Every nation, - every culture has its special habit(s) which may be considered as national habit(s). They are socially permitted and intricately associated with the life - style. They cause addiction. In western countries there are three national habits : drinking, smoking and taking tea/coffee. Similarly in India taking tea/coffee and chewing tobacco are the two socially accepted habits. Chewing of betel - quid with or without tobacco is an age old practice in India. From raw tobacco to very complex preparations (prepared by mixing tobacco with various other ingredients) are in use. Use of smokeless tobacco is now very popular all over the world including India. Public awareness regarding harmful effect of smoking, as well as propaganda from several tobacco companies that smokeless tobacco is less harmful are probably at the root for increase in consumption of smokeless tobacco.

It is now well established that smokeless tobacco, like smoking of tobacco is highly carcinogenic. It causes cancer mainly in the oropharyngeal regions, and increases the risk of cancer of several other body parts. India has the highest incidence of oral cancer in the world and as evidenced from epidemiological studies, practice of taking smokeless tobacco is considered as the causal factor for it.

The relationship between mutation and cancer is now almost beyond dispute. It is generally assumed that health hazards from mutational events can lead to cancer. With the development of modern toxicology attention has been focussed on genetic risk assessment.

Keeping all these in view in the present investigation an attempt has been made to evaluate potential genotoxic and cytotoxic effects of a widely used smokeless tobacco preparation, - 'gudakhu'. The use of gudakhu is
highly prevalent in the state of Orissa, and is spreading fast in the neighbouring states. It is a paste like preparation and rubbed over teeth and gums with a finger tip. Highly addicted persons practise it about 20 times a day. It is practised by individuals of all categories: men and women, aged and children, rich and poor. The ingredients of gudakhu are tobacco, lime, molasses, 'red-soil' and water.

The evaluation was based on experiments on laboratory mice, as well as examinations on habitual users. Both organic solvent (acetone) and water extracts of gudakhu were tested in animal system. Water extracts of different ingredients were also tested in mice. A battery of assay systems such as (i) chromosome aberration assay in bone marrow cells, (ii) micronucleus test (MNT) in bone marrow cells, (iii) MNT in regenerated hepatocytes, (iv) MNT in peripheral blood erythrocytes, (v) sister chromatid exchange analysis, (vi) spermatocyte chromosome analysis, (vii) sperm morphology assay and (viii) sperm count assay have been conducted to have a reasonably comprehensive idea on their effects on mitotic, meiotic and post-meiotic cells. All the assays were conducted for acetone extract of gudakhu, but for want of time, for others only 4 assays (i', vi, vii, and viii) were taken up. Further, experiments were conducted following single as well as chronic treatment. The latter was done particularly to simulate human exposure.

Study in habitual users comprises examination of buccal mucosa cells which are directly exposed to gudakhu, and of peripheral blood erythrocytes for presence of micronuclei.

The work has been presented in five chapters. The "Introduction" chapter includes in addition to introduction of the subjects, a review on the literature. Chapter-2 deals with the effect of gudakhu and its ingredients in mouse in vivo system. Besides, this chapter includes an introduction to various protocols adopted here, materials and methods in general for all the protocols, and positive
control experiments with cyclophosphamide and mitomycin C to standardize some protocols and to fix up some criteria for scoring different aberration types. An ancillary experiment was conducted in mice to find out if human saliva can modulate the genotoxic effect induced by gudakhu. The results of this experiment were presented in Chapter-3. Chapter-4 deals with the study of effect of gudakhu-use in habitual users. The work is summarized in Chapter-5.