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Review on Antioxidant Capabilities of Piper Betle Leaf: An Extensive Analysis

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Abstract

Ayurvedic medicine has long used betel leaf, a herb whose strong antioxidant qualities have drawn interest. By examining the phytochemical content, processes, and potential therapeutic uses of betel leaf, this study seeks to compile the body of research on the plant's antioxidant properties. According to the review, betel leaf extracts' strong antioxidant properties can be related to their high flavonoid, phenolic acid, and alkaloids content. The study evaluated the effects of solvent and variety variation on antioxidant activity and total phenol content by extracting six distinct kinds of betel leaf from different parts of India using five different solvents. To assess antioxidant activity, the following assays were used: DPPH, ABTS, FRAP, and PCL (Photochem Luminescence). Nevertheless, for TPC, DPPH, and all other antioxidant assays, the most feasible extraction medium was 80% ethanol, and then 80% methanol. Lipid peroxidation inhibition, antioxidant enzyme activation, and free radical scavenging are examples of antioxidant processes. We talk about the anti-aging, anti-inflammatory, anti-cancer, neuroprotective and cardiovascular health therapeutic potential of betel leaf antioxidants. This review emphasises the betel leaf's promising antioxidant qualities, highlighting its potential as a natural antioxidant agent for controlling and preventing disorders linked to oxidative stress.

Keywords – Betel leaf, antioxidants, phytochemical, Oxidative stress, Piper betel leaf extract

INTRODUCTION

The Piperaceae family comprises the perennial; evergreen Linn Piper betle which is also called paan. Betel leaf is a perennial creeper that produces glossy leaves and an inflorescence of white catkin. The thick, cylindrical spikes of the male betel leaf plant are different from the pendulous spikes of the female. The roots produced by each node serve as the plant's link to the support or host tree. Around the world, horticulture is frequently practised in tropical and subtropical regions. Worldwide, betel leaf variabilities number in the hundreds, with thirty types from Bengal and varieties in India. Although, male and female plants of the plant are different, they are all perennial root climbers that like shade [1]. Globally, the morphology, micrometrical features, cultivation region, size, colour, scent, and taste all influence the formation of different types of betel leaf. Betel leaf is grown in a number of Indian states, such as West Bengal, Tamil Nadu, Maharashtra, Orissa, and Uttar Pradesh [2].

Betel leaves are typically taken as a mouth refresher and digestive stimulant after meals. It possesses anti-inflammatory and antioxidant properties, among other medicinal attributes. Oxidative stress, defined as an unbalanced production of free radicals compared to antioxidant defences, has been connected to a variety of chronic ailments, such as neurological issues, cardiovascular disease, cancer. Using naturally occurring antioxidants as potential medicinal agents to treat oxidative stress has attracted a lot of interest for millennia, Ayurvedic medicine has utilised betel leaf, also known as piper betle, for its therapeutic benefits.

Recent research has shown that betel leaf has strong antioxidant properties, which are linked to the variety of phytochemicals it contains. The Piper betle's antioxidant and anti-inflammatory qualities have been linked to several sections, particularly the leaves. Increased anti- cancer, antioxidant, and radical scavenging activities have been associated with higher quantities of flavonoids and phenols found in leaves. The qualities of betel leaf's aroma are influenced by phenols, terpenes, and essential oil. The inherent antioxidant properties of phytochemicals, specifically the polyphenolic components found in betel leaf, help prevent oxidative damage, control oxidation, and mitigate the risk of stress-related illnesses including diabetes and cardiovascular disease. The bioactive substances found in betel leaves a multitude of advantages, such as an antimicrobial, an antitumor, an antidepressant, an antibacterial, an antifungal, anti-carcinogenic, anti-allergic, anti-larval, anti-filarial, anti-diabetic, and an anti-helminthic quality [3].

The betel leaf has a powerful flavour that is both aromatic and spicy, and it tastes strongly pungent or sweet. For instance, the Mitha variety has a sweet taste, but the Bangla and Sanchi kinds have a mild to intense spicy taste. Chemical and nutritional components, among other things, are responsible for the variation in taste among betel leaves [4]. The remarkable qualities of betel leaves, including their organoleptic, therapeutic, nutritional, functional, antioxidant, and antimicrobial qualities, among other advantageous attributes, propel food scientists, technologists, and manufacturers to employ these leaves and create innovative food products. During preparation, by blending essential oil with Piper betle extract, chemicals found betel leaf are utilised to enhance food safety aspects and prolong their shelf life. Researchers have also recommended utilising an essential oil, betel leaf, and extract as food preservatives that they provide consumers with essential nutrients through the creation of novel food products, pharmaceutical companies' medicine formulations, and cosmetic product development [5].

Natural Substance

The plant contains amino acids, terpenes, chavicol, P-cymene, oxalic acid, malic acid, estragole, and eugenol, among other related substances. The three primary forms of vitamin C that are found in leaves in reasonable amounts are carotin, ascorbic acid, and vitamin C. On top of that, they provide good levels of every important amino acid, except for arginine, histidine, and lysine. Proline and glycine are present in good proportions, whereas asparagine is present in large numbers. This leaf's essential oil gives it a fragrant flavour. β-sitosterol is present in the root [6,7].

Mechanism of action betel leaf

The primary source of betel leaf's antioxidant activity's mechanism of action (MOA) is the leaf's abundance of bioactive substances, including phenols, flavonoids, and alkaloids. These substances aid in the elimination of free radicals, which are erratic substances that may harm cells through oxidative stress. This is a condensed version of the MOA:

Scavenging Free Radicals Reactive oxygen species (ROS)

ROS and free radicals are immediately scavenged by the phenolic compounds in betel leaf, such as hydroxychavicol and eugenol, which reduces oxidative stress in the body.

Inhibition of Lipid Peroxidation

Betel leaf's antioxidant chemicals shield cells from oxidative stress that may result in diseases like cancer and cardiovascular conditions by preventing the oxidation of lipids in cell membranes.

Enhancing Antioxidant Enzymes

According to studies, betel leaf stimulates the body's natural antioxidant enzymes, which aid in the body's further detoxification of harmful oxidative chemicals. These enzymes include peroxidase glutathione, SOD & catalase.

Chelating Metal Ions

Iron and copper ions can be bound to by certain compounds in betel leaf through a process known as chelation. This keeps metal ions from activating the Fenton reaction, which is what forms dangerous free radicals.

Plant Profile:

Figure 1*: *A Piper Betle Leaf [8]

Scientific classification

Family

Piperaceae

Genus

Piper

Species

Betel

Kingdom

Plant

Order

Piperales

Based on its physical traits and essential oil content, betel leaf varieties are divided into five main groups: A Meetha, Kapoori, Bangla, Sanchi & Desawari.

Bangla has large, slender leaves with an elliptical lamina & a base of cordate. They also have nine principal nerves. A leaf's tip is short, sharp, and uncurled. Regarding other kinds, the petiolar sinus is more noticeable.

Figure 2*: *Bangla Paan

Desawari is characterised by its thin, large leaves with a lamina that has 7 to 9 nerves. The tip of the Desawari is short, acuminate, and curled. Its colour is pink.

Figure 3*: *Desawar Paan

The lamina is thin and has an undulating edge, whereas kapoori leaves are more elliptical. Kapoori leaves have acuminate apexes, and the petiolar sinus is barely noticeable.

Figure 4*: *Kapuri Paan

Meetha has big leaves with thick, cordate to broadly oval laminae. Waxy in texture, meetha leaves have three to five major nerves and yellowish spots. The apex of Meetha leaves are pointy and short. Its petiole features a conspicuous joint.mThe cordate leaf base of Sanchi has a long tapering apex and a more elliptical lamina. “Sanchi frequently has seven visible nerves”

Figure 5*: *Sanchi Paan

The approximate region in a major state where betel vines are grown [9]

Sr. No	STATE	COUNTRY
1	West Bengal	India
2	Assam	India
3	Kerala	India
4	Tamil Nadu	India
5	Gujarat	India

Table 1*: *Major state

Betel Leaf Extraction

Six distinct varieties of betel leaves were gathered from various parts of India for this investigation, and the leaves were extracted using five distinct solvents. As selection of extraction solvents was based on the plant phenolics' strong extraction**.**

Techniques

Solvent Extraction

Solvents

Water, Acetone, Methanol, and Ethanol Strategies:
Maceration, Soxhlet, and Perforation
Distillation by Steam
Extraction with Ultrasonic Assistance (UAE)
Extraction with Microwave Assistance (MAE)
SFE, or supercritical fluid Extraction:

Extraction Conditions Optimised

Methanol (50–70%) is the solvent.
30 to 40°C in temperature
Duration: one to two hotas
Ratio of Solvent to Leaf: 10:1–20:1.

The extracted phytochemicals are

Flavonoids: kaempferol and pierce tin
Phenolic Acids
Ferulic and Gallic A
Piperine is an alkaloids
Terpenoids (Caryophyllene, beta)
Flammable Oils: Eugenol and beta spinner

Recovery Ratio

Extract from Methanol: 10–20%
8–15% ethanol Extract
Water-based extract: 5–10%

Techniques for Purification

Chromatography in column
Chromatography with thin players
HPLC, or high-performance liquid chromatography

Supervision of Quality

The fingerprinting of HPLC
GC-MS, or gas chromatography-mass spectrometer
Magnetic Nuclear.

Precautions

Take care when handling betel leaves to prevent contamination;

Employ standardised extraction Techniques

Keep an eye on the extraction conditions to stop phytochemical re gradation

Note

Depending on the particular betel leaf variety, geographic area, experimental design, the extraction conditions and yield may change.

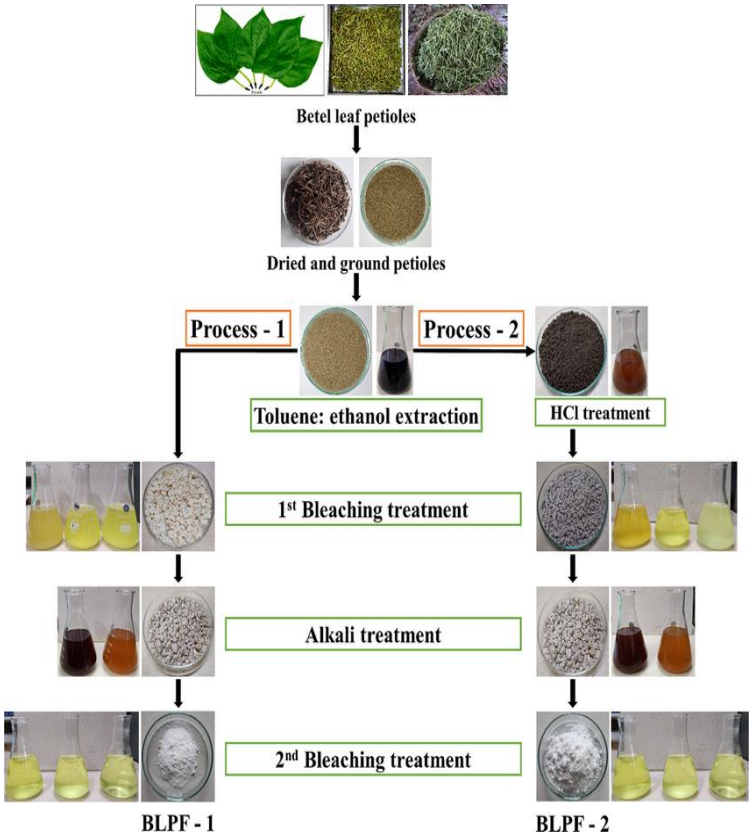

Figure 6*: *Extraction Process of Betel Leaf [10]

Techniques

Formulas

Sigma-Aldrich Fine Chemicals (St. Louis, MO) provided the following reference chemicals: ABTS+ (2, 2-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid), acid Gallic, the catechin, & 2, 2-diphenyl-1-picrylhydrazyl (DPPH). Merck (Darmstadt, Germany) supplied the Folin-Ciocalteu reagent, methanol, ethanol, ethyl acetate, acetone, acetic acid, and hydrochloric acid, while Sisco Research Laboratories Pvt. Ltd. Provided a TPTZ (tripyridyl-s triazine). Analytikjena (Konrad-Zuse-Strasse 1, Germany) is where the antioxidant kit (PHOTOCHEM ACW) that was used was bought. The potassium persulphate, hydrochloric acid, ferric chloride, ferrous sulphate, acetate buffer, and anhydrous sodium acetate were provided by Central Drug House (Pvt.) Ltd. (New Delhi, India).

Plant material and Extraction

India has a wide variety of betel leaf varieties based on form, colour, flavour, and aroma. These six, Banarasi Safeda (PA), Calcutta (PB), Desi Bangla, the Sofia (PF), Mumbai (PE), and Odisha's West Bengal, were gathered from several Indian regions, including West Bengal, Maharashtra, Bihar, & Uttar Pradesh. The leaves were stored at 40 C in the dark for 12 hours after being lyophilized in a Labconco freeze dryer located in Kansas City, USA.

One gram of freeze-dried powder from each species of betel leaf was dissolved in 25 millilitres of liquid (80 percent methanol, around eighty percent ethanol, eighty percent acetone, Eighty percent ethyl acetate, and distilled water) and added to a shaking isolator (Lab Tech, LSI-2005RL, Hyderabad, India) for two hours. After passing through muslin cloth, the extracts were centrifuged for 15 minutes at 4000 rpm. Once via Nylon-66 the membrane filter syringes with a membrane thickness of 0.45µm (mdi The Membrane Sciences LLC, California, Uk), the supernatant was preserved at 4oC for additional examination.

Calculating the Total Phenol Content (TPC)

With a small modification, the amount of total phenol (TPC) of many types of betel leaves was measured using the approach developed by Folin (Singleton and Rossi, 1965). One millilitre of freshly prepared (10-fold) Folin-Ciolateu reagent was added to the test instrument containing a 200 µL sample of leaf extract. Room temperature became maintained for the combination. Eight minutes later, after adding three millilitres of 7.5% (w/v) carbonate of sodium, the combination given the hand shake. After that, the mixture was let to stand at ambient temperature for sixty minutes. The absorbance of the sample at 765 nm was measured using a Shimadzu UV-2600 Kyoto, Japan UV-visible spectrophotometer. As the blank become acidified methanol. The findings were plotted against gallic acid to provide milligrams Georgian equivalents per gm dried weight (mg GAE per gram the dw). TPC's linearity committed between 0.05 and 0.5 mg GA/mL
(R2 = 0.9929 [11].

Calculating Total Flavonoids Content

To 1.0 millilitre of plant extract, added 0.3 millilitres of five percent. NaNO2. This mixture was given a two-minute standing period before 0.3 millilitres of 10 percent aluminium chloride was added. The mixture was given 3.4 ml of NaOH two minutes later, and it was left to stand for thirty minutes [12]. When the pH of aluminium chloride and sodium nitrite is alkaline, the flavonoids turn brick red. The complex's absorbance is measured at 510 nm. Afterwards, the sample's A absorbance against the blank was measured at 510 nm. For this determination, the Catechin is the benchmark.

Activity of the antioxidants

The activity of 1, 1 diphenyl-picryl hydrazyl (DPPH concentrations) the radical scavenging

Through the process of DPPH, which have been described with a major change, the antiradical efficiency was evaluated [13]. This method makes use of the stable, methanol-soluble free radicals as shown DPPH, which is readily accessible for purchase. Plant extracts in different quantities (250, 500, 750, and then 1,000 µg/ml) were collected within separate testing containers for a photometric assay. With the appropriate volumes, the plant extract's volume was changed to 1 ml. After adding 3.5 ml of a 0.1 mM the radical 1-diphenyl-2-picrylhydrazyl (DPPH) in a solution of methanol to these tubes, they are violently shaking. In the testing procedure the tube was left at room temperature for half an hour. As before, a control sample was created without the test extract, and the original baseline correction was performed using the solvent methanol. In the event of reduction by a radical component or a natural antioxidant, as the absorption band at 517 nm that DPPH possesses as in its most extreme configuration. The wavelength of 517 nanometres absorbance measurement was used to track the samples' variations. The results were compared using the activity of vitamin C as a benchmark. The proportion of DPPH discolouration in the samples was calculated using a particular formula:

$$\% \text{ inhibition} = A0 - A1 / A0 \times 100$$

As the IC50 values value, which represents the amount required for salvaging fifty percent of the DPPH, was calculated by graphing the percentage of lowered DPPH versus the concentration present in every sample.

The Potential assay of ferrous reducing inhibitors (FRAP)

The Ferric decreasing an antioxidant Potential technique, which is explained below, requires very little modification in reference 25—was used to determine the total antioxidants. Before usage, fresh preparations of Tripropyridyl triazine (TPTZ), the acetate buffer, and a ferric chloride e in a 10:1:1 ratio were made. The sample's various Solvent extracts (0.2 ml) were transferred into the experimental tube's functional FRP reagent (1.8 ml) was then Applied. Once each tube are at ambient temperature and dark, they are left to incubate for thirty minutes to react. Using a UV spectrophotometer, the generated colour at five hundred three nano meters, was calculated. Solutions containing 1 µg to 10 µg of the antioxidant ascorbic acid were made, and the optical density is calculated at 593 nano meters. A vitamin C derivative is used as a reference, so it's conc.vs optical density standard graph was created. The samples' concentrations were calculated using the conventional curve (µg/g) equivalent to the amount of ascorbic acid.

Acid thiazoline-6-sulphonic (2-2-azino-bis (3-ethyl Benzo) (ABTS) Test

The production of the colourful ABTS radical cation (ABTS•+), which reacts with antioxidants, is a step in the ABTS method used to measure the protective properties of betel leaf extract. First, the radical cation is formed by mixing 2.45 mM the solution of potassium per with 7 mM ABTS in a dark room temperature solution that is left for 12–16 hours. With a UV-Visible spectrophotometer, the solution has been diluted with the ethanol or a buffer containing phosphate to an absorbance of roughly 0.7 at 734 nm once the radical has generated, turning the solution green-blue. The produced ABTS•+ solution is then mixed with the antioxidant-rich betel leaf extract. At seven hundred thirty-four nm, the absorbance decreases as a result of the antioxidants in the extract scavenging the ABTS•+ radical. The sample's antioxidant capacity is directly correlated with the degree of decolorization. Antioxidant activity is measured in Trolox's equivalent antioxidant capacity (TEAC), and results usually correspond to the average anti-oxidant compounds such as Trolox. The Trolox concentration-response curve for five consecutively prepared stock standards that were prepared individually.

Photo Chemiluminescence (PCL) Assay

The mechanism of the photo chemiluminescence test was first reported by Popov and Lewin (1994) in the history of antioxidant analysis techniques. As this technique uses luminol, a chemiluminescent detection reagent, to produce superoxide radical anion photochemically. This luminol functions as a reagent for the detection of oxygen radicals and as a photosensitizer. The following Analytik Jena protocol was followed in order to prepare compound reaction mixes for assessments of soluble in water the antioxidant properties (ACW): To get the antioxidant ascorbic acid at the accepted value of 10 mmol/L, the vial holding reagent 4 was vortexed for 20 to 30 seconds. Using a ten microliter of conc and four hundred ninety µL of reagent 1.H_2SO_4 (95–97%) were added. The reagent 1 was used to dilute the stock solution 1:100.to create the working solution for reagent 4 (0.1 nmol/µL) Vitamin C in concentrations of0.5,1,2, and 3 nmol or 5 to 30 µL of working reagents solutions were used to produce the calibration curve. Reagent 1: 1490 µL, Reagent 2: 1000 µL, and Reagent 3: 25 µL were added to appropriately diluted samples (10µL).

$$L = L0 - L1$$

Analysis of statistics

Every technique activity and assay mentioned the procedure was performed three times, and the average ± standard deviation (SD) among the outcomes is used to represent data.

To determine the importance of any differences found in the samples of betel leaves, the data was subjected to an analysis of variance in one direction (ANOVA).

Analysis & Summary

Total Phenol Content

Plant-derived phenolics, or secondary metabolites, are a symbol of antioxidant qualities that shield human health from a variety of illnesses and are essential in lowering free radicals generated by oxidative processes (Podsedek, 2007). According to reports, the main pungent components of betel leaf that contribute to its antioxidant activity include eugenol, chavicol, allyl pyrocatechol, and chavibetol (The Wealth of India, 1989). A previous study's use of a highly polar solvent resulted in a lower value of total phenol concentration in betel leaf (Maisuthisakul, 2008). Some investigations have clarified the impact of the polarity of the solvent that is used on the total phenolics yield after extraction (Zhao et al., 2006). Using five distinct solvent systems, we attempted to take out as much polyphenol through the leaves of betel as you can in this study. The TPC results that were achieved. There was significant variation seen in each betel leaf variety based on the extraction solvent's polarity. In five different solvents, the TPC for six different varieties of betel leaf extract ranged from PA: 0.29 to 2.62 mg GAE/g dw; PB: 0.08 to 2.59 milligram GAE/g dw; PC: 0.09 to 2.38 mg GAE/g dw; PD: 0.07 to 2.87 mg GAE/g dw; PE: 0.16 to 2.07 mg GAE/g dw; and PF: 0.04-1.16 mg GAE/g dw. The observed ratios are methanol at greater than 80 percent acetone in excess of ethanol 80% greater than eighty percent ethyl acetate more than water, the descending order of contributing extraction solvent for TPC. The water extract had a lower TPC than the 80% methanol extract, which had the highest TPC. The optimal solvent was found to be discovered to be a P. betel water: methanol (1:1) extracts, P. betuloides along with P. wallichii with a considerably greater content of phenol than according to Rathee et al. (2006), the other solvent. However, a decreased TPC yield in an herb extract from Piper betel aqueous was further noted. Conclusion is consistent Using an outcome that were released. Of all the kinds, the PD variety from West Bengal had the highest TPC. Our results concur with earlier research showing that the West Bengal betel variety has a higher phenol content, as per Rathee et al. (2006), the Mysore and Sweet types.

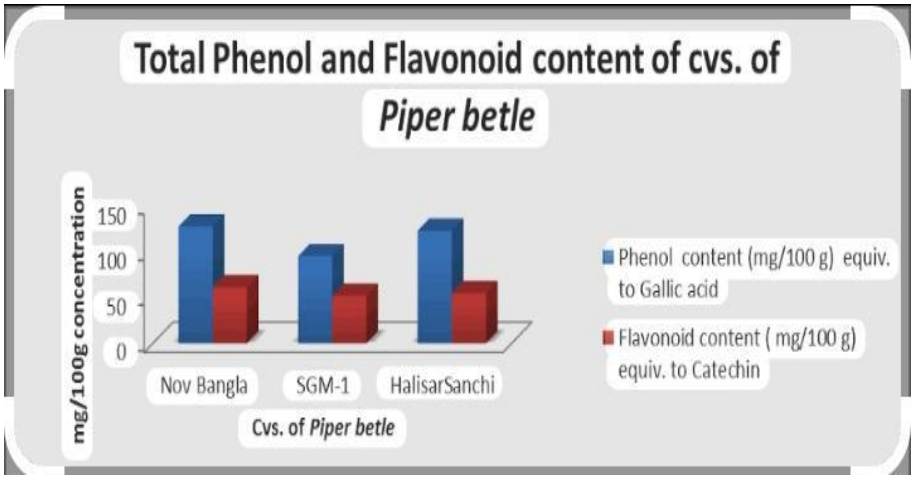

Figure 7*: *Total Phenol & Flavonoid content of CVS of Piper betel

Antioxidant Activity

Fig 8 shows that the PF (133 mg CE/g dw) 80% ethanol extract possessed the maximum degree of DPPH scavenging PE (127.5 mg CE/g dw), respectively, was the next action. As the PA water extract had minimum degree of engagements. The conclusion that, overall, 80% ethanol was a better solvent than 80% methanol. After being extracted with 80% ethanol, the DPPH assay showed a pattern of antioxidant capacity for betel leaf extracts that looked like this: PC>PB>PA>PF>PE>PD>PC.

Nevertheless, findings seemed to against the prior study that found 80% methanol to be a better solvent than 80% ethanol. Retarding PC and PA, in which PC and PA, in which results were never statistically a notable distinction ($P<0.05$) was observed between the activity of DPPH s of separate extracts of solvent for a specific variety when the solvents were eighty percent acetone and eighty per cent ethyl acetate. Three types of betel (Bangla, Sweet, and Mysore) were found to exhibit concentration-dependent DPPH radical scavenging in a different study (Rathee et al., 2006). The Mysore and Sweet varieties were found to have lower DPPH scavenging activity than the Bangla variety (IC50 52.43 µg/mL). Three different betel leaf kinds were studied using DPPH with seven different solvents, and the results indicate the activity of methanol and ethanol does not appear to differ much from one another as solvents. A methanol: water (1:1) extract's lowest IC50 value was Tamuly et al. (2013) reported that the concentrations of P. betle, P. betuloides, and P. wallichii were 36.5, 45.5, and 50.4 µg/mL, respectively. Both hydrophobic and lipophilic antioxidant systems can be tested using the ABTS. + assay; however, lipophilic antioxidant systems require the use of DPPH (Kim et al., 2002). Line graph displays the betel leaf extract values for the ABTS. + Assay. As contrast to the DPPH technique, the majority of the values indicate a marginally higher ABTS. + scavenging capability in both scenarios when catechin was utilised as the standard. Our results are consistent with earlier research (Khanam et al., 2012), which found that, when comparing the DPPH assay to the ABTS assay, most leafy vegetables had decreased antioxidant capabilities comparable to trolox, quercetin, and ascorbic acid.

Due to the close correlation between health and the superoxide radical (O2), one of the dangerous reactive oxygen species problems as well as possessing antioxidant qualities in nanomolar scope of the PCL test was selected for study on betel leaf extract as an antioxidant property. This works what's the first to describe the PCL method's ability to detect antioxidant activity in betel leaf extract. Similar to the ABTS and FRAP studies, the photochemical analysis of the PA, PB, PC, PD, and PF variety revealed that 80% ethyl acetate was the most effective extraction solvent. For the PE (31.98 mmol AA/g dw) type, 80% methanol exerted higher PCL values. It was established through comparison of all the techniques aside from the DPPH assay showed the best solvent for extracting antioxidant compounds was eighty percent ethyl acetate. The optimum solvent property for the betel leaf antioxidant investigation was ethyl acetate, which was corroborated by earlier data (Maisuthisakul, 2008). In the water extract and 80% a solution of ethyl acetate, PA and PF varieties displayed the best and lowest antioxidant activity, respectively.

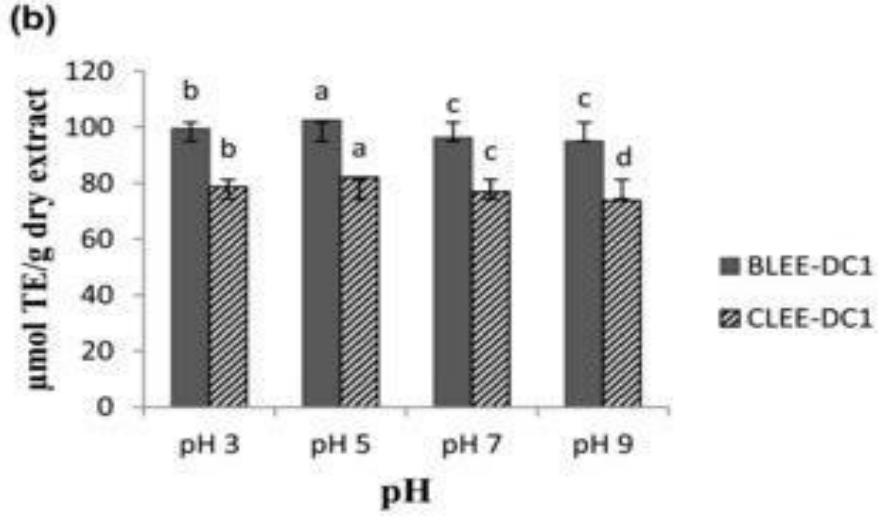

***Figure 8*:** *Graph showing the TPC of six various kinds of piper betle extracted using five distinct solvents*

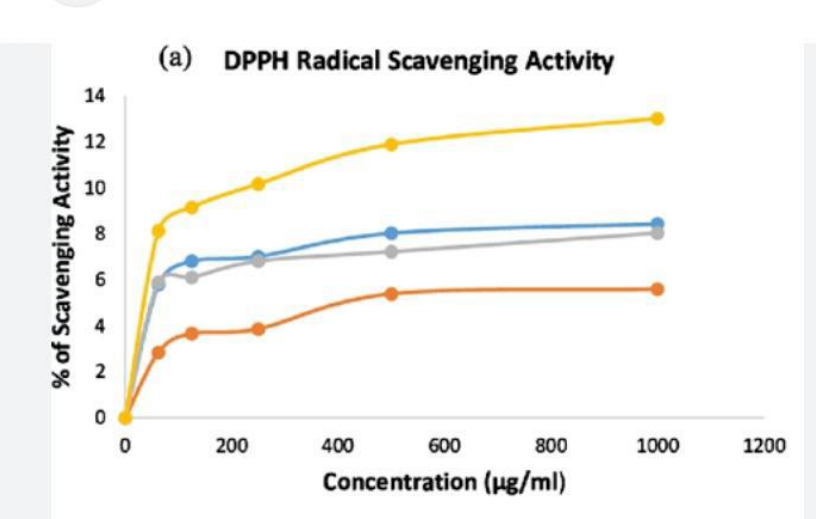

***Figure 9*: *Graphical representation of DPPH radical scavenging activity of betel leaf.* [14]**

Relation between TPC and Antioxidant Activity

Because of its high antioxidant content, betel leaf (Piper betle) is well-known for its therapeutic qualities. Since phenolic chemicals are strong antioxidants, there is a considerable correlation between total phenolic content (TPC) and antioxidant activity. The term "TPC" describes the concentration of phenols, which are organic substances that give off hydrogen atoms to neutralise free radicals and lessen oxidative stress. Research has indicated that betel leaf has a stronger antioxidant capacity in proportion to its TPC. Betel leaf contains phenolic components including flavonoids and tannins that scavenge reactive oxygen species (ROS) to prevent harm to cells. Assays that quantify the capacity to suppress free radicals, including DPPH and ABTS, are used to assess the antioxidant potential

TPC-rich betel leaf extracts have been shown to be successful in lowering oxidative stress indicators, indicating a significant correlation between TPC and general antioxidant efficacy. Furthermore, the anti-inflammatory, anti-cancer, and anti-diabetic qualities of betel leaf are facilitated by its antioxidant action. Because it increases the leaf's antioxidant activity, the total phenolic content of betel leaf is also important in identifying its health benefits. Correlation analyses between the factors under investigation were therefore examined within the extracts pertaining to every variable. Six varieties of betel leaf extracted in five different solvents reveal a high to weak association between the parameters under investigation [16,17,]. when examined in isolation. The correlation range between TPC and PCL was -0.52 to 0.94. Water had a 0.79 correlation and ethyl acetate had a strong positive correlation.

When compared to DPPH and PCL, the FRAP and ABTS assays show the highest correlation values with TPC. On the other hand, the PCL method's PF extract revealed an inverse correlation. Overall consistent correlation performance with TPC is demonstrated by the R-values of the PB variety across all approaches. Every value in the PCL method is less than that of the other ways [18].

Nutritional features of betel leaf

Betel leaf has a vast nutritional value that includes aromatic oils, protein-rich food, nutrients, minerals, digestive enzymes, and biological agents. These nutrients exist particularly

helpful when treating diseases such as liver function, brain, & heart illnesses. As shown in

above table·

Sr. No	Constituents	Approximate
1	Water	85-90%
2	Protein	3-3.5%
3	Fat	0.4-1.0%
4	Minerals	2.3-3.3%
5	Fiber	2.30%
6	Chlorophyll	0.01-0.25%
7	Carbohydrate	0.5-6.10%
8	Energy	44
9	Essential Oil	0.08-0.2%
10	Iodine	3.4
11	Iron	0.005-0.007%
12	Calcium	0.2-0.5%
13	Potassium	1.1-4.6%
14	Nicotinic acid	0.63-0.89
15	Vitamin C	0.005-0.01%

***Table 2*:** *Nutritional Features of Betel Leaf*

Betel leaf's health benefits

Health advantages including leaves of betel including powder, extract, pieces, and essential oil, can be utilised in various industries to create high-quality functional foods, medications, and other products that have limitless health benefits. Because of its analgesic and cooling properties, powdered and chopped leaf of betel can be used for treating a variety of conditions, "including joint discomfort, arthritic conditions, throat irritation, tremors, weakness, and headaches & nervous exhaustion [19]". Additionally, it is utilised to lessen dental-related problems, indigestion, coughing, asthma, bronchitis, and bad breath. Betel leaf juice has several applications such as treating endoparasites, cough, fever, asthma, exhaustion, skin and eye issues, and wound cleaning in children.

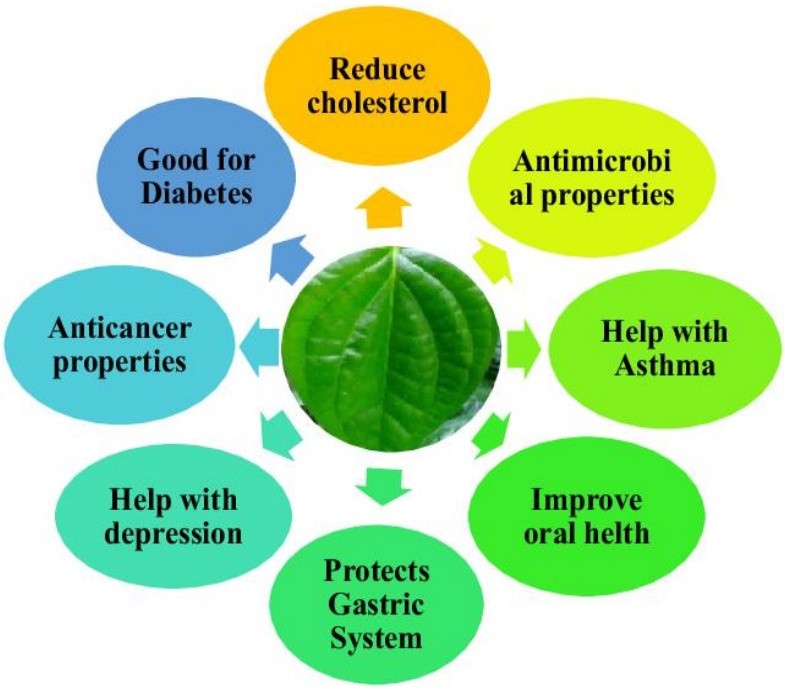

***Figure 10*:** *Health Benefits of Betel Leaf*

Contents of Piper Betle and their oil from a phytochemical perspective

Betel leaf's substance makeup is mostly linked to phenolic chemicals found in the natural world. Betel leaf extract contains many chemical components, including hydroxychavicol, piperol A and B, α-tocopherol, β-carotene, eugenol, and chavibetol and chavibetol acetate. Table 2 contains a list of the significant phytochemicals. Along with its derivatives, betel leaf includes the oxalic acid, the malic acid, the amino acids, chavicol, terpinene, p-cymene, carvacrol, the alley catechol, as well as estragole [20]. The living body receives substantial biological activity from these major and small chemicals found in essential oils [21]. 33 chemical components have been calculated by the essential oil's GC-MS study, primary volatile constituents and their relative percentage value· Numerous aromatic and therapeutic qualities are attributed to these substances. The main volatile substances found in essential oils were amines, and ester, ketone bodies, alkanes, alkenes, and aldehydes. The essential oil of betel leaf, namely the Tamluk Mitha kind, included 46 Chemicals. Similar to vellai kodi type, betel leaf essential oil has 65 chemical components that have distinct biological activities.

The ecological and geographical location, betel vine variety, nation, harvesting season, and meteorological conditions all affect both the qualitative and quantitative composition of extracted essential oil compounds. Each and every phytochemical molecule has a biological action; for example, eugenol has strong antioxidant, antifungal, antibacterial, anthelmintic, and nematicidal properties [22]. Additionally useful as an aromatic and fragrance ingredient, eugenol finds application in the food and cosmetics industries. Additionally, temporary dental fill-ins can be accomplished with a local anaesthetic. Next up is the chemical anethole, which functions as a sweet flavouring agent and has antimicrobial and antifungal properties. Within the food sector, estrazole is utilised for flavouring, food preservatives, and herbal medical items. Betel leaf contains linalool chemicals, which are used to treat skin conditions such as skin irritation and anticancer properties. In addition to having a faint creosote scent, hydroxy chloravicol has biological effects that include anti-inflammatory, anti-mutagenic, anticarcinogenic, antioxidant, and stomach ulcer healing. B-caryophyllene have a spice similar to black pepper and a scent similar to cloves; they are used to prevent diabetes, anxiety, and diseases similar to Alzheimer's. Iso-eugenol gives baked goods, chewing gum, and non-alcoholic drink flavouring agents its lovely aroma [23].

Sr. No	Component	Percentage of Components
1	Chavibetol	53.1
2	Caryophyllene	3.71
3	Chavibetol acetate	15.5
4	Allyl pyrocatechol Diacetate	0.71
5	Chavibetol methyl ether	0.48
6	Campene	0.48
7	f-Pinene	0.21
8	Eugenol	0.32
9	u-Limonene	0.14
10	a-Pinene	0.21
11	1,8-Cineol	0.04
12	Saprobe	0.11
13	Allyl pyrocatechol Monoacetate	0.23

Table 3*: *Major chemical Components of Betel Leaf

Potential of Betel Leaf as an Antioxidant

Antioxidants are substances that may scavenge or degrade the oxidative reactive species, hence inhibiting oxidation. They can be found in both natural and manufactured sources. Reactive oxygen species are made up of unsteady molecules of oxygen that can damage DNA and RNA in cells through reaction, moreover proteins found within living things. Molecules with unpaired electrons in one or more of their outer shells are known as free radicals. The body's mitochondria organelle produces adenosine triphosphate, which causes these free radicals when cells use oxygen to produce energy. The two byproducts generated during evaporation are reactive nitrogen species, or RNS, and oxygen species that are reactive (ROS). Depending on the concentration level, these byproducts have key roles in both positive and harmful consequences. All cell structures are harmed by ROS as well as RNS concentration that a condition called oxidative stress. As the substance that can be utilised to mitigate the effects of oxidative stress antioxidant substances are recognized to have a positive impact on biological system health. This antioxidant helps to avoid disorders caused by oxidative stress and has no adverse effects. Because free radicals are the source of many severe illnesses including diseases like Parkinson's, Alzheimer's, coronary artery, and malignancy, antioxidant activity can help avoid these conditions. Artificial antioxidants found in food and medicine, include butylated hydroxytoluene (BHT) and hydroxyanisole butylated (BHA), can have harmful effects. Efforts attempts has been made to gather organic antioxidants like tannins, saponins, and the polyphenols from plant sources in order to overcome these drawbacks. The maximal inhibitory concentration of 50%, the antioxidant capacity of the compound was evaluated using DPPH radicals for scavenging. Extract with a lower IC50 value has an increased level of antioxidant compounds because antioxidant ingredient in the extract has the ability to quench by giving DPPH radicals that are free electrons or hydrogen atoms. Antioxidant activity is correlated with the amount of the hydroxyl groups within the molecules, or flavonoids content, and the phenolic chemicals present in extracts. Strong contributors to antioxidant activity include hydroxyl chavicol, gallic acid, and eugenol. The yield of antioxidant chemicals extracted from betel leaves is significantly influenced by the different types of extracting Solvent.

Antioxidant compound extraction yield Possibility increased with the aid of a solvent with high polarity. A significant number of protective components were created by methanol extract [24]. The study investigated the effects of different solvents regarding the antioxidant's extraction method, polyphenolic, and bioactive substances included in extracted leaves .As the results showed that the given 80% of the solvent was methanol, the Banarasi Paan variety exhibited the greatest total phenolic compounds, ranging from the Calcutta Paan variety, which used 80% ethanol as the solvent of choice, had the greatest DPPH levels scavenging activity, measuring 133 mg/GAE/gdw .Other varieties ranged from 0.29 to 2.62 mg/GAE/gdw (milligram of gallic acid equivalents / gram in dry weight).This investigation leads us to the conclusion that the extraction bioactive chemicals is significantly influenced by the polarity of the solvent. The highest concentration of polyphenolic components with the greatest capacity of two scavenge DPPH signifies the highest level of antioxidant present in the extract [25]. 89.46% suppression of free radical scavenging activity was observed when betel leaf was extracted using an ethanol solvent. Higher amounts catechol in betel leaf extract contribute to its strong antioxidant qualities [26]. These 1.23% APC compounds are utilised to stop Fe (II)-produced lipid peroxide, homogenates of rat brain's activity, and gamma-ray degradation to the PBR322 DNA plasmid. These data demonstrate that betel leaf extract has a stronger antioxidative impact because of its capacity to scavenge H2O2 and O2 radical species. Nitrous oxide (NO) and hydroxyl radical to compare the activity of antioxidants, tests have been employed. The outcome indicates that nitrous oxide possesses hydroxyl radical scavenging with anbIC50 > 1000 µg/mL, but eugenol has better antioxidant activity (IC50 = 114.34 ± 0.46 µg/mL) [27].

Betel leaf's antioxidant qualities can be increased by using it in a range of herbal remedies. These are a few typical forms:

Infusions

Making tea by boiling betel leaves in water can extract useful components that, when ingested, provide antioxidant effects.

Powdered Form

To make consuming betel leaves easier, add powdered and dried leaves to soups, smoothies, or capsules.

Extracts

Betel leaf extracts made with water or alcohol can concentrate the antioxidant components; these extracts are frequently seen in dietary supplements.

Essential Oils

The antioxidant properties of betel leaf can apply oil as an essential oil topically or utilised as aromatherapy.

Utilising additional herbs

Ginger or turmeric is two more antioxidant-rich herbs that can be combined with betel leaf to increase its general health benefits. These preparations may be able to lessen chronic illness risk and stress related to oxidation by helping to neutralise free radicals, according to research [28].

Some Antioxidant-rich herbal formulations using betel leaf

Organic Betel Leaf Tea

Antioxidants like polyphenols, which are abundant in organic betel leaf tea, help scavenge free radicals, lessen oxidative stress, and boost heart and immune system health. Additionally, these antioxidants shield cells, which may delay ageing and enhance skin health. Boil a few organic betel leaves in water for five to seven minutes to prepare.

Betel Leaf Oil

The robust antioxidant natural betel leaves oil's activity is linked to the existence of several phenolic mixtures including chavicol, and Eugenol which are extracted from Piper betle leaves. By neutralising free radicals, these substances lessen oxidative stress and guard against cellular damage. Because of its antioxidant properties, betel leaf oil may be advantageous for several health uses, such as anti-inflammatory therapies, cosmetics products, and natural food preservatives. The robust antioxidant activity of natural betel leaf oil is attributed to the presence of several phenolic substances are considered to be essential for the t action of natural betel leaf oil including hydroxychavicol, & eugenol, which are extracted from Piper betle leaves. By neutralising free radicals, these substances lessen oxidative stress and guard against cellular damage. Because of its antioxidant properties, betel leaf oil may be advantageous for several health uses, such as anti-inflammatory therapies, cosmetics products, and natural food preservatives [29].

Betel Leaf Powder

Because it contains bioactive substances like tannins, flavonoids, and phenolics, betel leaf (Piper betle) is well-known for its antioxidant qualities. By lowering oxidative stress and averting cellular damage, these substances aid in the body's neutralisation of free radicals. Studies indicate that betel leaf powder may be useful in treating disorders including cancer and heart disease that are linked to oxidative stress. Its high phenolic content is thought to be responsible because it effectively scavenges the reactive oxygen species (ROS), contributing to its antioxidant qualities [30,31].

CONCLUSION

Betel leaf (Piper betle) has shown significant promise as a source of natural antioxidants, as highlighted by its rich phytochemical composition. This review consolidates findings from various studies that

illustrate the powerful antioxidant properties of betel leaf, primarily due to its high flavonoid, phenolic, and alkaloid content. These compounds not only neutralise harmful free radicals but also contribute to the prevention of long-term ailments including cardiovascular illnesses, neurodegenerative disorders, & cancer.

Furthermore, the findings emphasise the versatility of betel leaf extracts in traditional and modern therapeutic applications. The variety of solvents used for extraction has shown varying efficiencies in yielding antioxidant activity, with Methanol and ethanol often performing well.

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