



## Review Article

### CURCUMIN AND ITS PROMISING ROLE IN THE PREVENTION OF CANCER

Sana Afreen, Mir S Adil\*, Mohammed Nassir M, Muniba Suad, Sidhra Fatima  
Pharm. D, Deccan School of Pharmacy, Hyderabad –01, A.P., India

\*Corresponding Author Email: iampharmd@rediffmail.com

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#### ABSTRACT

Cancer is a disease in which cells grow abnormally in a group, uncontrollably deviating from the normal rules of cell division. It is regarded as the leading cause of death in economically developed countries and the second leading cause in developing countries. Cancer rates in India are lower than those seen in western countries, owing to the diverse populations and diets. The rate of colorectal, prostate and lung cancer in India are one of the lowest. Prevention of diseases through healthy diet and eating habits has been recognized in various mythological books. Turmeric or curcumin which is a common ingredient in the Indian curries has shown anti-oxidant and anti-inflammatory action, which helps it to act as a chemo-protective agent. The role of curcumin includes inhibition at multiple levels of several cell signaling pathways. The use of turmeric in Indian dishes could be a reason for low cancer rates; hence turmeric can be included in diet to prevent the development of tumor.

**Keywords:** cancer, curcumin, turmeric, chemoprevention.

#### INTRODUCTION

Cancer is a disease in which cells grow abnormally in a group, uncontrollably deviating from the normal rules of cell division. Cells normally receive signals that give indication whether the cells should divide, multiply or die. Some cells produce a degree of autonomy from these signals which results in an uncontrolled growth and proliferation. Such cells are termed as cancerous cells. It can be proved to be fatal, if the cancer cells are allowed to proliferate and spread. Metastasis, a process where tumor spreads is accountable for almost 90 % of cancer related deaths.<sup>1</sup>

#### Causes of Cancer

Cancer is regarded as the leading cause of death in economically developed countries and the second leading cause in developing countries. The reasons behind this cause are population aging, growth, increase in adoption of cancer associated lifestyles (smoking, physical inactivity and westernized diets), environmental pollution, diet and sunlight.<sup>2,3</sup> Various physiological and biochemical carcinogens like the ultra violet and ionizing radiations, tobacco smoke, asbestos, viral infections (hepatitis B virus cause liver cancer and human papilloma virus cause gastric

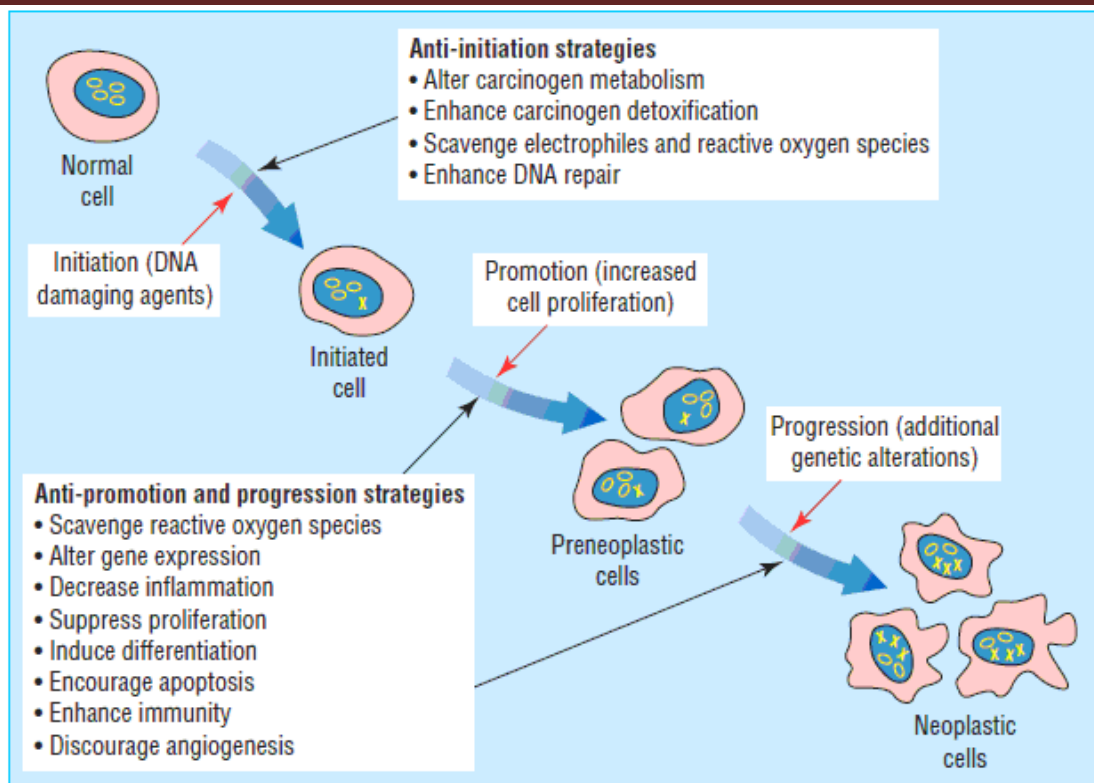
cancer) and parasites such as schistosomiasis causes cancer of bladder. Contamination of food by mycotoxins such as aflatoxins causes cancer of liver. Oxygen species may cause other kinds of cancer because over production of such free radicals can cause oxidative damage to bio molecules (lipids, proteins, DNA).<sup>4</sup>

#### Epidemiology

Prostate cancer, killing more men than any other cancer is the most prevalent malignancy in men in the United States and Western Europe. Patients with prostate cancer falling under the mean age group are 72-74 years and almost 85 % of the cases are diagnosed after the age of 65. Asia has the lowest rates (7.9 per 100,000 in India) and the highest in North America (137 per 100,000 in African-American men in the USA).<sup>5</sup>

#### Chemoprevention

The main objective of chemoprevention is to prevent arrest or reverse either the phase of initiation of carcinogenesis or the progression of neoplastic cells to cancer. For several decades, chemoprevention has been considered as an active area of interest for researchers. The use of retinoid to prevent cancer of the head and neck is a notable example.<sup>6</sup>



### Treatment and Cure

The process of carcinogenesis can be affected by interfering with modulation steps (initiation, promotion and progression) as well as the associated signal transduction pathway.<sup>4</sup> The treatment and cure for most human malignancies remain challenging due to alterations in multiple cellular signaling pathways and complexities in communication between multiple signaling networks. Research on differences between species response variation, varying lifestyles, dietary habits and response is still under as there is no standard treatment designed for a particular malignancy.<sup>7</sup>

### Role of Diet in Prevention of Cancer

Cancer rates in India are lower than those seen in western countries, owing to the diverse populations and diets. The rate of colorectal, prostate and lung cancer in India are one of the lowest.<sup>8</sup> The relationship between diet and health has been associated since the time immemorial. Prevention of diseases through healthy diet and eating habits has been recognized in various mythological books. Since nineteenth century, a modern approach has been undertaken using western scientific methodologies to reduce the burden of diseases from non-communicable diseases (NCD) such as cancer, coronary heart diseases (CHD) and other endemic conditions. It has been proved through various ecological, observational and laboratory studies that eating a diet high in fruits, vegetables and plant based foods, food containing low animal fat and salt content, tobacco free products, along with maintaining healthy weight and being physically active can reduce the risk of cancer and other chronic diseases.<sup>8</sup> Addition of dark chocolate in diet has proved to minimize the risk of cardiac diseases.<sup>9</sup> Dietary agents are known to suppress the transformation, hyper-proliferation, invasion, angiogenesis and metastasis of cancerous tumors. These agents contain biologically active constituents in addition to vitamins and minerals.<sup>10</sup> Epidemiological data suggest that

the risk of several types of cancer is reduced with consumption of spices. Spices are used as adjunctive therapy along with conventional cancer treatments<sup>7</sup>. Spices are known to possess medicinal properties and have been in the traditional systems of medicine for a long time. Recent decades have shown the chemistry and pharmacology of spices (their active constituents) and their health benefit effects.<sup>11</sup>

### Turmeric

Turmeric or curcumin which is a common ingredient in the Indian curries has been proven to be a potent anti-oxidant and anti-inflammatory agent. A promising additional property as a chemo protective agent of curcumin has also surfaced.<sup>8</sup> Curcumin (diperuloyl methane) [1, 7-bis (4-hydroxy-3-methoxy phenyl)-1, 6-heptadien-3, 5-dione], a derivative of turmeric is one of the most commonly used and highly researched phytochemicals.<sup>12</sup> Interesting information about the multiple mechanisms by which curcumin helps in chemotherapy and chemopreventive effects on cancer are provided by many sources. The role of curcumin includes inhibition at multiple levels of several cell signaling pathways, such as transcription factors (NF- $\kappa$ B and AP-1), cell cycle arrest (Cyclin P1), enzymes (COX2), TNF, survival pathways ( $\beta$  catenin and adhesion molecules), proliferation (EGFR and AKt). Curcumin downregulates anti-apoptotic genes [Bcl-2 and Bcl-X(L)] and up-regulates family proteins. A new dimension for molecular responses of cancer cells to curcumin at the genomic level is added by the cDNA microarray analysis.<sup>12</sup>

### Studies conducted on Curcumin

A study on human blood cell lines has shown suppression and destruction of blood cancer cells by turmeric. In many experimental studies, it has been shown that turmeric suppresses tumor initiation, promotion and metastasis.

Activated nuclear factor kappa-B (NFkB) appears to be associated with cancer cell growth in many cell types which may be blocked by turmeric. A carcinogenic bacterium, *helicobacter pylori* has been linked to the increased risk of adenocarcinoma of stomach and colorectal adenomas. The growth of as many as 19 clinical strains of *H. pylori* has been found to be inhibited by turmeric.<sup>8</sup>

### Limitations

Adequate concentrations of curcumin for pharmacological effects in certain tissues are limited due to poor absorption and low systemic bioavailability of curcumin.<sup>12</sup> Moreover in various animal and human pharmacokinetic studies, active levels of curcumin have been found in the gastrointestinal tract. The pharmacokinetic feature of low systemic bioavailability of curcumin prevents against using it in the prevention of malignancies which are at a distant from gastrointestinal tract.<sup>13</sup> To a great extent, the curcumin distribution in the target tissues is independent of systemic availability, thus its development in prevention of gastrointestinal malignancies would not curtail.<sup>13</sup> At present significant data advocating phase II, III clinical trials of curcumin has been shown for a variety of cancer conditions such as colon cancer, multiple myeloma and pancreatic cancer.<sup>12</sup>

### Curcumin potential against Cancer

The anti-carcinogenic activity of curcumin in animals by blocking the initiation of colon tumor by azoxymethane and promotion of skin tumor induced by TPA has been shown. Clinical trials using curcumin have been carried out in several laboratories and recently oncologists has considered curcuma as a potential third generation cancer chemo preventive agent. Curcumin is a potent anti-inflammatory agent inhibiting reactive oxygen generating enzymes such as lipoxygenase/cyclo-oxygenase, inducible nitric oxide synthase, xanthine dehydrogenase/oxidase. Curcumin also inhibits protein kinase C, I kappa-B kinase and EGF receptor tyrosine kinase. Curcumin additionally inhibits the expression of C-jun, C-fos, C-myc and iNOS and it also inhibits the activation of NF kappa B. curcumin blocks signal transduction pathways in the target cells and thus suppresses tumor promotion. Curcumin was bio transformed first to dihydrocurcumin and tetra hydrocurcumin, subsequently these compounds were converted into monoglucuronide conjugate.<sup>14</sup> Several studies has shown that the proliferation of both the androgen dependant prostate cancer cell line LNCaP and the androgen independent DU-145 line has been suppressed by the curcumin. The growth of heterotopically implanted LNCaP prostate cancer cells in nude mice is also suppressed by curcumin. Curcumin by interfering with growth factor receptor pathways, interferes with the activation of both the osteoblastic and osteoclastic components of the advanced prostate cancer phenotype and also by inhibiting the NFkB activation process.<sup>15</sup> It was reported recently that the growth of the implantation of PC-% prostate xenografts can be inhibited by administering curcumin prior to it. Studies has shown that curcumin

sensitizes the prostate cancer cells in culture to gamma-irradiation.<sup>5</sup>

### CONCLUSION

Despite the fact that cancer is difficult to cure at this moment, we are now aware that many forms of cancers are at least avoidable or preventable. Impressive breakthrough in determining cancer biology in recent years led us to find several ways to intercede in the carcinogenic process. Because oxidative and inflammatory stress contributes to malignant transformation, curcumin with its anti oxidative and anti-inflammatory properties would be a good agent for preventing most human malignancies.

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