



A Promising Role in the Cancer Prevention by Curcumin: Enriching the Clinical Translation

Unithirumala Amitha¹, Dr. Ruman Shaik²

¹Pharm-D, Department of Pharmacy Practice, Sree Dattha Institute of Pharmacy, Ibrahimpatnam, Hyderabad, Telangana-501510

²Junior Associate-Quality Assurance (Pharmacovigilance Officer), Indegene Private Limited, Bengaluru, India.

*Corresponding author's E-mail: amithabaradwajj14@gmail.com

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ABSTRACT

Cancer is a common disease that spreads throughout the blood circulation in the human body and destroys human life. The Human body has many numbers of cells; it grows divides and dies in the traditional manner. Sometimes the system goes wrong and an abandoned no of cells grows, which leads to cancer. The cancer cells combine together and form an extra mass of tissue known as tumour. As curcumin is shown to be non-toxic, further work is needed to substantiate the chemo preventive potentials of curcumin as the best alternative to chemotherapeutic agents which are adverse to cancer patients.

Keywords: Curcumin, Phytochemicals, Chemoprevention, anti proliferatives, Oxidative stress.

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INTRODUCTION

Cancer is a common disease that spreads throughout the blood circulation in the human body and destroys human life.¹ The human body has many cells; it grows divides and dies traditionally. Sometimes the system goes wrong and the abandoned no of cells grows, which leads to cancer. The cancer cells combine and form an extra mass of tissue known as a tumor.² Some of the tumors do not spread throughout the body but grow uncontrollably like a benign tumor.³ In Asia high prevalence of chronic viruses like hepatitis B and C, the Epstein Barr virus, and human papillomaviruses (HPV) increases the high risk of cancer.⁴ Cancer is the leading cause of death in economically developed countries and the second leading cause in developing countries.^{5,6} It is not possible to find out the specific cause of cancer.⁷ Various physiological and biochemical carcinogens like the UV and the ionizing radiations, tobacco smoke, asbestos, viral infections (hepatitis B virus cause liver cancer and human papillomavirus cause gastric cancer), and parasites such as schistosomiasis cause cancer of the bladder. Oxygen species may cause other kinds of cancer because overproduction of such free radicals cause oxidative damage to biomolecules (lipids, proteins, DNA).⁸

Phytochemicals are naturally occurring substances found in plants. There has been considerable scientific interest in the use of Phytochemicals that are derived from the

dietary components to combat human diseases, particularly cancer. India has a wealthy history of using plants for medicinal purposes. Turmeric (*Curcuma longa* L.) is a medicinal plant capaciously used in Ayurveda, Unani as well as Siddha medicine as a home remedy for various types of diseases. The dried ground rhizome of the perennial herb *Curcuma longa*, called as turmeric in English, Haldi in Hindi, and ukon in Japanese, has been used in Asian medicine as long as the second millennium BC.⁹

Chemoprevention

The term chemo-prevention was first invented by M. B. Sporn in 1976 who defined it as a preventive modality in which natural or synthetic agents can be employed to slow, stop, reverse, or prevent the development of cancer.¹⁰

The objective of the chemo-prevention is to avert arrest or reverse either the phase of the initiation of carcinogenesis and/or progression of the neoplastic cells to cancer. For several decades, chemo-prevention has been considered an active area of interest for researchers. The use of retinoids is to prevent cancer of the head and neck is a notable example.¹¹

Composition of Turmeric

Curcuma spp. contains turmerin which is a water-soluble peptide, essential oils (such as turmerones, atlantones and zingiberene) and curcuminoids including curcumin [1,7-bis-(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3, 5-dione]. Curcuminoids can be defined as the phenolic compounds which are derived from the roots of *Curcuma* spp. (Zingiberaceae). Curcumin (diferuloylmethane) is a low molecular weight polyphenol, which is first chemically characterized in 1910, which is generally regarded as the most active constituent and comprises 2–8% of most turmeric preparations.^{12, 13} Turmeric consists of proteins



(6.3%), fats (5.1%), minerals (3.5%), carbohydrates (69.4%) and moisture (13.1%).

The essential oil which is obtained by the steam distillation of rhizomes has α -phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpenes (53%)⁵. Curcumin (diferuloylmethane) is 3–4% which is responsible for yellow color and encompasses curcumin I (94%), curcumin II (6%), and curcumin III (0.3%)⁶. It has a melting point of 176–177°C; forms a reddish-brown salt with alkali and is soluble in ethanol, alkali, ketone, acetic acid, and chloroform.^{14, 15}

Anti-Cancer Effects of Curcumin

Chemopreventive agents are classified into various subgroups: Anti proliferatives, antioxidants, or carcinogen blocking agents. Curcumin, which belongs to all three subgroups, given its multiple mechanisms of action. The anticancer effects of curcumin result from multiple biochemical mechanisms that are involved in the regulation of programmed cell death and survival signals. The curcumin targets that are involved in the signaling pathways are transcription factors, growth factors, inflammatory cytokines, receptors, and enzymes. In various types of cancers, curcumin reveals anticancer actions through a combination of different various mechanisms including; survival signal reduction, proapoptotic promotion, anti-inflammatory actions, and reactive oxygen stress (ROS) scavenging to different degrees. The effects of curcumin on these signaling pathways are expected to be more complex in the legal setting, and the mechanism of curcumin's chemopreventive, chemosensitizing, and radiosensitizing results are more vigorously being studied now.^{16, 17} Oral curcumin administration has been shown to prevent the development of certain cancers of the skin, soft palate, duodenum, stomach, colon, liver, lung, as well as breasts of rodents.¹⁸

Curcumin has been shown to affect many cellular and molecular pathways which combat human diseases such as cancer. The main molecular targets of the curcumin appear to be gene expression, transcription factors, growth factors and their receptors, nuclear factors, and hormone receptors.

Studies Conducted on Curcumin

Since 1987, the National Cancer Institute (NCI) has tested over 1,000 different potential agents for chemoprevention activity, out of which only about 40 promising agents were moved to clinical trials.¹⁹ Curcumin, the Indian spice known as "Haldi", is one such agent that is currently under clinical investigation for cancer chemoprevention. Three polyphenols were isolated from *Curcuma longa*, of which curcumin (bis- α,β -unsaturated β -diketone) is the most abundant, potent, and extensively investigated.²⁰ Curcumin has been used empirically as a remedy for many illnesses in different cultures. The very first clinical report of anticancer properties of curcumin was from Kuttan and co-workers, who used 1% curcumin ointment on skin

cancerous lesions with a reduction in smell in 90% of the patients.²¹ 10% of patients experienced a reduction in pain and lesion size. In a study of oesophageal cancer prevention in curcumin-fed F344 rats, the chemopreventive activity of curcumin was observed not only in the initiation phase but also in post-initiation phases.²²

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. A carcinogenic bacterium, *helicobacter pylori* has been linked to the increased risk of adenocarcinoma of the stomach and colorectal adenomas. The growth of as many as clinical strains of *H. pylori* has been found to be inhibited by turmeric.²³

Several studies of cancer prevention at different stages have illustrated the multi-targeted anticancer effects and chemopreventive effects of curcumin and suggested it as a very favorable agent for chemoprevention.

Limitations

Adequate concentrations of curcumin for pharmacological effects in certain tissues are limited due to poor absorption and low systemic bioavailability of curcumin.²⁴ Moreover, in various animal and human pharmacokinetic studies, active levels of curcumin have been found in GIT. The pharmacokinetic feature of low systemic bioavailability of curcumin prevents using it in the prevention of malignancies that are at a distance from GIT.²⁵ At present, the data advocating phase II, III clinical trials of curcumin has been shown for a variety of cancer conditions such as colon cancer, pancreatic cancer, and multiple myeloma.²⁴

CONCLUSION

The fact that cancer is difficult to cure at this moment but we are now aware that many types of cancers are at least preventable. We know that Oxidative stress, as well as inflammatory stress, contributes to malignant transformation, curcumin with its anti-oxidative and anti-inflammatory properties would be a better agent in the prevention of human malignancies. Many studies on curcumin are still in the preclinical stage at present. A clinical trial stage is necessary to unlock the potential of curcumin formulations to improve anticancer medications and research for mankind. As curcumin is shown to be non-toxic, further work is needed to substantiate the chemopreventive potentials of curcumin as the best alternative to chemotherapeutic agents which are adverse to cancer patients.



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