

Chapter 20

Chemopreventive and Therapeutic Potential of Phytopharmaceuticals Against Oral Cancer: Evidence-Based Reports From Preclinical Studies in Animal Models

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ABSTRACT

Oral cancer is a major public health problem in both developing and developed countries. It is believed to be the eighth most common cancer considering a major risk factor of worldwide morbidity and mortality. Major risk factors of this deadly disease are lifestyle (consumption of smoking and smokeless tobacco, alcohol, betel quid, etc.), unhealthy food, and poor dental care and viral infections. These factors are responsible for mutations in the DNA leading to the initiation of carcinogenesis. Oral carcinogenesis is a multistep process having three distinct phases: initiation, promotion, and progression. Modern cancer treatments (chemotherapy, surgery, radiation therapy, and immunotherapy) are associated with lots of side effects. Thus, phytopharmaceuticals are being used as alternative medicines in the prevention of oral carcinogenesis. Phytopharmaceuticals (such as resveratrol, sulforaphane, quercetin, etc.) have immense potential to prevent cancer development in every phase of carcinogenesis and more importantly, these compounds have fewer side effects.

DOI: 10.4018/978-1-7998-6530-8.ch020

INTRODUCTION

Induction of oral carcinogenesis is a complex process that takes place when epithelial cells are subjected to genetic changes. It is a serious public health issue and an important cause of morbidity and mortality in South Asian countries especially in India and Bangladesh (Sharma et al., 2018; Kumar et al., 2019). Oral cancer is considered as the eighth most common cancers in the world and may occur in the lips, mouth, cheeks, and tongue. According to the most recent report of GLOBOCAN 2018 estimate, there are 3,54,864 new cases of oral cancer (lip and oral cavity) and out of which 1,17,384 death cases were reported worldwide (Bray et al., 2018). In India, it is the third most common type of cancer and 20 cases per 1,00,000 individuals have been recorded (Tanaka and Ishigamori, 2011; Danaraddi et al., 2014; Scrobota et al., 2016). Despite the development in this area in the last 20-30 years, the 5-year survival of the disease is ~50% (Bodhade and Dive, 2013; Bhavana and Lakshmi, 2014). International agency for research on cancer (IARC) predicted that worldwide new cases of oral cancer will increase up to 1.7 million by 2035 (Coelho, 2012).

Oral carcinogenesis, like other cancers, is a sequential multistep process involving three common stages- initiation, promotion, and progression. Initiation involves genetic mutations that cause irreversible alteration of a normal cell. Promotion is generally involved in increased proliferation of initiated cells that lead to progressive dysplasia. Progression is associated with the accumulation of mutated cells that help in the transformation of progressive dysplasia into malignant or invasive phenotype. These genetically mutated cells evade the cell cycle checkpoints that regulate cellular proliferation.

Oral cancers are of three types based on the clinic-pathological perspective- carcinomas of the lip vermilion, carcinomas of the oral cavity proper, and carcinomas in the oropharynx. Cancers of the oral cavity may be premalignant or malignant. The most common premalignant lesions are Leukoplakia, Erythroplakia, and Lichen planus. These premalignant (precancerous) lesions have a higher risk of malignant transformations. The malignant lesions of the oral cavity include squamous cell carcinoma (SCC), Lymphomas, Salivary gland adenocarcinomas, Sarcomas, and Melanomas. Approximately 90% of the oral cancer is SCC.

The modern cancer treatment includes chemotherapy, surgery, radiotherapy, targeted therapy, and immunotherapy (Barhoi et al., 2020). However, the results of these cancer interventions are not promising and are associated with side effects and normal cells also get affected. Therefore, development of alternative medicines with fewer side effects is in constant demand in the field of cancer biology for their therapeutic potential.

Herbal medicines or phytotherapy is gaining importance due to its diversified chemical constituent having medicinal property and more importantly, herbal medicines have very fewer side effects. More than 80% of the world's population primarily depends on herbal medicines for curing various diseases including cancer (Ekor, 2013; Carmona and Pereica, 2013). Scientific evidence supports that vitamins and herbal medicines play a significant role in cancer prevention and increases the quality of life of cancer patients (Albabbain et al., 2018).

Chemoprevention by using phytopharmaceuticals is a promising strategy to control the progression of the carcinogenesis process. Chemoprevention can be defined as the use of natural or chemically synthesized drugs or biological agents to prevent suppress or reverse carcinogenesis at its initial phases (initiation and promotion) or prevent the invasive potential of malignant cells (Ranjan et al., 2019). In the progression phase, chemoprevention ends and chemotherapy starts on. Clinical and epidemiological studies suggest that several phytopharmaceuticals like resveratrol, curcumin, garlic, etc. have chemopreventive

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