

## PHARMACOLOGICAL EFFECTS OF ARECANUT

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### Introduction

The arecanut (*Areca catechu*) is one of the major plantation crops cultivated in India and South Asian countries. The arecanut endoplasm or seed is surrounded by the pericarp. The endoplasm is used for masticatory purpose. Consumption of arecanut consists of varying different combinations of ingredients such as betel leaf, spices, tobacco and lime. The chewing of arecanut produces stimulant effect due to the presence of the alkaloid arecoline. The betel quid chewing may produce complex reactions and interactions with in the quid ingredients.

Arecanut can be used as an external application to ulcers, skin disorders, diarrhoea and urinary disorders. Arecanut was used as an anthelmintic, and vermifuge in veterinary medicine. Arecanut powder is used as dentifrice. Chewing of dried nuts are said to sweeten the breath, strengthen gums and teeth and also act as a digestive agent. Arecoline hydrobromide, a commercial salt, is a stronger stimulant to the salivary glands. It is used for colic in horses.

Biochemical compounds present in the arecanut are polyphenols (20%), fat (15%), starch (20%) and alkaloids (0.5%). Arecoline (methyl-1, 2,5,6 tetrahydro 1-methyl nicotinate) is the main alkaloid and trace amount of other alkaloids are arecaidine, guvacoline, arecolidine, guvacine. Arecoline content of arecanut could influence the nervous system, psychotic activity for chewers of arecanut.

In this article, the recent research advances on betel quid chewing and its effect on the nervous system and also studies conducted on arecoline as a therapeutic agent in psychiatric and neurological disorders are summarized below.

### Parasympathetic action

Arecoline, which is the key alkaloid content of arecanut seems to have the physiological effect on the central and autonomic nervous system. Arecoline is a natural product parasympathomimetic tertiary amine and acts as both muscarinic and nicotinic receptor agonist activities. The parasympathetic action of arecoline promotes stimulation of central nervous system, vertigo, secretion of saliva, increase in intestinal tone, meiosis, tremor, hypotension, bradycardia.

Recently conducted human studies show that betel quid chewing produces a state of well-being, euphoria, heightened alertness, sweating, salivation, a hot sensation in the body and increased capacity to work. In the presence of lime, arecoline and guvacoline in areca nut are hydrolyzed into arecaidine and guvacine. Although it is chemically unstable due to the ester moiety, it does penetrate into the brain. Action of arecoline is similar to that of muscarine externally and as pilocarpine internally whereas it is used to contract the pupils. It could be used in ocular treatment equivalent to pilocarpine.

The muscarine agonist activity of

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arecoline is due to its similarity to acetylcholine that is formed by protonation of nitrogen atom of arecoline. Arecaidine and guvacine show strong gamma-aminobutyrate (GABA) uptake inhibitory properties. The adrenaline and noradrenaline levels are increased after betel nut ingestion. Piper betel leaves contain phenolics. It has synergic effects with arecoline to stimulate the release of catecholamines. This action seems to suggest that arecanut has sympathetic action.

#### Central and autonomic nervous action

Human studies show that betel quid chewing produces an increase in heart rate, blood pressure, sweating and body temperature. In addition the Electroencephalography (EEG) shows widespread cortical desynchronization indicating a state of arousal. In autonomic function tests, both the sympathetic skin response and RR interval variation in the electrocardiogram (ECG) are affected. These results indicate that betel quid chewing mainly affects the central and autonomic nervous systems.

#### Attention and visuospatial

Alzheimer patients showed improved cognitive performance during continuous intravenous administration of the muscarinic cholinergic agonist arecoline at different doses. This may have therapeutic significance, as verbal ability tended to improve at low doses of arecoline, whereas attention and visuospatial ability tended to improve at higher doses of arecoline.

#### Schizophrenia

Arecoline might exert a crude atypical-like antipsychotic effect. Such an action may explain the favorable effect on negative

symptoms and the generally mild extrapyramidal symptoms and tardive dyskinesia among betel-chewing people with schizophrenia. The compounds that mimic arecoline are under investigation as potential novel drug therapy for schizophrenia.

#### Psychiatric Diseases

Major depressive disorder patients when administered with arecoline by intravenous route showed a significant correlation between the magnitude of heart rate increase and the latency of onset of the second Rapid Eye Movement (REM) sleep period suggesting some central cholinergic sensitivity. Arecoline could be used as a pharmacological tool for studying central nervous system.

#### Serial learning

Subcutaneous administration of arecoline significantly enhanced serial learning in normal human subjects and the degree of enhancement was inversely proportional to the subject's performance. Thus arecoline seems to have enhanced learning performance.

#### Conclusion

Recent human studies on betel quid chewing seem to have effects on the central and autonomic nervous systems and it has also been observed that arecoline, arecaidine and several phenolic compounds may have a stimulating effect on the sympathetic system. Arecoline is a natural product parasympathomimetic tertiary amine and acts as both muscarinic and nicotinic receptor agonist activities, which are mediated by central cholinergic mechanisms. Therapeutic trials have been conducted on arecoline to use for some psychiatric

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