Preface
Areca nut (the endosperm of *Areca catechu*), the fourth most commonly used psychoactive substance in the world used by approximately 600 million people, has long been a public health problem. Although its popularity has declined in the recent years, it is still widespread in Asia, particularly the South Pacific islands, Southeast Asia, Papua New Guinea, Indonesia, Bangladesh, Pakistan and India. Various physiological and pathological effects of habitual areca nut use are listed. Areca nut quid chewing has claimed to produce a sense of well being, euphoria, warm sensations of the body, sweating, salivation, palpitation, heightened alertness, tolerance to hunger, diminished thirst, combat of cold and increased capacity and stamina to do work.

Arecoline has been found to be the most abundant and potent muscarinic agonist present in areca nut which can cross blood brain barrier and induce a range of parasympathetic effects (Asthana *et al*., 1996). 7.5 mg/gm weight of arecoline has been found to be present in areca nut (Rooban *et al*., 2005). Arecoline caused bronchospasm (Walland *et al*., 1997), an increase in total mood disturbance, and also increase in heart rate (Asthana *et al*., 1995) mean systolic blood pressure and pulse (Nurnberger *et al*., 1983). Areca nut components and arecoline, have long been considered to be the major etiologic factors in the pathogenesis of oral and oropharyngeal cancers (Stich *et al*., 1981).

Arecoline is reported to have hepatotoxic, cytotoxic, genotoxic and mutagenic effects in various cells (Chou *et al*., 2009). It shows strong correlation to the incidence of oral submucosal fibrosis, leukoplakia and oral cancer, and has also been found to impose toxic manifestations in immune, hepatic and other defense systems of the recipient (Das
Gupta et al., 2006). Arecoline has been found to increase testosterone release in vitro (Wang et al., 2008). It has also been found that arecoline inhibits pineal activity but stimulates testicular function (testosterone level) and its target organ, presumably via muscarinic cholinergic receptors in rats (Saha et al., 2007).

All these neurological effects suggest that chewing areca nut quid influences the central and autonomic nervous system at various levels. The detrimental effects of chewing areca nut and associated morbidities are no less. Besides causing diarrhoea, dizziness, constipation, epigastric discomfort, increase in blood pressure increased risk of peptic ulceration, chewing areca nut is associated with various oral conditions including areca nut chewer’s mucosa, chewer’s lichenoid mucositis, oral submucous fibrosis and oral squamous cell carcinoma (Boucher and Mannan, 2002). Hence, it is important to concentrate on the ill-effects of this ethnic, socio-culturally accepted habit and help in the prevention and treatment of all associated morbidities.

For understanding the detrimental effects of chewing areca nut, the physiological effects of its individual components have to be understood. Betel nut contains different types of chemicals like tannins, polysaccharides, fats and alkaloids. The four major alkaloids isolated in areca nut are arecoline (7.5 mg/g weight), arecaidine (1.5 mg/g weight), guvacoline (2.0 mg/g weight) and guvacine (2.9 mg/g weight) (Rooban et al., 2005). Most of the effects of betel chewing are thought to be related to arecoline, the major alkaloid of areca nut.
Arecoline displays cell-transformation ability, genotoxic (Jeng et al., 2001) and clastogenic effects (Stich et al., 1981), and also chromosome and DNA damaging capacity (Sinha and Rao, 1985a). It also induces hepatotoxicity, depletes intracellular thiols (Chang et al., 2001a), jeopardizes the antioxidant environment of the recipient and disturbs reactive oxygen species (ROS) production (DasGupta et al., 2006). Arecoline suppresses cell immunity, affects lymphoid organs, depletes lymphocytes, and suppresses primary antibody response (Selvan et al., 1993).

Arecoline is known to induce hormonal changes including an increase in plasma corticosterone, prolactin and growth hormone levels (Nurnberger et al., 1983). Arecoline stimulates the HPA axis (Calogero et al., 1989) leading to elevation of mean ACTH, cortisol and β-endorphin levels.

Thus, betel nut, chewing is likely to cause health hazards and diseases owing to the presence of arecoline in the betel nut. Though considerable attention has been directed towards the ill-effects of arecoline, several arenas in this regard, especially the influence of pineal on testis, has remained unexplored. In the current thesis, an attempt is made to investigate the hormonal responsiveness of the pineal-testicular axis to arecoline in normal as well as in experimentally stress-induced rats. Since the overall study of this vast area is beyond the scope of our research work, we have concentrated on exploring certain aspects in this area of research.