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A Review on Anticancer Agent: Curcuma Longa

Wagadare Megha B and Kale Hrushikesh R
Samarth College of Pharmacy, Belhe, Maharashtra, India

Abstract: *Cancer is the second leading cause of death in the world and one of the major public health problems. Despite great advances in cancer treatment, cancer incidence and mortality remain high. Therefore, the search for more effective and less toxic cancer treatment strategies is still at the forefront of current research. Curcumin, the active component of the plant Curcuma longa, has received much attention in the last two decades as an antioxidant, anti-inflammatory and anti-cancer agent. In this review, a summary of the medicinal chemistry and pharmacology of curcumin. Natural products with immunomodulatory activity are widely used in the treatment of many diseases including autoimmune diseases, inflammatory disorders and cancer. They have gained much interest in recent decades as therapeutic agents because they provide cost effective and less toxic products than synthetic chemotherapeutic agents. recent advances in drug delivery systems to deliver curcumin to cancer cells have been highlighted as agents that have the ability to enhance. recent advances in drug delivery systems to deliver curcumin to cancer cells were highlighted..*

Keywords: Immuno modulator, antioxidant, anticancer, autoimmune diseases, cancer

I. INTRODUCTION

Cancer is the second most life-threatening disease and one of the major public health problems worldwide. In 2018, there were approximately 1.73 million new cases of cancer and more than 609,000 deaths in the United States alone. Despite tangible advances in cancer treatment, the reported incidence and mortality rates have not decreased over the past 30 years. Understanding the molecular changes that contribute to the development and progression of cancer is a key factor in cancer prevention and treatment. Curcumin has been widely used in Ayurvedic medicine for centuries because it is non-toxic and has a number of therapeutic properties including antioxidant, analgesic, anti-inflammatory and antiseptic activity. Recently, curcumin has been found to exert anticancer effects through its effect on various biological pathways involved in mutagenesis, oncogene expression, cell cycle regulation, apoptosis, tumorigenesis, and metastasis. Curcumin is one such potential candidate, and this review presents an overview of the current in vitro and in vivo data supporting its therapeutic activity in head and neck cancer, as well as some of the challenges regarding its development as an adjuvant chemotherapy agent.

1.1 Anticancer Activity

Anticancer drug, also called antineoplastic drug, any drug that is effective in the treatment of malignant, or cancerous, disease. There are several major classes of anticancer drugs

1. Alkylating Agents,
2. Antimetabolites,
3. Natural Products,
4. Hormones.

Cancer treatment is complicated in that the drugs used target human cells, albeit cells that have undergone genetic changes and are dividing at a rapid and uncontrolled rate. However, some anticancer drugs can differentiate between normal tissue cells and cancer cells to some extent, and the rate at which cancer cells proliferate may actually play a role in the apparent selectivity of the agents. For example, alkylating agents that act on cells in all phases of the cell cycle appear to be most toxic to cells in the synthesis, or S, phase when DNA is in the process of replication and unpaired nucleotides (the nitrogen containing units of DNA and RNA) are most vulnerable to alkylation (the addition of alkyl groups). In the late 20th and early 21st centuries, the identification of molecular properties unique to cancer cells has fueled the development of targeted cancer therapies that have a relatively high degree of specificity for cancer cells.

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1.2 Curcumine Longa

Fig.1: Curcuma longa.

1.2.1 Macroscopic Study

- Botanical Name: Curcumin Longa
- Family: Zingiberaceae
- Synonym : Turmeric
- Biological Source: Dried Rhizome

Chemical Constituents:

ROOTS	aromaticaSalisb. 8,9-Dehydro-9-formyl-cycloisolongifolene (2.7–36.8%), germacrone (4.3–16.5%), ar-turmerone (2.5–17.7%), turmerone (2.6–18.4%), ermanthin (0.8–13.3%), β-sesquiphellandrene (0.3–11.3%), and ar-curcumene (0.3–10.5%). C. aromaticaSalisb.
Methanol Extract of Rhizomes of Curcumin Longa	4-Hydroxycinnamoyl (feruloyl) methane Bis(4-hydroxycinnamoyl) methane, Caffeic acid Ferulic acid, Protocatechuic acid, Vanillic acid ,a-Tocopherol
Ethyl Acetate Extract of Curcumin Longa	Curcumin 1, demethoxycurcumin 2 and β-sitosterol-3-O-β-d-glucopyranoside 3

1.2.2: Microscopy

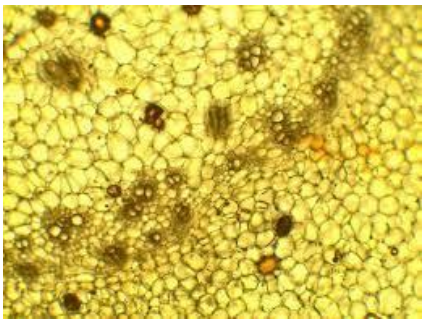

Fig.2 T.S of curcoma longa

1. Vessels
2. Oleoresins
3. Trichomes Covering
4. Calcium Oxalate Peisms
5. Calcium Oxalate Clusters

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Table: Measure of Discrimination.

MICROSCOPIC FEATURE	DIMENSION (MICRO MITER)
VESSELS	0.052
OLEORESINS	0.335
TRICHOMES COVERING	0.297
CALCIUM OXALATE PEISMS	0.252
CALCIUM OXALATE CLUSTERS	0.329

1.3: Mechanism of Action (Curcumin Longa)

The main mechanisms of action by which curcumin exerts its unique anticancer activity include induction of apoptosis and inhibition of tumor proliferation and invasion by suppression of various cell signaling pathways. According to the mode of action, chemopreventive substances are classified into different subgroups: antiproliferative, antioxidants or carcinogen blocking agents. Curcumin belongs to all three subgroups, due to its multiple mechanisms of action. The anticancer effects of curcumin mainly result from many biochemical mechanisms involved in the regulation of programmed cell death and survival signals. Curcumin targets involved in signaling pathways include transcription factors, growth factors, inflammatory cytokines, receptors and enzymes. In various types of cancer, curcumin exhibits anti-cancer effects through a combination of different mechanisms including; reduction of survival signal, pro-apoptotic support, anti-inflammatory action and reactive oxygen stress (ROS) to varying degrees. The effects of curcumin on these signaling pathways are expected to be more complicated in real-world settings, and the mechanisms of curcumin'schemopreventive, chemosensitizing, and radiosensitizing effects are now being more intensively studied.

II. STUCTURAL ACTIVITY RELATIONSHIP

1Modification of the chemical structure not only affects the binding to the receptor and the pharmacological activity of the drug molecule, but also changes its pharmacokinetics and physicochemical properties. Determination of essential pharmacophores in a drug molecule requires a thorough study of its natural and synthetic analogues. The chemical structure of curcumin is shown in Figure 3. As can be seen, it consists of two phenyl rings substituted with hydroxyl and methoxyl groups and connected through a seven-carbon keto-enol linker (C7). While curcumin occurs naturally, its derivatives are generally produced by a chemical reaction between aryl aldehydes and acetylacetone. This assembly method can provide more chemical analogues, such as compounds with alkyl substituents on the middle carbon of the linker (C7 part). A SAR study of curcumin derivatives shows that the presence of a coplanar hydrogen donor group and a β-diketone group is essential for antiandrogenic activity in the treatment of prostate cancer. In addition, a scan of 50 curcumin analogs showed that shortening the linker from seven carbon atoms (C7) to five carbon atoms (C5) improves antiandrogenic activity. As a result of the introduction of a methyl group at both C2 and C6 positions, a new derivative of curcumin was produced. This derivative exhibited a steric inhibitory effect on metabolizing enzymes such as alcohol dehydrogenase and showed significantly higher activity than curcumin in inhibiting endothelial cell proliferation and invasion both in vitro and in vivo. Dimethylcurcumin or ASC-J9 (5-hydroxy-1, 7-bis (3, 4-dimethoxyphenyl)-1, 4, 6-heptatrien-3-one) is a newly developed curcumin analog that enhances androgen receptor degradation and has been used for prostate cancer treatment In addition, it also demonstrated a significant antiproliferative effect against estrogen-dependent breast cancer cells..4:

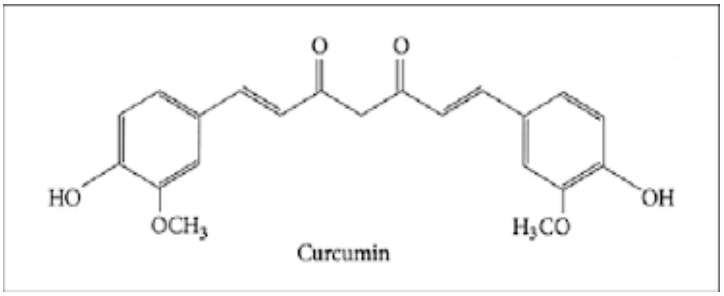

Fig. 3 structure of curcuma longa.

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The conjugation reactions occur on the hydroxyl groups (4-OH) attached to the phenyl rings of curcumin. Thus, curcumin's kinetic stability can be enhanced by masking the 4-OH groups . Another study has revealed a correlation between the hydrophobic property of the benzyl rings and androgen receptor affinity .

III. CONCLUSION

Several therapeutic procedures are available for the treatment of cancer, which are chemotherapy, radiotherapy and immunotherapy. In most cases, unwanted side effects such as gastrointestinal upset, kidney damage, and other complications are associated with this compound. This compound includes the alkaloid compound phenol and, in addition to the indicator curcumin, the active component of Curcuma longa extract, has been widely studied in the past. several decades for its anti-inflammatory, antioxidant, anti-cancer and anti-androgenic effects. Curcumin has shown significant anticancer effects against several different types of cancer, including prostate cancer, breast cancer, colorectal cancer, pancreatic cancer, and head and neck cancer in vitro and in vivo. In addition, its efficacy and safety in cancer patients either alone or in combination with other anticancer agents have been demonstrated in several clinical trials in human subjects. Curcumin is believed to exert its anticancer activity through multiple mechanisms, interfering with various cellular pathways and inducing/inhibiting the production of various types of cytokines, enzymes or growth factors such as MAPK, EGF, NFκB, PKD1, COX-2, STAT3, TNF - a, and IκKp. However, the anticancer application of curcumin has been limited mainly due to its low water solubility, which results in low cellular absorption and poor oral bioavailability, as well as low chemical stability. Various approaches such as structural modification and the use of drug delivery systems have been developed to overcome these limitations. The key pharmacophores contributing to the biological activity of curcumin are known to be the hydrogen donor group, β-diketone group, phenyl rings and substituent groups on them. Chemical modification of these groups has led to curcumin derivatives with higher potency and/or increased solubility or stability in water. In addition, various types of delivery systems have been developed to deliver curcumin to cancer cells or animal xenografts using various natural or synthetic polymers, lipids or proteins, some of which have improved the stability and/or cellular uptake of curcumin, thus leading to a stronger anticancer response. This compound has antioxidant properties and inhibition of DNA cell cycle damage induction of apoptosis inhibition of angiogenesis in tumor cell and its anticancer effect are new and more effective.

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