

**Chemoprevention in oral cancer – A double edged sword**

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**Abstract**

‘Prevention is better than cure’. This holds good for the current scenario in the management of oral cancer and potentially malignant disorders. Oral cancer is the most common and deadliest of all oral lesions. Cancer chemoprevention is one of the method to reverse, suppress, or prevent carcinogenic progression to invasive cancer by using either natural or chemical components. The recent clinical trails shows very promising and successful results. But at the mean time, it has not become the main stream line treatment in managing the potentially malignant disorders or either cancer. The reason for this is because of the low effectiveness, high toxicity and lack of long term clinical trial results. This article highlights the

both face of the single coin which means the merits as well as demerits of the chemopreventive agents.

**Keywords :** Chemoprevention, Oral cancer.

**Introduction**

According to Robbins Cancer has been defined as an autonomous new growth of tissue or an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of normal tissue and persists in the same excessive manner even after cessation of stimuli which evoked the change. The term oral cancer is used to describe any malignancy that arises from oral tissues. Ninety to ninety five percent of all oral malignancies are squamous cell carcinoma.<sup>2</sup>

The most prevelant and the one of the sixth major causes of death is Oral cancer.<sup>1</sup> In India, the age-standardized

incidence rate of oral cancer is 12.6 per 1,00,000 population.<sup>3</sup> Oral carcinogenesis is a complex multistep process controlled by various endogenous as well as environmental factors. Most important risk factor for oral cancer are tobacco use, either smoking form or smokless. Alcohol has synergistic effect along with this smoking habit.<sup>4</sup> The other risk factors includes viruses, genetics and positive family history.<sup>4,5</sup>

Prevention of oral cancer can be divided into three stages: primary, secondary, and tertiary prevention.<sup>6</sup> Quitting or discontinuing of smoking and alcohol forms the primary<sup>7</sup>, early diagnosis and management of patients with potentially malignant disorders; mass screening of population at risk forms secondary<sup>8</sup> and prevention and early detection of recurrent lesions or second primary tumors in already treated cases or its precursors detection and reduction of complications forms the tertiary<sup>9,10</sup>.

The use of specific natural and synthetic agents is directed toward secondary chemoprevention that has evolved as a promising strategy to inhibit, suppress or control the incidence of carcinogenesis<sup>11</sup>.

### Definition

**Chemoprevention** of cancer is a means of cancer control in which the occurrence of this disease is prevented by administration of one or several compounds either naturally occurring fruits and vegetables or chemical compounds.<sup>12</sup>

**Biochemoprevention** is also one of the most commonly used term in cancer chemoprevention which uses the combination of a chemical substance with a biological factor like interferon- $\alpha$  in prevention [20].(Biomed research international)

**History<sup>12</sup>**: Chemoprevention of cancer was first defined by Sporn in 1976. The authors of the concept of neoplasm chemoprevention are L.W. Wattenberg and M.B. Sporn. Their studies made in the 1960s and 1970s

provided the basis for further research in that respect [17, 18].

### Classification<sup>13</sup>

The chemopreventive agents can be divided into two general classes based upon their mechanism of action upon the carcinogenic agents:

- Blocking Agents
- Suppressing Agents

The blocking agents act either by inhibiting the metabolic activation of carcinogens thereby, it stops these agents from reaching or reacting with critical target sites or by enhancing detoxification systems and by trapping reactive carcinogens, as tumor promoters via; and the suppressing agents prevent the evolution of the neoplastic process in cells that would otherwise become malignant.<sup>13</sup>

The second classification is based on the chemical structure and pharmacological actions.<sup>14</sup>

**1. Antimutagens/carcinogen blocking agents** : Phase II metabolic enzyme inducers – N-acetyl-L-cysteine – Polyphenols – Curcumin, dehydroepiandrosterone (DHEA)

**2. Antiproliferatives** : Retinoids/Carotenoids:  $\beta$ -carotene, 13-cis-retinoic acid, vitamin A. – Glucose-6-phosphate dehydrogenase inhibitors – Aspirin

### 3. Antioxidants

**Ideal feature of chemopreventive agent<sup>15</sup>** :

1. A known mechanism of action
2. High efficacy against multiple sites
3. Little or no toxic effects
4. Capability of oral administration
5. Human acceptance.

**Mechanism of action(MOA)<sup>12</sup>**:The mechanism of action of chemopreventive agents vary from each individual type. The summary of its MOA is described in the table 1.

### Different chemopreventive agents

A variety of grains, cereals, nuts, soy products, olives, beverages confer a protective effect against cancer [24]11. In particular, natural products consist of a wide variety of biologically active phytochemicals including phenolics, flavonoids, carotenoids, alkaloids and nitrogen containing as well as organosulfur compounds, which have been shown to suppress early and late stages of carcinogenesis[25] Recently, the bioactive triterpene, lupeol, commonly found in fruits like fig, mango,etc, has attracted interest in the context of chemoprevention attributable in large part to its antioxidant [26] , apoptosis-inducing and antiproliferative anti-mutagenic, anti-inflammatory [27] properties as well as its efficacy in inhibition of in vivo and in vitro cancer growth. Triterpenes represent a varied class of natural products, which occur commonly and are found in fruits, vegetables and other parts of several medicinal plants e.g . Arbutus unedo, Tipuana tipu, etc [28] have seen tremendous efforts by researchers worldwide to develop this wonderful molecule as a chemopreventive agent.

S.N.	Name of the chemopreventive agent	Possible mechanism of action	Trade names
1.	Retinoids & Vitamin A		
2.	Beta Carotene		
3.	Vitamin E		
4.	Vitamin C		
5.	Vitamin K		
6.	Dietary agents		
7.	Newer drugs		
8.			

### Second face of the coin of chemopreventive agent :

#### Clinical Efficiency

Despite almost 40 years of research in chemoprevention of HNSCC, no standards have been developed for that method as yet.

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**Legends Table**

Table 1 : Summary of mechanism of actions of different chemopreventive agents

Sl no :	MOA	Examples
1.	Inhibition of activated protein -1 (AP-1)	-----
2.	Inhibitors of cell proliferation and apoptosis	Curcumin Green tea 6- gingerol Resveratrol
3.	Inhibitors of COX-2	Curcumin NSAIDS
4.	Inhibitors of angiogenesis	Curcumin Resveratrol Catechins Vitamin E
5.	Inhibitors of cell cycling	Curcumin Resveratrol Catechins
6.	Molecular targeted agents : H-ras gene COX-2 EGFR P53	