General Summary
Betel nut chewing is a common practice of millions of people for increased capacity of work, euphoria and heightened alertness. It contains arecoline which has multiple adverse effects on general physiology (hepatotoxicity, immunosuppression, antioxidant suppression, induction of oral cancer), as well as, endocrine functions. The current objective is to investigate the role of arecoline on pineal-testicular axis at ultrastructural and hormonal levels under normal and conditions of diabetes, hypothyroid and stress in rats. Our findings are summarized as follows:-

(1) intraperitoneal injection of arecoline (10 mg/kg body wt daily for 10 days) inhibits pineal activity evidenced by ultrastructural degeneration of pinealocytes with depletions of pineal and serum melatonin and N-acetyl serotonin (NAS) levels and elevation of serotonin levels in rats. However, testes (Leydig cells) and male sex accessories functions are stimulated by arecoline, because Leydig cells showed ultrastructural stimulation with elevation of serum testosterone titre. Testosterone-dependent male sex accessories functions are also stimulated at prostatic ultrastructural level, with increased levels of fructose and sialic acid of the coagulating gland and seminal vesicle, respectively. It may be concluded that arecoline may be useful in treatment of infertility, but prolonged use of arecoline (by betel nut chewing) may increase the risk of developing prostate cancer due to over expression of the androgen receptor and G1 cell cycle regulatory proteins in the prostate;

(2) pineal-testicular axis is suppressed in alloxan-induced diabetic rats. Arecoline that inhibits pineal activity does not aggravate pineal dysfunction in diabetes. Arecoline can prevent testis and its accessories dysfunctions in diabetic rats. The
findings suggest that insulin deficiency may be responsible for pineal suppression, whereas both hypersecretion of corticosterone and insulin deficiency are involved in testicular dysfunction followed by regression of sex accessories. Arecoline may have biomedical importance to treat infertility under diabetic conditions;

(3) hypothyroidism induced by propylthiouracil causes pineal and testicular (including sex accessories) dysfunctions in rats. Though arecoline inhibits pineal activity, it cannot aggravate pineal dysfunction in hypothyroid rats. Arecoline cannot prevent testicular dysfunction in hypothyroidism. The findings suggest that thyroid hormone (T₃) deficiency may be responsible for pineal-testicular dysfunction in experimentally-induced hypothyroid rats. Antagonadal relationship of the pineal gland is perhaps abolished in hypothyroid rats;

(4) auditory stress by noise and metabolic stress by inanition (food deprivation) and water deprivation cause stimulation of pineal activity, which arecoline cannot further aggravate in rats. The findings suggest that pineal hormones may be considered as stress hormones that are involved to counteract stress in rats. Hypersecretion of corticosterone and/or adrenomedullary hormones (epinephrine and norepinephrine) may be responsible for pineal stimulation in stress. Both auditory and metabolic stresses cause dysfunctions of the testis and its accessories, which arecoline does not alter during stress in rats. Corticosterone and/or medullary hormones, and melatonin are perhaps involved in inducing testicular dysfunction in stress. Arecoline cannot prevent testis and its accessories dysfunctions induced by stress.