

Use of Piper Betel to combat COVID19

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Chymotrypsin like protease is a ratified target in the design of potential anticoronavirus inhibitor. In a recent research conducted by TCS, India 31 molecules out of 1600000 have been identified as the most effective protease inhibitors against COVID 19. One of those is Aurantiamide, a plant constituent derived from 'Piper aurantiacum', mostly available in India, Nepal, Vietnam, Thailand and other Asian countries. Still the process is under in vitro state. This "Aurantiamide" in the form of Aurantiamide acetate has anti-cancer, anti-inflammatory and antinociceptive activities as yet traced. The combined application of Hydroxychloroquine and Azithromycin is reported as a treatment of COVID 19 till now. This article is on the usage of Piper Betel leaf as a potential herbal medicine to grow human body's self defence mechanism against either the reception of such pathogens or in viral load reduction of affected patients.

Keywords: Betel Piper, COVID19, Herbal Medicine

Introduction

Social distancing is the only solution to combating coronavirus at present all over the world. No vaccine as yet is introduced for novel coronavirus. Before COVID19 no vaccine for SARS or MERS too was invented. So, the only way as per the small sample size survey is to combining Hydroxychloroquine and Azithromycin for viral load reduction and elimination in COVID19 patients.

Chymotrypsin like protease is a ratified target in the design of potential anti-coronavirus inhibitors. In recent research conducted by TCS, India 31 molecules out of 1600000 have been identified as the most effective protease inhibitors against COVID19. One of those is Aurantiamide, a plant constituent derived from 'Piper *aurantiacum*' mostly available in India, Nepal, Vietnam, Thailand and other Asian countries. Still, the process is under in-vitro state. This "Aurantiamide" in the form of

Aurantiamide acetate has anti-cancer, anti-inflammatory, and antinociceptive activities as yet traced. 'Piper Betel', the member of the same 'Piperaceae Family' have all the qualities of 'Piper *aurantiacum*' and different therapeutic activities reported in Piper Betel plant are Anti-microbial, Anti-diabetic, Anti-oxidative & Anti-hemolytic, Anti-dermatophytic, Anti-bacterial, Gastroprotective, Analgesic and Anti-inflammatory, Anti-fertility, Anti-hepatotoxic, Skin Antiseptic, Radioprotective, Immunomodulatory, Antidepressant, Antinociceptive activities. The antioxidant and anti-inflammatory activity of Betel leaf extracts has the capacity to combat influenza-like illness. Further, if commercially available influenza-specific antivirals are tested in combination with Betel leaf ingredients, they may show a synergistic activity and the effective dose of antivirals may be reduced thus minimizing the drug pressure and development of resistant viral strains in treated individuals. Different Betel leaf varieties have shown decreasing influence on pancreatic trypsin and chymotrypsin activities too.

Coronavirus & Chymotrypsin like protease's role in spreading of its pathogens to a human body

Briefly, in the structural analysis of coronavirus four types of proteins have identified as Spike glycoprotein, Envelope protein, Membrane protein and Nucleocapsid protein. Initial attack to human body is done by this Spike glycoprotein. Then with the help of Furin enzyme of the host cell it forms a partnership relation with the cell's surface receptor. After the perfect matching of the pathogen and the receptor through a process of two poly protein synthesis and with the help of Chymotrypsin like protease or enzyme this virus spreads all over the body. So why the coronavirus 3 Chymotrypsin like protease is a validated target in the design of potential anti-coronavirus inhibitors.

Fever, Cough, Shortness of breath - these symptoms may appear 2-14 days after exposure and reported illnesses have ranged from mild symptoms to severe illness and death for confirmed coronavirus disease 2019 (COVID-19) cases.

Why Piper Betel?

- Chemical constituents: The Piper Betel leaf has been described to have Piperol-A, Piperol-B, methyl piper betlol and they also have been isolated. The Betel leaves have starch, sugars, diastases and an essential oil composing of terpinen-4-ol, safrole, allylpyrocatecholmonoacetate, eugenol, eugenyl acetate, hydroxyl chavicol, eugenol, piper betol and the Betel oil contains

cadinenecarvacrol, allyl catechol, chavicol, p-cymene, caryophyllene, chavibetol, cineole, estragol, etc. as the key components. Phytochemical analysis on leaves revealed the presence of Alkaloids, Tannins, Carbohydrate, Amino acids, and Steroidal components. The chief component of the leaves is a volatile oil in the leaves from different countries, called Betel oil and contains 2 phenols, Betel phenol (Chavibetol and Chavicol). Codinene has also been found.

- Description of chemical constituents:

- Chavibetol

Chavibetol is a natural chemical compound of the phenylpropanoid class. It is the most important component of the essential oil from the leaves of the Piper Betel plant. It is an aromatic compound with a spicy odor and is an isomer of eugenol.

- Eugenol

Eugenol, one of the principal constituents of Betel leaf, has also been shown to possess anti-inflammatory property in a variety of animal models of studies with various inflammogens. Antimicrobial, analgesic, anti-oxidant, antiviral and anticancer activity, other identified activities such as its anti-ulcerogenic potential and effect on osteoporosis and especially its effect on the central nervous system (CNS) encompassing seizure control, Parkinson's disease, antidepressant effects etc.

- Hydroxychavicol (HC)

The new, immature leaves contain various beneficial bioactive compounds, among which Hydroxychavicol is the most important phenolic compound which is reported to possess anticarcinogenic, antinitrosation, antimutagenic effects. Beside this, it has a considerable potency to act as an anti-inflammatory, antioxidant, antibacterial, anti-platelet and antithrombotic effects without impairing haemostatic function. In the aqueous extract of Betel leaf it is reported to exhibit useful bioactivities – antimutagenic and anticarcinogenic activities, whereas isolated from the chloroform withdrawal from aqueous extract of Piper Betel leaves show inhibitory action against oral cavity pathogens. 0.5% Hydroxychavicol inhibited the biofilm produced by anaerobes and biofilm produced in pooled saliva. The use of Hydroxychavicol

as an oral care agent. Hydroxychavicol show compelling anti-inflammatory action by considerably inhibits the phrase of the proinflammatory cytokine TNF- α . Methyl chavicol, a biogenic oxygenated aromatic compound, reported to have antioxidant activity.

➤ Allylpyrocatechol

The phenolic constituent allylpyrocatechol obtained from the leaves, show action against obligate oral anaerobes responsible for halitosis. The leaf extract also has a stimulatory outcome on pancreatic lipase and antioxidant activity. Oral administration of APC at different doses accelerates the rate of remedial of gastric lesion induced by indomethacin due to its antioxidative and mucin defensive properties.

➤ Quercetin

Quercetin is one of the most important dietary flavonoids belong to a group of flavonols. It occurs chiefly as glycosides, but other derivatives of quercetin have been recognized as well. Joined substituent's changing the biochemical activity and bioavailability of molecules when compare to the aglycone. Quercetin has also been verified to exhibit the antiviral, antibacterial, anticarcinogenic and antiinflammatory properties. The anticarcinogenic property of quercetin result from its important impact on an increase in the apoptosis of mutated cells, inhibition of DNA synthesis, inhibition of cancerous cell growth, decrease and alteration of cellular signal transduction pathways. Animal evidence suggest Quercetin's antioxidant effects provides protection of the brain, heart, and other tissues adjacent to ischemiareperfusion injury, toxic compounds, and other factors that can persuade oxidative stress.

➤ β -Caryophyllene

$^1\beta$ -Caryophyllene is a chief volatile compound establish in huge amounts in different spice and food plants. β -caryophyllene has shown to posses potent anti-inflammatory properties. β caryophyllene is an FDA-approved food additive and it is apparently a non-toxic compound with no genotoxic or cytotoxic effect in vivo. Clinical studies prove its efficiency in treating

¹ (Review study on potential activity of Piper betle- VandanaDwivedi, ShaliniTripathi Journal of Pharmacognosy and Phytochemistry2014; 3(4): 93-98)

endometriosis. β -caryophyllene exerts anti-inflammatory activity by acting as a potent, selective and nonpsychoactive full agonist for CB2 receptor in vivo. The Piper Betel used as anti-depressant, CNS stimulant, Immunomodulator, antioxidant, antibacterial, antiulcer, cardiovascular, anti-diabetic, anti-infective. Piper Betel, found to be safe in terms of hepatotoxicity, renotoxicity, hematotoxicity.

Conclusion

Piper Betel Leaves are widely used as a mouth freshener after meal. This plant is extensively grown in Bangladesh, India, Sri Lanka, Malaysia, Thailand, Taiwan and other Southeast Asian countries. Its common name is Betel in English, 'Paan' in India and Bangladesh. Indian system of medicine and health has adopted the use of Betel leaves in various ways. Scientific research on the leaf of this plant reveals that it possesses many beneficial bioactivities and its extract from Betel leaves has a great potential to be used in developing commercial products. Due to the numerous benefits, Betel vine is grown for its leaves. The best conditions for commercial Betel vine cultivation are those of tropical rain forests, which provide cool shade, considerable humidity and an adequate supply of soil moisture.

Although the zeal and zest for discovering novel pharmaceutical leads from plant extracts have dwindled in recent years, the dominance of plants as superior sources of new drug discovery is unchallengeable. As mentioned earlier about the application of Hydroxychloroquine and Azithromycin against COVID19 as the one and only solution, a backup plan for using Piper Betel extract in its raw form may be potentially viable logic for growing self-defenced mechanism of a human body against it. As Betel leaf extracts have the capacity to combat influenza like illness and if commercially available influenza specific antivirals are tested in combination with Betel leaf ingredients, they may show a synergistic activity and the effective dose of antivirals may be reduced thus minimizing the drug pressure and development of resistant viral strains in treated individuals.

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