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## INTRODUCTION

Cancer, an age-old disease described by Charaka and Susruta, as “Ghatak” is a public health challenge in our country as it is the major cause of morbidity and mortality. Oral squamous cell carcinoma is defined by WHO “ as an invasive epithelial neoplasm with varying degrees of squamous differentiation and a propensity to early and extensive metastasis, occurring predominantly in alcohol and tobacco users in the 5<sup>th</sup> and 6<sup>th</sup> decades of life. ” It is the sixth most common neoplasm in the oropharyngeal region worldwide with a high incidence rate in developing countries. In India it accounts for 30% of all malignancies with a mean age distribution of 55 years in the adult population (**Prasad, 2014**). The disease has a male predilection.

The various predisposing factors of oral squamous cell carcinoma include tobacco related habits, alcohol consumption, chronic inflammation, viral infection and genetic predisposition (**Markopoulos, 2012**). Tobacco along with alcohol accounts for 40% of carcinomas and 60% of death due to cancer worldwide. In our country 30-40% of individuals in 15 -30 years age group use tobacco out of which 40-50% develop oral cancer and 42% of all deaths are tobacco related (**Shukla and Shukla, 2012**). In addition to these factors there is substantial evidence to suggest the role of free radicals, oxidative stress, microorganisms like *Streptococcus mutans*, and fungi like *Candida albicans* in carcinogenesis (**Mohd Bakri et al., 2010; Valko et al., 2006 and Schwartz et al., 2012**).

Cancer is characterized by various hallmarks such as sustaining proliferative signaling, avoiding immune destruction, evading growth suppressors,

tumor promoting inflammation, enabling replicative immortality, inducing angiogenesis, activating invasion and metastasis, dysregulating cellular energetics, genome instability and mutation, resisting cell death, **(Hanahan and Weinberg, 2011)**. Among the various hallmarks of cancer, evasion of apoptosis or resisting cell death is one of the most important factor. Mutations of the genes regulating apoptosis or the tumor suppressor genes like p53 leads to evasion of apoptosis that ultimately leads to cancer.

Carcinogenesis is a multistep process characterized by genetic and epigenetic alterations of DNA that underlie all three phases namely (i) initiation (ii) promotion (iii) progression. This process is characterized by transformation of normal cells into neoplastic cells with uncontrolled proliferative potential. It is noteworthy that free radicals and oxidative stress play a key role in carcinogenesis by causing DNA damage and dysregulating intracellular signaling pathways, thereby leading to the conversion of normal cells into malignant cells with an oncogenic phenotype **(Valko *et al.*, 2006)**.

Chemotherapy, surgery, and radiotherapy are the current treatment measures for oral cancer, yet the five-year survival rate is 62% worldwide and 35% in Indian and South East Asian countries **(Shukla and Shukla, 2012)**. The age standardized five-year survival rate in Chennai is about 35 to 36% **(Mallath *et al.*, 2014)**. Moreover the above mentioned treatment measures are often mutilating as they cause functional impairment, esthetic impairment and adverse effects such as nausea, vomiting and immunocompromised state. Therapy to benefit oral cancer patients is still lacking. With regard to the socioeconomic status in the Indian

scenario, to deliver an affordable and equitable cure for cancer is yet another challenge. A therapeutic approach that would be cost effective and would possess antioxidant, antimicrobial antimycotic and anticancer properties would not only aid in management of the disease but also aid in biochemoprevention thereby reducing cancer burden in our nation.

In this context, herbs are regarded rich in phytochemicals such as polyphenols, flavonoids, alkaloids, terpenoids, tannins, and glucosinolates. These constituents possess antioxidant, antimicrobial, antimycotic and anticancer properties. The use of herbs for the management of various diseases has been practiced since several hundred years ago by Charaka and Susruta, but with the advent of modern medicine, traditional medicine has lost its importance. An attempt to re-explore the medicinal properties of herbs would aid in management of diseases like cancer.

*Trigonella foenum-graecum* L. commonly termed as fenugreek belongs to the family Fabaceae. It is an annual semi arid crop that originated from the Mediterranean region and Asia. It was part of Indian diet for more than 3000 years and one of the oldest medicinal herbs. **(Parthasarathy *et al.*, 2008)**. The polyphenols of *Trigonella foenum-graecum* L. exert antioxidant activity **(Kaviarasan *et al.*, 2007)**. The bioactive oils, volatile oils and alkaloids of *Trigonella foenum-graecum* L. (seeds) possess antimicrobial and antimycotic properties **(Omezzine *et al.*, 2014)**. **Shaban *et al.*, (2009)** and **Balsevich *et al.*, (2009)** have reported the anticancer effects of the herb against leukemia and breast cancer respectively.

*Cinnamomum verum* J. Presl is commonly termed as true cinnamon or Ceylon cinnamon is indigenous to Sri Lanka. It has been cultivated in other countries like India, Madagascar, Seychelles, South East Asia and Brazil since early times. It is an evergreen tree with strongly aromatic barks and leaves. It exerts antioxidant activity (**Mathew and Abraham, 2006**). Cinnamaldehyde of *Cinnamomum verum* J. Presl (bark) possess antimicrobial and antimycotic properties (**Ferhout et al., 1999; Shreaz et al., 2011**). **Chulasiri et al., (1984); Varalakshmi et al., (2014) and Manal et al., (2012)** have reported the anticancer effects of *Cinnamomum verum* J. Presl in human cancer (KB) cells, mouse leukemia L1210 cells, Hep2G2 cell lines respectively.

*Carica papaya* L. commonly known, as papaya is a tree cultivated in many parts of India for its fleshy fruits. It finds its origin in Southern Mexico and Costa Rica. Later the plant was cultivated as a plantation crop in other places like India, Hawaii, Australia, Sri Lanka and South Africa. **Iyawe, (2011) and Norshazila et al., (2010)** have reported the antioxidant activity, **Nwachukwu and Umechuruba, (2001) and Onkar and Ali, (2011)** have reported the antimicrobial activity of the leaves and seed extracts of *Carica papaya* L. **Morimoto et al., (2008)** have reported the anticancer effects of papaya leaves against various cell lines other than oral squamous cell carcinoma. **Nakamura et al., (2007)** have reported the anticancer effects of papaya seeds and its active compound benzyl isothiocyanate against promyelotic leukemia HL-60 cells.

With the available information the present study was conducted to assess *in-vitro* anticancer and antimicrobial effects of fenugreek seed (*Trigonella foenum-graecum* L.), cinnamon bark (*Cinnamomum verum* J. Presl) and papaya leaf and seed (*Carica papaya* L.) extracts in oral squamous cell carcinoma cell line and selected microbial strains along with their antioxidant potential.