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FORMULATION AND EVALUATION OF *PIPER BETEL L.* NANOSUSPENSION

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ABSTRACT

One promising 21st-century strategy is nanotechnology. In addition to their potential benefits in clinical treatment, the manufacturing of nanoparticles with varying sizes and shapes makes this a fascinating field of study. It greatly advances the development of biological medicine and the improvement of phytomedicines' bioavailability, and it is at the forefront of bringing a plethora of new products and methods to the modernizing therapeutic and pharmaceutical fields. Herbal medication delivery is entering a new era thanks to nanosuspensions. Since ancient times, herbal remedies have been widely used worldwide. The release of physiologically active chemicals is necessary for the effectiveness of various species of medicinal plants. Most of the extract's active ingredients suffer from limited absorption and poor bioavailability since they either contain extremely large molecules or are poorly soluble in water, making them unable to cross the lipid membranes of the cells. Despite their incredible in vivo potential, many phytomedicines show little to no in vivo activity because of inadequate absorption. Some extracts are not used in clinical settings as a result of these challenges. The use of herbal extracts has been widely recommended as a way to improve bioactivity while lowering the required dosage and associated negative effects. The introduction of nanosuspension technology is the consequence of innumerable formulation scientists' efforts, and it has developed into a strong contender for the more effective and noticeable delivery of poorly soluble medications.

Keywords: *piper betel, pan, nano suspension, suspension, antimicrobial fraction*

Introduction

A wide range of secondary metabolites, including phenolic compounds (chavicol, hydroxyl chavicol), volatile oils (safrole, eugenol, isoeugenol, eugenol methyl ester), fatty acids (stearic and palmitic), and hydroxyl fatty acids (stearic, palmitic, myristic), are abundant in the leaves of the Piper betel plant. These compounds demonstrate antibacterial properties in vitro and may be used as a practical, affordable, and safe antibacterial for the treatment of microbial infections. Traditionally, piper betel has been used as a carminative, compost, antiseptic, antifungal, and antibacterial agent. Additionally, it has been used as a general tonic and to treat worms and stomach issues. As a stimulant, it is frequently chewed alongside betel nut (Areca catechu).

VERNACULAR NAMES :

- Sanskrit :Tamboolavalli, Tamboola, Tamboolavallika
- English: Betel leaf plant
- Hindi: Pan
- Malayalam: Vetta,Vettila
- Bengali: Pan

TAXONOMICAL CLASSIFICATION

- Kingdom - Plantae
- Division - Magnoliophyta
- Class - magnolipsida
- Order - piperales
- Family - piperaceae
- Genus - piper
- Species - Betel

CHEMICAL CONSTITUENTS:

Plant contains terpine, p-cymene,chavicol, allyl catechol, eugenol, estragol, oxalic acid, malic acid amino acids. Leaves contain good amounts of vitamins particularly nicotinic acid, ascorbic acid and carotin. They also contain significant amounts of all essential amino acids except lycine, histidine and arginine. Large concentrations of asparagines are present while glycine and proline occur in good amount. Essential oil of leaf gives it the aromatic flavour. Beta-sitosterol is present in the root.

VARIOUS PROVED THERAPEUTIC VALUES OF PIPER BETEL:

Antimicrobial Activity:

The antibacterial activity of an aqueous and methanol extract of Terminalia catappa L., Manilkara zapota L., and Piper betel L. leaves against ten Gram positive, twelve Gram negative, and one fungal strain, Candida tropicalis, was investigated by Nair and Chanda (2008). The antifungal assay employed fluconazole as a reference, and the antibacterial assay used piperacillin and gentamicin. The three plants' levels of action against the examined bacteria varied. The examined microbial strains were significantly inhibited by the methanolic extract compared to the aqueous extract. Piper betel was the most potent antibacterial herb.

Antihistaminic activity:

The pharmacological assessment of the ethanolic and essential oil extracts of P. betel Linn. leaves was conducted for their antihistaminic activity on guinea pigs in Hajare et al. (2011). The isolated guinea pig tracheal chain preparation showed a right side shift of the dose response curve (DRC) of histamine. Chlorpheniramine maleate was used as a standard drug.

Anti-inflammatory effects:

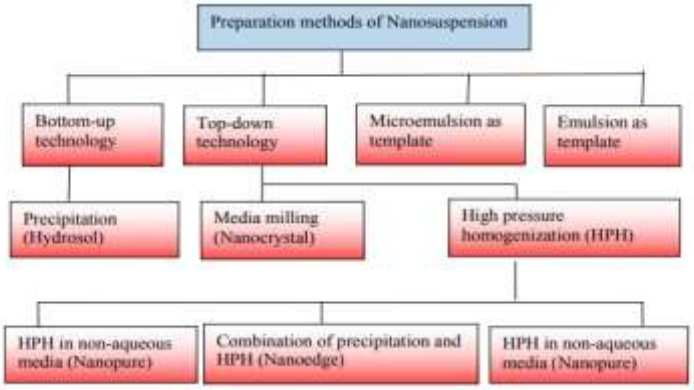
In the complete Freund's adjuvant-induced model of arthritis in rats, the ethanolic extract of betel leaf has been reported to possess anti-inflammatory activities at non-toxic concentrations. Eugenol, one of the principal constituents of betel leaf, has also been shown to possess anti-inflammatory effects in various animal models of studies with various inflamogens. The betel leaf is a common household remedy for inflammation in the oral cavity.

Antioxidant effects:

The constituents of betel leaves, eugenol, hydroxychavicol, and alpha-tocopherol, have also been demonstrated to raise the levels of GSH in mouse skin and liver, according to studies by Azuine et al. (1991) and Bhide et al. All of these findings collectively demonstrated that betel leaf extracts and some of its constituents enhanced cellular antioxidants and, at least in part, mediated the chemopreventive effects.

NANOSUSPENSION

Very finely dispersed solid medication particles in an aqueous or organic medium for parentral and pulmonary or oral and topical delivery are known as pharmaceutical nanosuspensions. Solid particles in nanosuspension typically have an average particle size of 200–600 nm, with a particle size dispersion of less than one micron. Nanoparticles are not the same as nanosuspensions. Drugs are transported by lipidic nanoparticles. By maintaining the medicine in the necessary crystalline state with smaller particles, nanosuspension technology improves bioavailability by increasing the rate of dissolution.



ADVANTAGES OF NANOSUSPENSION:

- It can be applied for the poorly water soluble drugs.
- Rapid dissolution and tissue targeting can be achieved by iv route of administration.
- Oral administration of nano suspension provide rapid and improved bio availability.
- Long term physical stability due to the presence of stabilizers.
- Nanosuspensions can be incorporated in tablets, pellets, hydro gels.

DISADVANDAGES:

- Physical stability, sedimentation and compaction can causes problems.
- It is bulky sufficient care must be taken during handling and transport.
- Uniform and accurate dose cannot be achieved unless suspension.

MATERIALS AND METHODS

AUTHENTICATION OF PLANT:

It is an identification process of combination of art and science. Correct botanical identification of drug is very important for good quality of formulation.If the starting raw material is not good, then final formulation quality is not guaranteed.A first stage is identification of the plant species or botanical verification by the currently accepted Latin binominal name and synonyms.

Collection of the leaves:

Healthy plant leaves of *piper betel L.* were collected from nearby farm. The leaves were cleaned properly in running tap water and were shade dried. It was powdered in a mechanical mixer. The powder was sieved in a No.60 sieve and kept in a well closed container in a dry place.

EXTRACTION:

It is the treatment of plant with solvent where by the medicinally active constituents are dissolved and most of the inert matter remains undisclosed. Two plants are used for this formulation by using different extraction technique.

PROCEDURE:

The powder drug was placed inside a thimble made from thick filter paper, which is loaded into the main chamber of the Soxhlet extractor. The Soxhlet extractor is placed onto the flask containing the extraction solvent ethanol. The Soxhlet is then equipped with condenser.The solvent vapour travels up a distillation arm and floods into the chamber housing the thimble of solid. The chamber containing the solid material slowly fills with warm solvent. When the Soxhlet chamber was almost fill, the chamber is automatically emptied by a siphon arm with the solvent running back to the distillation flask.This cycle was allowed to repeat for many times. After many cycle the desired compound is concentrated into the distillation flask. This procedure was taken upto 48 hours to get a concentrated *piper betel L.* extraction.

EVAPORATION OF SOLVENT:

The evaporation of solvent was carried out by the equipment called, Heading mantel. The extract was heating under the low temperature to avoid the loss of phyto chemical of the plant.

The extract was evaporated until the solvent is evaporated and the extract get concentrated.

Then, the crude extract was stored in an beaker in a sterile condition to avoid the microbial contamination.

PREPARATION OF PIPER BETEL . LNANOSUSPENSION:

Nano-precipitation method was followed with a slight modification for the preparation of nanosuspensions.*Piper betel L.* leaves extract (200mg), was dissolved in 15 ml of acetone and 5ml of ethanol (3:1) ratio andthe whole preparation was allowed for sonication for 60 seconds and add 1ml of triethanolamine. The resultant solution was then subjected for stirring in a magnetic stirrer and inorder to minimize coalescence and the mixture was continously stirred at 500rpm for 6hrs at room temperature to allow solvent evaporation and nanoparticle formation . the resultant nanosuspension was consequently cooled down to -18 degree celsius to obtain nano suspension.

EVALUATION TEST OF NANO SUSPENSION

DRUG CONTENT TEST:

Nanosuspension equivalent to 10mg of the drug was taken in 100ml volumetric flask and diluted up to 100ml with methanol. The absorbance of resulting solution was measured at 231.0nm and drug content was calculated. This test was done by pour-plate technique. The bacterial culture and liquid agar medium are mixed together. After mixing the medium, the medium containing the culture poured into sterilized petridishes, allowed solidifying and then incubated. After incubation no microbial growth appear on the surface.

PARTICLE SIZE AND PDI:

Mean particle size and size distribution analysis was carried out using Malvern Zetasizer Nano Series Nano- S90, which follows principle of LASER light diffraction or also called Photon correlation spectroscopy (PCS). It is based on the measurement of the Brownian motion of particles.

ZETA POTENTIAL:

Zeta potential is a physical properties of nano suspension. The zeta potential can be measured by determining the velocity of the particles in an electric field (electrophoresis measurement) in collodial systems according to electric double layer theory, there is a net balance of attractive as well as repulsive forces. However, if the particles have low zeta potential values then there will be less stability.

RESULT AND DISCUSSION

The evaluation and formulation of nanosuspension using *piper betel L.* was prepared and submitted

Nanosuspension is a commercially possible approach to solving the poor solubility as well as poor bioavailability problems of the drugs. Productions techniques such as media milling and high-pressure homogenizer are used for large scale production of nano-suspensions. Nanosuspensions can be administered through oral, parenteral, pulmonary, ocular and topical routes. A nanosuspension not only improves the solubility and bioavailability but also modifies the pharmacokinetics of drug and thus improves drug safety and efficacy. The main goal of this review was to describe the various preparation techniques for production of nanosuspensions. it was observed that preparing nanosuspensions is a state -of-art technology that requires a suitable technique among the various possible methods. Production techniques such as media milling and high-pressure homogenization have been successfully employed for large scale production. The advances in production methodologies using emulsions or microemulsions as templates have provided still simpler approaches for production but with some limitations.

PARTICLE SIZE AND PDI:

Particle size of optimized formulation is 904.9nm and PDI is 0.643 as the smaller particle size may in turn bring about more bio-availability.

ZETA POTENTIAL:

The reduced zeta potential values of -39.3mV indicated that the prepared nanosuspension possess a higher degree of long-term stability.

CONCLUSION:

The drug's poor oral bioavailability may be caused by poor solubility, poor permeability, or poor stability in the gastrointestinal tract (GIT). Nanosuspensions solve the twin problems of poor solubility and poor permeability across the membrane. Using a nanosuspension formulation, the bioavailability of poorly soluble oleanolic acid, a hepatoprotective agent, was improved, and the therapeutic effect was significantly enhanced, indicating higher bioavailability due to the lyophilized nanosuspension powder dissolving 90% in 20 minutes as opposed to 15% in 20 minutes for a coarse powder.

In this study we have taken an effort to prepare nanosuspension formulation of*Piper betel L.* and the vesicles formed are quite stable. From the results of the present experimental investigation, it may be concluded that the formulation of *piper betel L.* nanosuspension showing small vesicle size, by the evaluation test of particle size and zeta potential.

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