BETEL LEAF USED IN COUGH SYRUP

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Abstract:
Piper betel Linn. an important species of the Piperaceae family is an evergreen and perennial creeper, with glossy heart-shaped leaves that are magnificent reservoirs of phenolic compounds with antiproliferative, anti-mutagenic, antibacterial and antioxidant properties. Phytochemical studies show that Piper betel contains a wide variety of biologically active compounds whose concentration depends on the variety of the plant species. Many research studies on Piper betel has reported that it contains important chemical constituents such as chavibetol, chavibetol ace-tate, caryophyllene, allylpyrocatechol diacetate, campene, chavibetol methyl ether, eugenol, a- Pinene, f-Pinene, uLimonene, safrole, 1-8-cineol, and allylpyrocatechol monoacetate. These components are valued as a stimulant for its medicinal properties like anti-fungal, anti-nociceptive, anti-cancer, immunomodulatory, antihalitosis, anti-diabetic, gastroprotective, anti-allergic, anti-fertility, antifilarial, anti-larvicidal, wound healing and anti-dermatophytic. The present re-view is an attempt to highlight various traditional uses as well as pharmacological reports on Piper betel L.

Index Terms - (Tulsi, Vasa, Trikatu, Zingiber officinale, Piper nigrum, Piper longum, Shunthi )

INTRODUCTION:

Cough is a protective reflex that helps to expel irritant matter and is necessary for preventing mechanical obstruction to breathing. It is the most common symptom affecting a large popula-tion and presenting to general practitioners. It can also be associated with the pulmonary dis-eases like common cold, pneumonia and chronic bronchitis. Up to 40% of patients with chronic cough remain unexplained in specialist clinics and are observed creating serious health problems. Both acute and chronic cough have significant impacts on health-related quality of life. Drugs that suppress cough are designated as anti-tussives. Some of them act on the central nervous system to inhibit cough while others produce their effects locally. Centrally (codeine and ephedrine) and peripherally (bromhexine and guaefenesin) acting anti-tussives produce known side effects such as sedation, constipation, drowsiness and addiction. Therefore, a need is felt to develop an effective anti-tussive and expectorant drug without any side effects.

In present study, selected Ayurvedic cough syrup consists extracts of Ocimum sanctum (Tulsi)Aerial, Adhatoda vasica (Vasa) Leaves, Trikatu [Compound of Shunthi (Zingiber officinale) Rhizome, Marich (Piper nigrum) fruit and Pippali (Piper longum) fruit], Zingiber officinale (Shunthi) Rhizome, Glycyrrhiza glabra (Yashtimadhu) Root, Solanum
xanthocarpum (Kan-takari) Whole plant along with powder of Navasar and Menthol. Each of these ingredients is reported to have direct or indirect anti-tussive effect.

Expectorant: A type of cough medicine use to clear mucous from your air way. You make taken expectorant to help relieve congestion if you have cold or the flu.

**TYPES OF COUGH**

Mainly there are two types of cough, which are classifies as follows.

- Wet cough
- Dry cough

<table>
<thead>
<tr>
<th>Wet cough</th>
<th>Dry cough</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Productive and effective cough.</td>
<td>● Non effective and infective cough.</td>
</tr>
<tr>
<td>● It expels secretion mucous or foreign material from respiratory tract.</td>
<td>● It expels secretion or mucous from lungs.</td>
</tr>
<tr>
<td>● The main purpose of wet cough is to remove the foreign matter or mucous from respiratory tract by which inspection is caused.</td>
<td>● Dry cough is chronic in nature and it is caused by dry irritation, smoke or dust.</td>
</tr>
</tbody>
</table>

Table 1 Types of Cough

![Classification of drugs for cough](image)

**REVIEW OF BETEL LEAF:**

The betel leaf is an evergreen and perennial, creeper, with glossy heart-shaped and white catkin. The genus Piper (Piperaceae) is largely distributed in tropical and subtropical regions of the world. Piper betel is cultivated in India, Sri Lanka, Malaysia, Indonesia, Philippines, Island, and East Africa.
TAXONOMICAL CLASSIFICATION:

- **Kingdom**: Plantae
- **Division**: Magnoliophyta
- **Class**: Magnoliopsida
- **Order**: Piperales
- **Family**: Piperaceae
- **Genus**: Piper
- **Species**: Betel

COMMON NAME:

- **Sanskrit**: Tambool, Mukbhushan.
- **Hindi**: Paan.
- **Marathi**: Khauch Paan.

SIGNIFICANCE OF BETEL LEAVES:

<table>
<thead>
<tr>
<th>Guna (Quality)</th>
<th>Laghu, Ruksha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rasa (Taste)</td>
<td>Tikt</td>
</tr>
<tr>
<td>Vipak (Metabolism)</td>
<td>Katu</td>
</tr>
<tr>
<td>Virya (Potency)</td>
<td>Ushan</td>
</tr>
<tr>
<td>Prabhav (Impact)</td>
<td>Hridya</td>
</tr>
</tbody>
</table>

Table 2. Significance of Betel Leaves
VERITIES OF BETEL LEAF:

Based on the morphological characters and essential oil content, betel vine varieties are divided into five main groups viz, Bangla, Desawari, Kapoori, Sanchi, and Meetha.

1. **Bangla** is large thin leaves with nine main nerves and ovate lamina with cordate base. Leaf apex is pointed and short, not curved. Petiolar sinus is more prominent than other varieties.

![](image1)

Fig 3. Bangla.

1. **Desawari** is large thin leaves and cordate lamina with seven to nine nerves. Leaf of Desawari is pinkish, and leaf apex is short, acuminate, and curved.

![](image2)

Fig 4. Desawari.

2. **Kapoori** leaves are more elliptical, and lamina is thin with undulated margin. Leaf apex of Kapoori is acuminate, and petiolar sinus is inconspicuous.

![](image3)

Fig 5. Kapoori.

1. **Sanchi** consists of a cordate leaf base with more elliptical lamina and long tapering apex. Normally seven nerves are seen in Sanchi.

![](image4)

Fig 6. Sanchi.
CHEMICAL CONSTITUENT OF BETEL LEAF:

Leaves contain protein 3-3.5%, carbohydrate 0.5 - 6.10%, minerals 2.3-3.3%, and tannins 0.1 - 1.3%. It contains calcium, phosphorus, iron, iodine, potassium, vitamin B, vitamin C and vitamin A. It also contains some aromatic compounds and stable oils like phenol and terpene. Besides, it contains eugenol, chavibetol a-pinene, f pinene, 1, 8 cineole and hydroxychavicol. Major constituents of common betel were found to be safrrole (48.7%) and chavibetol acetate (15.5%). The presence of allylpyrocatechol, caryophyllene, anethole, stearic acid, carvacrol, polyphenol, alkaloids, saponin, are also found in betel Leaf.

<table>
<thead>
<tr>
<th>Chemical constituents</th>
<th>% of chemical constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chavibetol</td>
<td>53.1</td>
</tr>
<tr>
<td>Chavibetol acetate</td>
<td>15.5</td>
</tr>
<tr>
<td>Caryophyllene</td>
<td>3.71</td>
</tr>
<tr>
<td>Allylpyrocatehol diacetate</td>
<td>0.71</td>
</tr>
<tr>
<td>Chavibetol methyl ether</td>
<td>0.48</td>
</tr>
<tr>
<td>Eugene</td>
<td>0.32</td>
</tr>
<tr>
<td>a-Pinene</td>
<td>0.21</td>
</tr>
<tr>
<td>f-Pinene</td>
<td>0.21</td>
</tr>
<tr>
<td>Safrrole</td>
<td>48.7</td>
</tr>
<tr>
<td>1, 8-Cineol</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Table 3. Chemical constituents of Betel Leaf

Fig 7. Structure of chemical constituents.
AYURVEDIC USES:

**Scanty or Obstructed Urination:**
Betel leaf juice is credited with diuretic properties. Its juice, mixed with dilute milk and sweetened slightly, helps in easing the passage of urine.

**Weakness of Nerves:**
Betel leaves are beneficial in the treatment of nervous disorders. The juice of a few betel leaves, with a teaspoon of honey, serves as a good tonic. A teaspoon of this mixture can be taken twice a day.

**Headaches:**
The betel leaf has analgesic and cooling properties. It can be applied to relieve intense head-aches.

**Respiratory Disorders:**
Betel leaves are useful in pulmonary afflictions suffered in childhood and old age. The leaves, soaked in mustard oil and warmed, may be applied to the chest to relieve a cough or difficulty in breathing.

**Constipation:**
In the case of constipation in children, a suppository made of the stalk of betel leaf dipped in castor oil can be introduced in the rectum. This instantly relieves constipation.

**Sore Throats:**
Local application of the leaves is effective in treating sore throat. The crushed fruit or berry should be mixed with honey and taken to relieve an irritating cough.

**Wounds:**
Betel leaves can be used to heal wounds. The juice of a few leaves should be extracted and applied to the wound. Then a betel leaf should be wrapped over it and bandaged. The wound will heal with just a single application within two days.

**Boils:**
The herb is also an effective remedy for boils. A leaf is gently warmed till it gets softened and then coated with a layer of castor oil. The oiled leaf is spread over the inflamed part. This leaf has to be replaced, every few hours. After a few applications, the boil will rupture draining out all the purulent matter. The application can be made at night and removed in the morning.

**Drying Of Betel Leaf:**
Drying is also known as dehydration, which removes the moisture from the product and thus avoids spoilage. Drying is a well-known preserving technique to enhance the shelf life of leaves and to prevent post-harvest losses. Drying implies many advantages, like longer shelf life, being easy to handle, and requiring a minimum space to store. To preserve the phyto-chemical compound, the rapid drying method is used. Drying alters both physical and chemical properties of a product, thus the selection of a drying technique is an essential factor. Generally, drying methods like sun drying, shadow drying, vacuum drying, cabinet tray drying and oven drying were used for drying. Researchers concluded that 50°C was found to be the optimum temperature for drying betel leaves in cabinet drying. This study focuses on the drying of betel leaf in solar tunnel drying and cabinet tray. In the drying process, betel leaf varieties of Pachaikodi and Vellaikodi were used. Visually, Pachaikodi betel leaf variety is dark green in colour while the Vellaikodi betel leaf variety is light green in colour. The drying characteristics, proximity and colour of dried betel leaf were also investigated.
RAW MATERIAL:

Pachaikodi and vellaikodi varieties of betel leaf were collected from the local farmers of Sriperambuthur. The freshly collected betel leaves were sorted, de-petiolized and washed be-fore drying.

PREPARATION OF BETEL LEAVES FOR DRYING:

The fresh betel leaves were sorted by removing pest damaged leaves, and petioles were re- moved from the leaves. The petiole-removed leaves are washed to remove dirt particles. Thewater drained from the leaves. After removal of excess water, drying was carried out with two different techniques, such as solar tunnel drying and tray drying.

DRIYING OF BETEL LEAVES:

150g of betel leaves were weighed accurately and the drying process was carried out in a suntunnel dryer and a cabinet tray dryer.

(i) Tray drying. Betel leaves are sorted, washed, strained from excess water, weighed and placed in a tray for drying. The betel leaves were dried at 50°C in a cabinet tray dryer. Drying continues until a constant weight is reached. After complete drying, the dried leaves were ground and sieved in a sieve. The sieved pow-der was packed in airtight LDPE pouches and stored at 4°C for further usage.

(ii) Solar tunnel drying. Betel leaves are sorted, washed, strained from excess water, and weighed. The weighed betel leaves are uniformly distributed on the filter pa- pers and placed in the solar tunnel dryer for drying. The temperature of the solar tunnel dryer varies from 28°C to 38°C. Drying was carried out until it reached a constant weight.

(iii) Vacum Drying. 10 grams of betel leaf was distributed uniformly as a thin layer on a tray and dried in vacuim oven on temperature 30, 50, 70 and pressure 1, 0.5 and 0.0 atm for each temperature respectively. The weight of sample measured in every 15 minutes for 3 hours.

FIG 8. Dried leaves of betel plant

EXTRACTION OF BETEL LEAF:

Extraction methods comprises the separation of medicinally active portions of plant tissues from the inactive/inert components by using selective solvents. During extraction, solvents dif-fuse into the solid plant material and solubilize compounds with analogous polarity. Now day's pharmaceutical agencies begin processing of medicinal and aromatic flora in their system by means of the usage of extraction of energetic components. There are numerous approaches like distillation, effleurage, maceration, expression, solvent extraction and fluid extraction are to be used for extraction of plant element. The goal of systematized extraction approaches for crude drugs (medicinal plant parts) is to obtain the pharmaceutically energetic elements and to ex-clude undesired material by remedy with a selective solvent known as menstruum. The extractthus received, after standardization, may be used as a medicinal agent as such inside the shape of tinctures or fluid extracts or in addition processed to be incorporated in any dosage form including drugs and tablets.

These products contain a complicated combination of many me-dicinal plant metabolites, together with alkaloids, glycosides, terpenoids, Flavonoids and lignans and many others. The standard strategies of medicinal plant extraction encompass mac-eration, infusion, percolation, digestion, decoction, hot continuous extraction (Soxhlet), aqueous-alcoholic extraction through fermentation, counter-current extraction, microwave-as-sisted extraction, ultrasound extraction (sonication), supercritical fluid extraction and phytonic extraction (using hydrofluorocarbon solvents). For aromatic plants, hydrodistillation tech- niques (water distillation, steam distillation, water and steam distillation),
hydrolytic maceration followed by way of distillation, expression and enflure (cold fat extraction) may be taken into account. Some of the modern extraction methods for aromatic plant life consist of headspace trapping, strong section micro extraction, protoplast extraction, microdistillation, thermomicrodistillation and molecular distillation. Extraction of the bioactive plant elements has usually been a tough project for the researchers. In this chapter, an attempt has been made to offer an outline of sure extractants and extraction approaches with their advantages and drawbacks.

Choice of solvents:

Successful evaluation of biologically active compounds from plant parts are largely dependent on the sort of solvent used within the extraction system. Properties of a ideal solvent in plant extractions consists of, low toxicity, ease of evaporation at low temperature, fast physiologic absorption of the extract, preservative action, incapability to cause the extract to form complex or dissociate. The circumstances affecting the choice of solvent are amount of phytochemicals to be extracted, rate of extraction, variety of various compounds extracted, variety of inhibitory compounds extracted, ease of subsequent handling of the extracts, toxicity of the solvent in the bioassay method, ability health hazard of the extractants. The preference of solvent is biased by using what is supposed with the extract. Since the end product will include traces of residual solvent, the solvent must be nonpoisonous and need not intervene with the bioassay. The desire will even depend on the targeted compounds to be extracted.

Alcohol: The better activity of the Ethanolic extracts compared to the aqueous extract can be attributed to the presence of higher amounts of polyphenols in comparison to aqueous extracts. It manner that they're greater efficient in cell walls and seeds degradation which have nonpolar character and cause polyphenols to be released from cells. More beneficial reason behind the decrease in activity of aqueous extract may be ascribed to the enzyme polyphenol oxidase, which degrade polyphenols in water extracts, while in methanol and ethanol they may be inactive. Moreover, water is a better medium for the occurrence of the micro-organisms compared to ethanol. The higher concentrations of greater bioactive flavonoid compounds have been detected with methanol 70% due to its higher polarity than pure ethanol. By including water to the pure methanol up to 30% for making ethanol 70% the polarity of solvent was elevated. Additionally, methanol was found easier to penetrate the cell membrane to extract the intracellular ingredients from the plant material.

- Water: Water is prevalent solvent, used to extract plant products with antimicrobial property. Though traditional healers use generally water but plant extracts from organic solvents have been found to offer more consistent antimicrobial property as compared to water extract. Also water soluble flavonoids (in general anthocyanins) haven’t any antimicrobial importance and water-soluble phenolics only important as antioxidant compound.

LERATURE REVIEW

Maran et al., 2013; Muruganandam et al., (2017):

Several extraction variables such as extraction temperature, extraction time, and material to solvent quantity were optimized to get maximum extraction yield by using Box-Behnken design (BBD) coupled with response surface methodology (RSM). Response surface methodology, a valuable tool helps to determine the optimum values of experimental parameters and builds a mathematical model to evaluate the interaction effect between variables with a reduced number of experiments (Maran et al., 2013; Muruga-nandam et al., 2017)

ECCLES, ET AL., (2013):

Globally, breast cancer is the most common disease in women with new cases incidence of 1.38 million per year
Zulharini M et al., (2018):

used methanolic extract of red betel leaf to evaluate the cytotoxic and anti-migration activity towards metastatic breast cancer. Red betel leaves (Piper crocatum Ruiz dan Pav) has been known as herbal medicine containing biphenolic, such as apigenin and luteolin de-rivatives which have cytotoxic activity toward cancer cells.


studied the in-vitro antifungal activity of hydroxychavicol isolated from piper betel leaf. The minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) were determined using broth microdilution method. Hydroxychavicol exhibited inhibitory effect on fungal species of clinical significance with MICs ranging from 15.62 to 500 μg/ml for yeasts, 125 to 500 μg/ml for Aspergillus species and 7.81 to 62.5 μg/ml for dermatophytes. The antifungal activity exhibited by this compound warrants its use as an anti-fungal agent particularly for treating topical infections as well as gar- gle mouthwash against oral Candida infections.

Majumdar B et al., (2003):

studied the healing effect on treatment with ethanol extract of P. betel at a dose of 150mg/kg body weight daily for 10 days, after induction of peptic ulcer by NSAID in albinorats. During the healing process, on treatment with extract of piper betel, antioxidant factor, e.g., superoxide dismutase and catalase activity, mucus and total gastric tissue sulphahydryl group were increased. Overall it can be suggested that the antioxidant or free radical scavenging activity of the plant extract may be responsible for its healing property 13.

Ld et al., (2014):

evaluated the gastroprotective activity of hot aqueous extract (HAE) and cold ethanolic extract (CEE) of P. betel against ethanolinduced gastric ulcers in rats. The parameters evaluated were (a) effects of HAE on mucus content adhering to the wall of the gastricmucosa, (b) acidity (total and free) (c) volume and (d) pH of the gastric juice. Oral administration of HAE and CEE provided marked dependent (HAE r² = 0.97; CEE r ² = 0.96) and significant (P≤ 0.05) than that of misoprostol, the reference drug.

Kanjwani DG et al., (2008):

evaluated immunomodulatory activity of methanolic extract of Piper betel. The MPbconsisted of a mixture of phenols, flavonoids, tannins, and polysaccharides. Both in-vitro as well as in-vivo evaluation were carried out. The effects of MPB on lymphocyteproliferation, interferon-γ receptors and the production of nitric oxide were measured in-vitro.

Arambewela LS et al., (2005):

investigated the anti-diabetic activities of aqueous and ethanolic extracts of Piper betelleaves in rats. This was tested in normoglycaemic and streptozotocin (STZ)-induced diabetic rats using oral administration of hot water extract (HWE) and cold ethanolic extract (CEE). In normoglycaemic rats, both HWE and CEE significantly lowered the blood glucose level in a dose-dependent manner. In glucose tolerance test, both extractsmarkedly reduced the external glucose load.

Arambewela LS et al., (2011)

reported that Piper betel has antinociceptive activity. About 200 and 300 mg/kg doses of Piper betel extract markedly reduced the licking time in early and late phases of the formalin test in a bell-shaped dose-response curve. In the formalin test, the pain in the early phase is caused due to the direct stimulation of the sensory nerve fibers by forma-lin, while the pain in the late phase is due to the inflammatory mediators, like histamine, prostaaglandin, serotonin, and bradykinin.
NILUGAL ET AL., (2014);
investigated the wound healing capability of Piper betel leaves and stem extract. The enhanced rate of wound contraction and the drastic reduction in healing time in male albino rats, which might be due to enhanced epithelialization was observed. The results showed wound healing and repair, accelerated by applying ointment formulation containing Piper betel leaves and stem extract, which was highlighted by the full thickness coverage of the wound area by an organized epidermis.

L.S. RARAMBWEWA ET AL., (2011):
Anti-larvicidal activity of Piper betel was observed. The piper betel essential oil at different concentrations, i.e. 500, 100, 50, 25, 12.5 and 6.25 ppm concentrations were used, and motility was recorded between 1 to 24 h. Mortalities of 43% and 100% were observed for 100 and 500 ppm concentrations, respectively, within 1 h. The concentration of oil used was 1%, 0.8%, and 0.5% respectively and the mortality rate of 100% was observed in 1% betel oil solution within 1 h.

Anti-dermatophytic Activity of Piper betel cream was studied by Nopamart Chatcha-wanchonteera et al., in 2006. Crude ethanolic extracts of Piper betel leaves (Piperaceae), Alpinia galangal rhizomes (Zingiberaceae) and Alliums ascalonicum bulbs (Liliaceae) were previously tested against selected dermatophytes (Microspore canis, Microsporum gypseum, and Trichophyton mentagrophyte). The results suggested a promising anti-fungal property of Piper betel extracts than its counterparts. In a study conducted by for anti-dermatophytic activity 10% Piper betel cream was formulated, subjected to physical and microbial limit tests, and evaluated for its effect against dermatophytes in vitro.

PHARMACOLOGICAL ACTIVITY
A large number of natural products are being used in the treatment of many diseases as traditional medicine in several countries. Piper betel belongs to the family Piperaceae and has over 2000 species. The plant is indigenous to India. Piper betel leaves are shown to be effective against several human pathogens, although the mechanisms involved have not been elucidated. Extracts of Piper betel are used for the treatment of various ailments since ages due to its essential properties like anti-oxidant, anti-cancer, anti-allergic, etc.

GASTROPROTECTIVE:
Study evaluated the gastroprotective activity of allylpyrocatechol (APC), the major antioxidant constituent of Piper betel, against indomethacin-induced stomach ulceration in a rat model. Results showed both APC and misoprostol effectively healed stomach ulceration. The protective activity was attributed to antioxidant activity and the enhancement of mucus content of gastric tissues.

GASTROPROTECTIVE ACTIVITY:
The healing effect on treatment with ethanol extract of P. betel at a dose of 150 mg/kg body weight daily for 10 days, after induction of peptic ulcer by NSAID in albino rats. During the healing process, on treatment with extract of piper betel, antioxidant factor, e.g., superoxide dismutase and catalase activity, mucus and total gastric tissue sulphahydryl group were increased. Overall it can be suggested that the antioxidant or free radical scavenging activity of the plant extract may be responsible for its healing property. LD evaluated the gastroprotective activity of hot aqueous extract (HAE) and cold ethanolic extract (CEE) of P. betel against eth-anol-induced gastric ulcers in rats. The parameters evaluated were (a) effects of HAE on mucus content adhering to the wall of the gastric mucosa, (b) acidity (total and free) (c) volume and (d) pH of the gastric juice. Oral administration of HAE and CEE provided marked dependent (HAE, r² = 0.97; CEE, r² = 0.96) and significant (P ≤ 0.05) than that of misoprostol, the reference drug. The HAE significantly increased the mucus content adhering to the wall of gastric mu cosa and inhibited the volume of gastric acid, and hence concluded that both HAE and CEE of P. betel leaves have a strong gastroprotective activity.
WOUND HEALING ACTIVITY:

The enhanced rate of wound contraction and the drastic reduction in healing time in male albino rats, which might be due to enhanced epithelialization was observed. The results showed wound healing and repair, accelerated by applying ointment formulation containing Piper betel leaves and stem extract, which was highlighted by the full thickness coverage of the wound area by an organized epidermis. The animals treated with ointment formulation containing 10% Piper betel leaves and stem showed significant results when compared with providone iodine and control group. From this investigation, it can be concluded that Piper betel has the potential ability in wound healing.

ANTI-ALLERGIC ACTIVITY:

The effects of Piper betel ethanolic extract on the production of histamine and granulocyte macrophage colony-stimulating factor (GMCSF) by murine bone marrow mast cells (BMMCs) and on the secretion of exotoxin and IL-8 by the human lung epithelial cell line, BEAS-2B, were investigated in-vitro. The extracts significantly decreased histamine and GM-CSF production by an IgE mediated hypersensitivity reaction and inhibited exotoxin and IL-8 secretion in a TNF-α and IL-4-induced allergic reaction. The results suggested that Piper betel may offer a new therapeutic approach for the control of allergic diseases through inhibition of production of allergic mediators.

ANTI-LARVICIDAL ACTIVITY:

Anti-larvicidal activity of Piper betel The piper betel essential oil at different concentrations, i.e. 500, 100, 50, 25, 12.5 and 6.25 ppm concentrations were used, and motility was recorded between 1 to 24 h. Mortalities of 43% and 100% were observed for 100 and 500 ppm concentrations, respectively, within 1 h. The concentration of oil used was 1%, 0.8%, and 0.5% respectively and the mortality rate of 100% was observed in 1% betel oil solution within 1 h. Betel solutions ranging in concentration from 1% to 4% were prepared using 1% Tween 80, sodium lauryl sulfate (0.05 g/ml as a stabilizer) and methylparaben (0.01 g/100 ml, as preservative). The 4% and 3% preparations of the oil of betel were effective in killing 100% of the larvae of C. megacephala within 3 h, while betel oil at 2% concentration killed 97% of C. megacephala larvae within 4 h. This shows that betel oil is effective in the treatment of wound myiasis.

ANALGESIC:

Study evaluated the analgesic activity of piper betel leaf using eddy’s hot plate and heat conduction method. Results showed a dose-dependent response. The aqueous extract of leaf was safe up to 1000 mg/kg b.w. p.o. dose.

ANTIDEPRESSANT:

Study evaluated the antidepressant activity of ethanolic extract of P. betle leaves in Swiss albino mice. Results showed significant antidepressant effect as indicated by reduction in duration of immobility. The 100 mg extract dose effect was greater than that of imipramine.

ANTIBACTERIAL:

According to the study, PB was effective against all pathogens tested, including Rastonia, Xan-thomonas, and Erwinia. Additionally, tests revealed that PB solvent extract had a more powerful effect than streptomycin. The ethanol extract of P. betel showed the greatest zone of inhibition against Gram negative and Gram positive bacteria, with the greatest bactericidal activity against E. coli, P. aeruginosa, and S. aureus. The study of crude aqueous extract of P. betel demonstrated activity against most of the test bacteria.

ANTIOXIDANT:

Study showed a leaf extract to inhibit the radiation-induced lipid peroxidation process effectively, attributed to its ability to scavenge free radicals involved in initiation and propagation steps with elevation of the antioxidant status in the study animals.

ANTIMICROBIAL:

Study evaluated an aqueous extract of fresh leaves for antimicrobial activity. Results showed effective inhibitory action against the tested organisms (E. coli, Vibrio cholera, S. typhi, and S. paratyphi A and B).
ANTITUMOR:

Study evaluated a methanolic extract of Piper betel leaves and fractions for antitumor activity against Ehrlich ascites carcinoma in Swiss albino mice. Results showed significant antitumor activity, which may be attributed to augmentation of endogenous antioxidant potential.

ANTICHLINESTERASE INHIBITORY ACTIVITY:

Study evaluated three leaf varieties Kaliganga, Meetha, and Haldi—for acetylcholinesterase inhibitory properties. Aqueous extracts of both fresh and dry leaves of all varieties inhibited acetylcholinesterase activity in a dose dependent manner. The AChE inhibitory property of P. betle may have a beneficial effect on memory function.

ANTIDERMATOPHYTIC:

An ethnoveterinary study evaluated crude ethanolic extracts of P. betel leaves, A. galanga rhizomes, and A. escalonicum bulbs against selected zoonotic dermatophytes (M. canis, M. gypseum, and T. mentagrophytes) and yeast-like Candida albicans. All the extracts caused concentration dependent suppression of fungi growth. Testing showed Pb cream formulation with potential therapeutic values for treatment of dermatophytosis.
<table>
<thead>
<tr>
<th>S.no.</th>
<th>Plant part/ Extract</th>
<th>Activity/Animal/ Model</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Aqueous extract of the fresh <em>Piper betle</em> leaves.</td>
<td>Antimicrobial activity/Various microorganisms/disc diffusion method.</td>
<td>Aqueous extracts showed effective inhibitory action against the microorganisms</td>
<td>Shamsheem Pasha MD; et al., (2013)</td>
</tr>
<tr>
<td>4.</td>
<td>Aqueous extract of the fresh <em>Piper betle</em> leaves.</td>
<td>Antioxidative &amp; anti-thrombolytic activity/Microorganisms (<em>Streptococcus pyogenes</em>, <em>Staphylococcus aureus</em>, <em>Pseudomonas aeruginosa</em> &amp; <em>Escherichia coli</em>).</td>
<td>The antioxidative &amp; anti-thrombolytic activities were attributed to the high concentration &amp; combined activity of flavonoids &amp; polyphenols.</td>
<td>Chakraborti Devjani; et al., (2011)</td>
</tr>
<tr>
<td>6.</td>
<td>Aqueous and ethanol extract of the <em>Piper betle</em> leaves.</td>
<td>Antibacterial Activity/ Gram positive (<em>Bacillus subtilis</em>, <em>Staphylococcus aureus</em> &amp; <em>Micrococcus luteus</em>) &amp; Gram negative (<em>Escherichia coli</em> &amp; <em>Pseudomonas aeruginosa</em>) bacteria/ Agar diffusion method.</td>
<td>The study reveals that both the aqueous and alcoholic extracts be active beside the strains of bacteria which are common cause of infections.</td>
<td>Kaveti Balaji; et al., (2011)</td>
</tr>
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<td>7.</td>
<td>The hot water <em>Piper betle</em> leaves extract.</td>
<td>Gastroprotective activity.</td>
<td>The study showed that it can protect against indomethacin-induced gastric ulceration due to its antioxidant and mucin protecting properties.</td>
<td>Pradhan D.; et al., (2013)</td>
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<td>8.</td>
<td>The petroleum ether extract &amp;methanol extract of the <em>Piper betle</em> leaves.</td>
<td>Insect Attractant Property/Field tests in a cornfield.</td>
<td>Field tests in a cornfield using trap contain the extracts, which does not detect adult moths of <em>Ostrinia sallentals</em>.</td>
<td>Yusoff Z.; et al., (2005)</td>
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<td>9.</td>
<td>The methanolic extract of the <em>Piper betle</em> leaves.</td>
<td>Analgesic and anti-inflammatory activity/ Carrageenan induced hind paw edema model, hot plate, writhing and formalin tests/ Swiss albino mice and Wistar Rats.</td>
<td>The dose produced a significant increase in pain threshold in hot plate method whereas significantly reduced the writhing caused by acetic acid &amp; caused significant inhibition of carrageenan induced paw edema.</td>
<td>Akbar Fahima; et al., (2012)</td>
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<td>12.</td>
<td>The <em>Piper betle</em> leaf infusion.</td>
<td>Skin Antiseptic/ pre-surgery cataract patients.</td>
<td>Results showed that 20% <em>Piper betle</em> leaf infusion to have an antiseptic</td>
<td>Husnun Amalia; et al., (2009)</td>
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</tbody>
</table>
PROPOSED METHODOLOGY:

MACERATION PROCESS

Coarse powder of sample

Placed in closed vessel

Whole of the selected solvent (menstruum) added

Allowed to stand for 7 days shaking occasionally

Liquid strained off

Solid residue (marc) pressed to recover as much as occluded solution

Strained and expressed liquid mixed

Clarified by subsidence or filtration

Evaporation and concentration

CONCLUSION:

Since the traditional times, piper betel is consumed frequently as cough syrup. According to numerous research studies, the medicinal importance of the herb as discussed above evidently prove that betel leaf is one of the most promising commercial botanical. It has shown to possess a lot of therapeutic activities such as anticancer activity, antifungal activity, antinociceptive activity, immunomodulatory activity, anti-halitosis activity, anti-diabetic activity, gastropro- tective activity, anti-allergic activity, antifertility activity, anti-filarial activity, anti-larvicidal activity, wound healing activity and antidermatophytic activity. In consideration of the proven therapeutic values of P. betel proper characterization could be useful for long term research for drug development.
REFERENCES:


16. Sharma R.K, Goyal A.K and Bhat R.A; Antifertility Activity of Plants Extracts On Female Reproduction: A