept	0.9761	-	-	0.9761	0.9761
Peak 1 Mean by Intensity ordered by area (nm)	128	-	-	128	128
Peak 2 Mean by Intensity ordered by area (nm)	5276	-	-	5276	5276
Peak 1 Area by Intensity ordered by area (%)	98.9	-	-	98.9	98.9
Peak 2 Area by Intensity ordered by area (%)	1.096	-	-	1.096	1.096
Derived Mean Count Rate (kcps)	2.554E+04	-	-	2.554E+04	2.554E+04
Detector Angle (°)	173	-	-	173	173

1a. Particle size distribution

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.

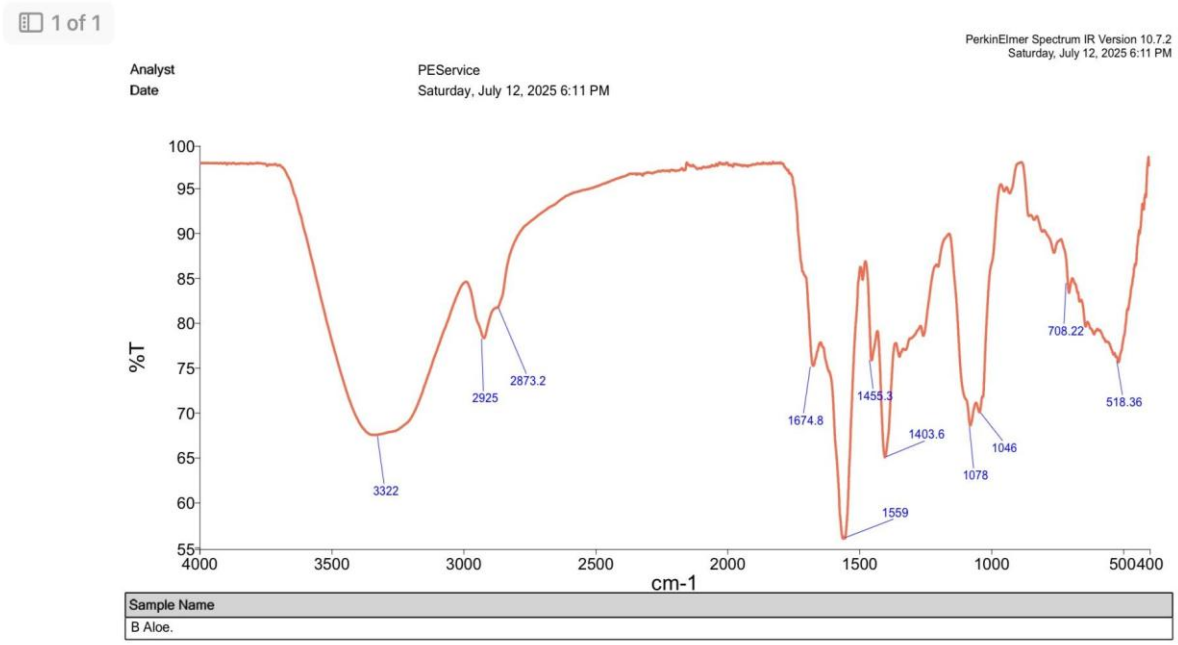


Name	Mean	Standard Deviation	RSD	Minimum	Maximum
Zeta Potential (mV)	-26.98	-	-	-26.98	-26.98
Conductivity (mS/cm)	0.03449	-	-	0.03449	0.03449
Wall Zeta Potential (mV)	0	-	-	0	0
Zeta Deviation (mV)	0	-	-	0	0
Derived Mean Count Rate (kcps)	3941	-	-	3941	3941
Reference Beam Count Rate (kcps)	2199	-	-	2199	2199
Quality Factor	2.099	-	-	2.099	2.099

1b. Zeta potential

3.3. FTIR

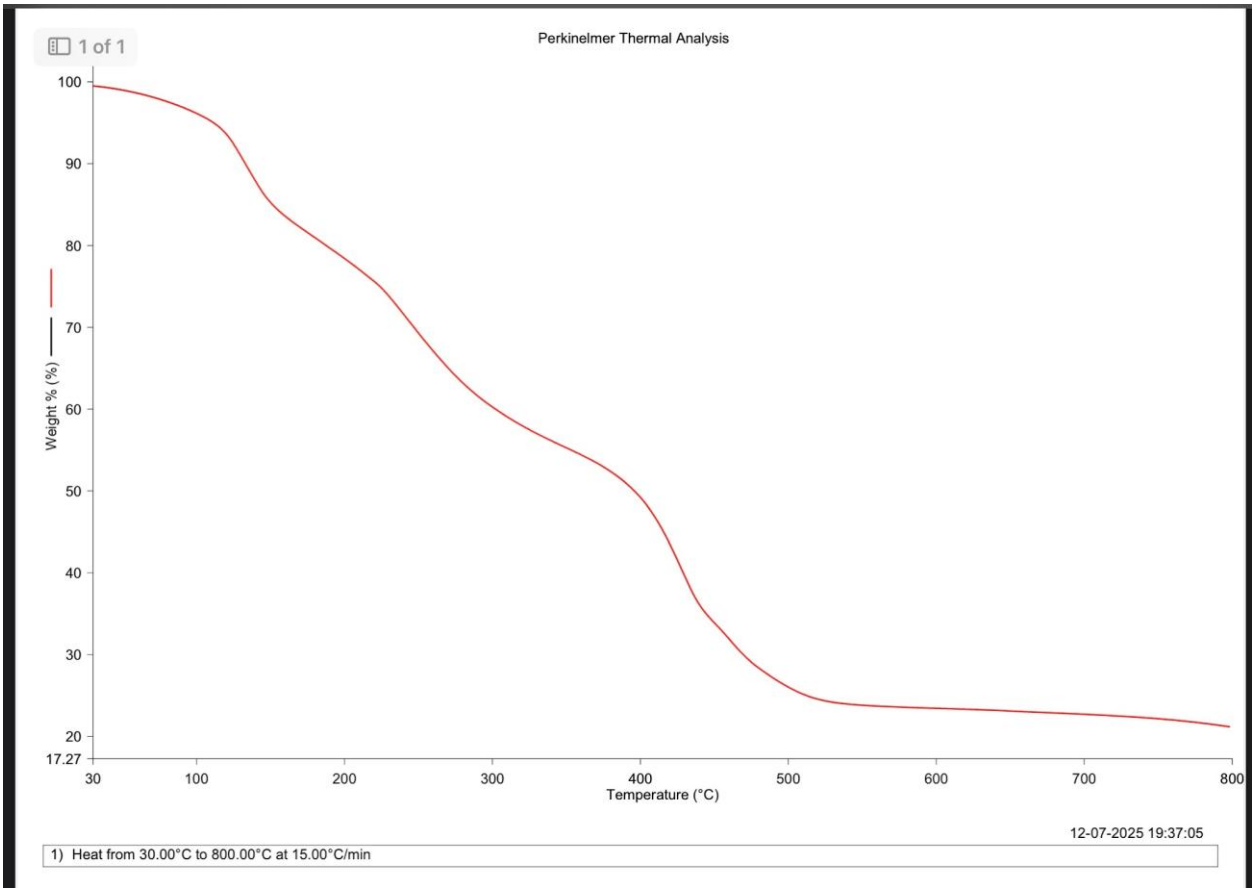
Fourier Transform Infrared spectroscopy (FTIR) obtains an infrared spectrum of a substance, revealing information about its chemical composition and structure. FTIR spectroscopy is widely used in various fields for analysing organic and inorganic compounds. Figure 2 depicts that OH ions are emitted initially, followed by NH3 ions, showing that the sample dimensionally emits organic compounds.



2. FTIR

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. TGA

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).

4. ANTI-MICROBIAL ASSAY

4. DISCUSSION

This study aims to formulate an aloe vera-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).

Aloe vera is a perennial plant in the Zingiberaceae family. Curcuma longa is the source of the Asian spice turmeric. Its use in traditional medicine is attributed to its anti-inflammatory, antioxidant, anticariogenic, antiviral, and antimicrobial qualities (Vijayapremakumar et al. 2021). Studies have shown that aloe vera gel actively contributes to wound healing and aids in immune system control.

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.

5. CONCLUSION

Butea monosperma nanoemulsion with aloevera-based gel aids a promising effect as an adjunctive therapy in the management of trigeminal neuralgia. topically. The topical route of application is the prescribed one in the management as well. 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.

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