CHAPTER 1
INTRODUCTION
Every year 400,000 new cases of oral cavity and pharynx cancer occur worldwide and more than 50% of which occur in India. Each year over 200,000 people die of the disease, and over a third of these deaths occur in India[1]. The most commonly involved sites of tumor development in the Indian population are buccal mucosa and tongue[2]. The major risk factors for oral cancer are chewing tobacco either alone or with allied products and alcohol consumption. Precancerous lesions of leukoplakia and sub mucous fibrosis are also prevalent in India due to these habits[3].

Advances in surgery, radiation and chemotherapy have not changed the survival rates[4]. The clinical staging of oral cancer has limited prognostic importance as the patients with comparable stages respond differently to the same therapy. Several studies have focused on defining tumor-specific molecular markers that can either detect cancer at an early stage or can predict patient’s outcome [4, 5]. However, clinicopathological factors and molecular biomarkers that could identify patients at early stage or patients at highest risk of recurrence/lymph node metastasis are still undefined [6].

At present there is paucity of sensitive and specific early diagnostic and prognostic markers of OSCC. In human system it is not possible to get all the stages of oral carcinogenesis and tissue size is also a major limitation. Cancer progression is multistage development process and involves accumulation of genetic lesions resulting into alterations in cell proliferation and differentiation pathways[7]. During carcinogenesis many biochemical pathways involved in development, differentiation, proliferation, apoptosis, cell signaling, cell cycle, angiogenesis etc. get altered [8]. Experimental chemical carcinogenesis is being widely used to investigate the process of carcinogenesis. Rodent models like mouse, rats and Hamsters using chemical carcinogens such as 4NQO, DMBA etc. are being routinely used to study oral carcinogenesis process [9].
There is a need to devise critical tools for the early detection of OSCC and the monitoring of disease progression. In addition, the identification of therapeutic targets is an attractive strategy to further relieve the burden of OSCC. Among these tools, validated biomarkers are viewed as the most important tool[10]. Therefore there is a critical need to discover new specific and sensitive biomarkers in OSCC.

Proteomics is a promising approach in the identification of proteins which may be used as markers for early detection of cancers and prediction of regional lymph nodal metastasis [11]. It has been successfully employed in studies of various tumors, tissues and body fluids. Many studies on oral cancer patients led to identification of possible biomarkers for early diagnosis/ prognosis. Development of oral biomarkers by using genomics and proteomics approaches have been reviewed earlier by R. Ralhan [10]. Various proteomics platforms have been used to identify the biomarkers for early diagnosis and prognosis of Oral cancer[5, 12-15].

In spite of the fact that a large number of molecules have been identified as potential early diagnostic and prognostic markers for oral cancer, none of them has reached the clinics. In order to sequentially dissect the molecular events during different stages of oral carcinogenesis, proteomic analysis on samples obtained at sequential stages of rat lingual carcinogenesis was carried out. We used iTRAQ-LC-MS system for precise detection of differences in protein profile at various stages of lingual carcinogenesis.