ISBN: 978-93-90847-83-9

2. Turmeric: A Neutraceutical Boon

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2.1 Introduction:

The natural plant products are being used for various purposes throughout human history. These natural products are derived as secondary metabolites from higher plants that act as natural defence mechanism against diseases and infections. Many of the natural products have pharmacological and biological activity, hence they are exploited in drug discovery and drug design. Medicines derived from plants are shown to play vital role in health care from ancient and modern times (Newman and Cragg 2007; Prasad and Aggarwal 2011). About 61% of at least 877 drugs introduced worldwide between 1981 and 2002, can be traced back to their origins in natural products. These include vincristine and vinblastine (from *Vinca rosea*), etoposide (from May apple), irinotecan and topotecan (from *Camptotheca acuminata*), paclitaxel and abraxane (from *Taxus brevifolia*), solamargine (from *Solanum dulcamara*), masoprocol (from *Larrea tridentata*), arglabin (from *Artemisia glabella*), alitretinoin (from *Daucus carota*) and others (Prasad and Tyagi 2015).

Figure 2.1: Turmeric Cultivation

In 1989, the term "Neutraceuticals", an union of 'Pharmaceutical' and 'Nutrition' was proposed by Stephan De Felice. According to De Felice, Neutraceuticals can be defined as, "A part of food that provides medical or health benefits, including the prevention and/or treatment of a disease" (Karla 2003; Hay et al., 2019). Turmeric is one of the most studied plant materials due to its medicinal properties. Curcuma longa belong to the family Zingiberaceae, a rhizomatous Perennial herb, native of Southeast Asia and Africa that are ideal places for growth and cultivation. (Pal et al., 2020; Priyadarshini 2014). Turmeric, commonly known as haldi is used as an Ayurvedic medicine for the treatment of cough, diabetes, anorexia, and sinusitis (Nelson et al., 2017). It is also used as one of the ingredients in various food preparations for its characteristic natural color and it acts as a preservative as well (Kotra et al., 2019). It also has wide applications in the dyeing, drug, and cosmetic industries. India is the largest producer and exporter of turmeric in the world accounting for more than 50% of the international trade, thereby fulfilling 90% of the global demand and it has considerable importance in Indian economy (Olojede et al., 2009; Pal et al., 2020). Hence it is the spice of India, also known as "Indian saffron".

2.2 Turmeric:

The genus *Curcuma* comprises of 70 perennial rhizomatous species, which are distributed widely throughout tropical and subtropical regions of the world. Turmeric is popularly consumed in the countries of its origin for a variety of uses, such as dietary spice, a dietary pigment, and an Indian natural medicine for the treatment of various diseases (Yadav and Tarun 2017). The portion of the plant rhizome is powdered and medicinally used. The dried *Curcuma longa* or Turmeric has many names such as Curcum in the Arab region, Indian Saffron, Haridra (Sanskrit, Ayurvedic), Jianghuang (Yellow Ginger in Chinies), Kyoo or Ukon (Japanies) (Labban 2014). The rhizome of the plant that is used medicinally is usually cleaned, boiled, dried and pulverized to get a characteristic yellow powder. (Yadav and Tarun 2017).

2.2.1 Classification of Turmeric:

Figure 2.2: Rhizome of Curcuma Longa

Kingdom: Plantae
Class: Lilliopsida: Monocotyledons
Sub class: Commelinids
Order: Zingiberales
Family: Zingiberaceae
Genus: *Curcuma*
Species: longa

The wild Turmeric is called *Curcuma aromatica* and the Domestic species is called *Curcuma longa* (Chattopadhyay *et al*., 2004; Yadav and Tarun 2017).

2.3 Components of Turmeric:

The active components of turmeric are the flavonoid which constitute 90% Curcuminoids, a mixture of Curcumin or diferuloylmethane (71.5%), monodexmethoxycurcumin (19.4%), and bisdesmethoxycurcumin (9.1%). Curcumin has a melting point of 176–177°C; forms a reddish- brown salt with alkali and is soluble in oil, acetic acid, ethanol, ketone and chloroform and insoluble in water (Nasri *et al.,* 2014).

Water soluble curcumin can be prepared by fusion of sodium dodecyl sulfate, cetylpyridinium bromide, gelatine, polysaccharides, polyethylenegylcol and cyclodextrins into various surfactant microemulsions (Iniaghe *et al*., 2009).

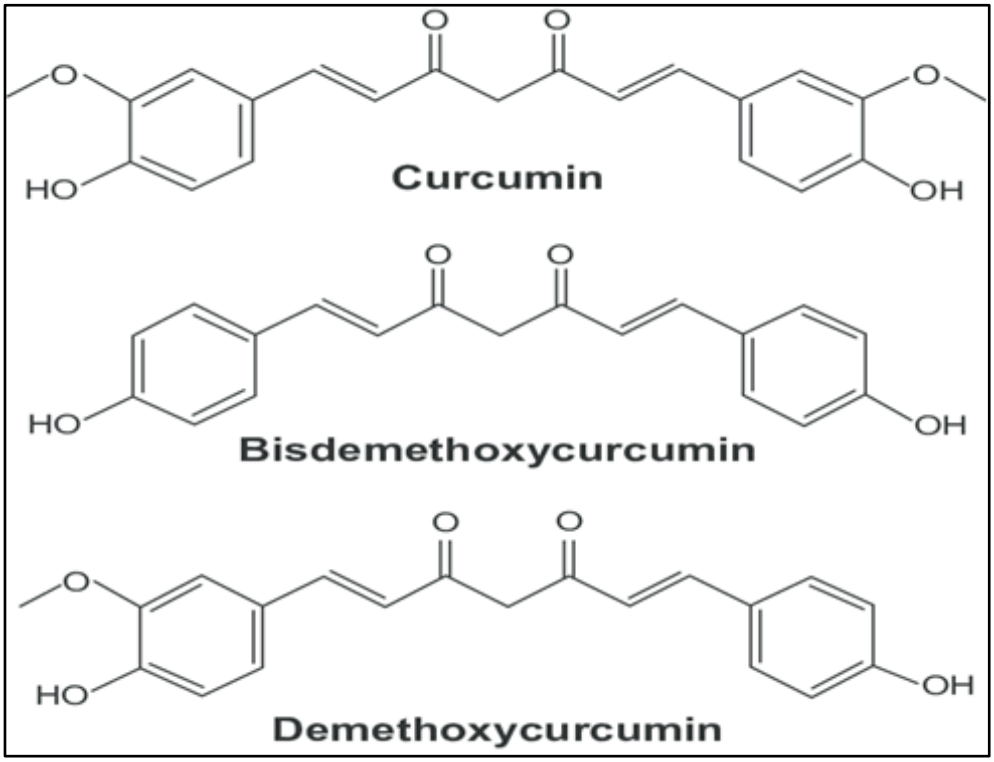

Figure 2.3: Isoforms of Curcumin

2.4 Nutritive value of *Curcuma longa*:

Turmeric is a major source of macro and micro nutrients. It is a good source of energy, and rich in dietary fiber. In ancient times turmeric was known as "Golden Spice" because of its various medicinal properties, which helps in controlling many diseases and also enriching the taste and colour of the food (Mishra and Goel 2020).

The nutritional values of turmeric include moisture (8.92%), crude fiber (4.60%), ash (2.85%), fat (6.85%), crude protein (9.40%), and carbohydrates (67.38%) respectively. The fiber has found to clean the digestive tract of consumere by removing carcinogens from the body and it can also arrest excessive absorption of cholesterol.

It is also adding in bulk to foods and it controls the excessive intake of starchy foods and it may act as guard against metabolic problems such as hypercholesterolemia and diabetes mellitus (Mughal 2019).

Table 2.1: Constituents of *Curcuma longa*

	Composition (w/w)
Curcuminoids	1-6
Volatile Oils	3-7
Fiber	2-7
Mineral matter	3-7
Protein	6-8
Fat	5-1
Moisture	6-13
Carbohydrates	60-70

(Source: Nelson *et al*., 2017)

Table 2.2: Major nutrients in *Curcuma longa* g/100g

Constituents	**Amounts**
Protein	7.66
Ash	6.13
Fat	5.03
Total dietary fiber	21.38
Carbohydrate	49.22
Energy	1174 kJ

(Source: Yadav and Tarun 2016; Mishra and Goel 2020)

Table 2.3: Minerals content in Turmeric mg/100g

Constituents	Amount
Calcium	122
Iron	46.08
Copper	0.44
Sodium	24.41
Potassium	2374
Phosphorus	276
Zinc	2.64

Table 2.4: Vitamins content in Curcuma longa mg/ µg/ 100g

Constituents	Amount
Thiamine	0.06
Riboflavin	0.01
Niacin	1.55
Pantothenic acid	0.13
Biotin	0.76 µg
Total folate	13.86 µg

2.5 Phytocomponents of Turmeric:

Turmeric contains carbohydrates, protein, fat, minerals, and moisture. The essential oil (5.8%) obtained by steam distillation possesses Sesquiterpenes (53%), zingiberene (25%), α- phellandrene (1%), sabinene (0.6%), cineol (1%), and borneol (0.5%). Curcumin (3–4%) is responsible for the yellow colour, and comprises curcumin I (94%), curcumin II (6%) and curcumin III (0.3%) (Ammon and Wahl, 1991). The derivatives of curcumin, Demethoxy and bisdemethoxy have been isolated from turmeric. The melting point of curcumin is at 176-177°C. In rhizome many phytochemicals have been reported such as tumeroneα, tumeroneβ, curzerenone, curdione, mono- and di-demethoxycurcumin. The volatile oils of leaves of *C. longa* have been analyzed by Gas Liquid Chromatography and reported to contain linalool, caryophyllene, geraniol, α-pinene, β-pinene, sabinene, myrcene, α-phellandrene, 1, 8-cineole, p-cymene, C8-aldehyde, and methyl heptanone (Golding *et al*., 1982).

Table 2.5: Biochemical contents in dried turmeric rhizome

Compound	Biological activity
Curcuma longa	Antitumor, Anti-protozoan, anti-inflammatory and Wound-healing

Compound	Biological activity
Methylcurcumin	Anti-protozoan
Demethoxycurcumin and Bisdemethoxycurcumin	Antioxidant
Volatile Oil	Anti-inflammatory, Antibacterial, Antifungal
Curcumin	Antibacterial, Anti-protozoan, Antiviral, Antitumor and Antioxidant

Well known five bisabolane sesquiterpenes and unique sesquiterpene, (6S)-2-methyl-6-(4-hydroxyphenyl-3-methyl)-2-hepten-4-one, two new bisabolane sesquiterpenes, (6S)-2-methyl-6- (4-hydroxyphenyl)-2-hepten-4-one, (6S)-2- methyl-6- (4-formylphenyl)-2-hepten4-one, and two calebin derivatives, 4''-(4'''-hydroxyphenyl3'''-methoxy)- 2''-oxo-3''-butenyl-3-(4'-hydroxyphenyl)- propenoate and 4''-(4'''-hydroxyphenyl)- 2''-oxo-3''-butenyl-3-(4'-hydroxyphenyl- 3'-methoxy)-propenoate have been isolated from Turmeric (Khajehdehi, 2012; Nasri et al., 2014).

Table 2.6: Biological properties of turmeric and its compounds

Component	Quantity	Reference
Curcumin	3.1-3.4%	Verma *et al*., 2018
Anthocyanins	18.9-37.0g/g	Verma *et al*., 2018
Phenols	0.15-0.62%	Verma *et al*., 2018
Tannins	0.32-0.76%	Verma *et al*., 2018
Protein content	3.6-6.8%	Verma *et al*., 2018
Sugars	20.5-43.4%	Verma *et al*., 2018
Oil	3.7-5.3%	Verma *et al*., 2018
Ash	6.9-9.8%	Verma *et al*., 2018
Moisture	90.2-91.3%	Verma *et al*., 2018

Source: (Mishra and Goel 2020)

2.6 Neutraceutical properties of Turmeric:

Turmeric has several therapeutic, food and Pharmacological activities. The active component of Turmeric is known as Curcumin. Many researchers have reported the medicinal properties of Turmeric.

This phytochemical present in turmeric have shown to have a variety of biological functions, such as antimicrobial, antioxidant, anti-inflammatory, anti-carcinogenic, Hepatoprotective properties, etc., and the numerous pharmacological effects of curcumin and established its ability to act as a potential therapeutic agent against several chronic diseases have been confirmed (Labban *et al*., 2014; Nasri *et al.*, 2014).

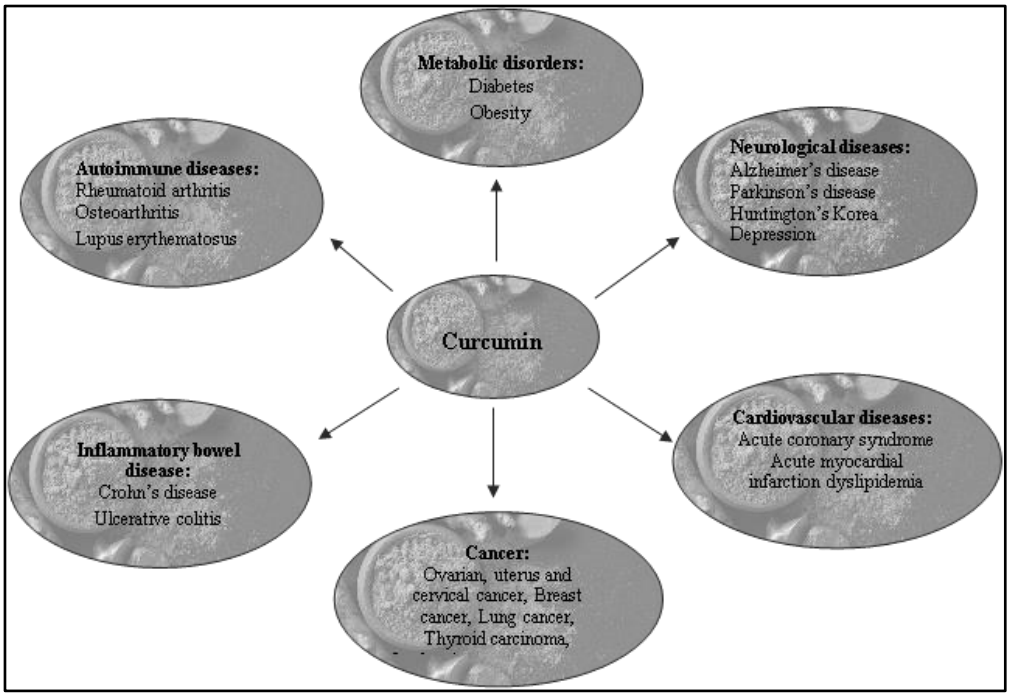

Figure 2.4: Health Beneficial Effects of Turmeric

2.6.1 Cardiovascular Diseases:

Cardiovascular disease is the leading cause of death at global scale (World Health Organisation, 2018). The concerning situation have been associated with many risks factors such as dyslipidemia, high blood pressure, reduced or lack of physical activity, obesity, tobacco consumption, as well as psychological conditions such as stress and depression. In order to bring to the lower grade of developing cardiovascular disease, a best management or avoidance of aforementioned habits are necessary for both healthy and the high-risk group of peoples (Yusuf *et al*., 2001; World Health Organisation, 2018).

Many reports have shown that Curcumin is a beneficial treatment for cancer, which at molecular level can have impact on growth, development and spread of cancer cells. Curcumin act as anti-carcinogenic compound. Although there are various mechanisms, induction of apoptosis plays an important role in its anti-carcinogenic effects. It induces inhibition of cell-cycle progression and apoptosis, both are preventing cancerous cell growth in rat aortic smooth muscle cells (Boonrao *et al*., 2010). The Curcumin also prevent colon carcinoma through arrest of cell-cycle progression independent of inhibition of prostaglandin synthesis. It suppresses human breast carcinoma through multiple pathways. Curcumin also produces nonselective inhibition of proliferation in several leukaemia, no transformed haematopoietic progenitor cells and fibroblast cell lines. On the effectiveness of Curcumin on cardiovascular risk factors in individuals with coronary artery disease, it has been determined that serum triglyceride, LDL and VLDL cholesterol levels decrease considerably in the group of individuals taking Curcumin and it has been used as a safe and well tolerated adjunct strains to control hyperlipidemia.

The curcumin significantly down regulates both p53 and estrogen receptor (ERα) protein levels with decrease in T-47D cell viability. Other studies involving different breast cancer cell lines treated with Curcumin, such as BT-483 and MDA-MB-23, have shown a significant decrease in cell proliferation. Curcumin has been studied as a chemo preventive agent in numerous clinical trials, and it will be examined in vivo and in vitro studies for its effects. The potential and suitability of Curcumin as a treatment modality in hormone dependent breast cancer has been reported (Hallman *et al*., 2017).

2.6.2 Curcumin in Autoimmune Disease:

Many reports were demonstrated as Curcumin inhibits inflammation in many autoimmune and inflammatory diseases such as atherosclerosis, arthritis, experimental autoimmune neuritis and encephalomyelitis. Curcumin decreases the growth expression of adhesion molecules, β3 and β7 integrins, and thereby decrease joint inflammation in Rheumatoid Arthritis and also decrease the expression of pro-inflammatory cytokines (Hay *et al*., 2019; Shpitz *et al*., 2006). Curcumin is a potent anti-inflammatory agent with specific lipoxygenase- and COX-2- inhibiting properties. In vitro, and in vivo studies have demonstrated its effects through decreasing both acute and chronic inflammation (Nasri *et al*., 2014). The turmeric derived polyphenols were suggested in portal inflammation. Many reports have been published on dietary supplements trials of turmeric in various populations. It has been shown that a 5% overall incidence of abnormal liver function associated turmeric dietary supplements use including transaminases, LDH, alkaline phosphatase and/or bilirubin (Lukefahr *et al*., 2018).

Curcumin has been shown to have anti-inflammatory effects on Osteoarthritis through the inhibition of NF-$_{\kappa}$B and the suppression of important regulators of inflammation such as TNF- α, IL-1β, IL-6, MCP1, prostaglandin E2 activator protein-1. The administration of curcumin appears beneficial for the treatment of systemic lupus erythematosus, an inflammatory and chronic autoimmune mediated disease recognized by the accumulation of auto-antibodies and immune complexes in distinct organs. Actually, Curcumin can manage to recover an imbalance present among T-helper cell subsets, regulatory T cells, and dendritic cells observed in these patients (Hay *el al*., 2019; Perkins *et al*., 2017).

2.6.3 Cardiovascular and Anti-Diabetic Effects:

Turmeric exercise cardio-protective effects mainly by antioxidant activity, lowering lipid peroxidation, anti-diabetic activity and inhibiting platelet aggregation. Cardiovascular diseases such as acute coronary syndrome, acute myocardial infraction and dyslipidemia, were against curcumin (Hay *et al*., 2019; Essa *et al*., 2019). It inhibits oxidative stress, apoptosis and inflammation and exerts cardio protective effects. Apart from this, curcumin can be useful for lipoprotein metabolism because it is involved in the reduction of low-density lipoprotein cholesterol and triglycerides and augmentation of high-density lipoprotein. A review reported that 18 atherosclerotic rabbits administered with 1.6-3.2 mg/kg/day of turmeric extract showed a decreased susceptibility of LDL to lipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels. Turmeric will decrease blood glucose level in diabetic rats as well as decreases the complications in diabetes mellitus (Nasri et al., 2014; Selvi *et al*., 2015).

A recent report has been shown that curcumin can be used as a safe and well tolerated adjunct to strains to control hyperlipidemia. Clinical studies need to be performed to discover optimal dosages for cardiovascular protection and lipid or glucose lowering activities (Nasri *et al*., 2014).

2.6.4 Antioxidant Activity:

Turmeric has been reported as a powerful scavenger of oxygen free radicals. Its antioxidant activity is comparable to vitamin C and E. Curcumin can crucially inhibit the generation of reactive oxygen species (ROS) such as H_2O_2, super oxide anions and nitrite radical generation by activated macrophages (Labban 2014). Its derivatives, bisdemethoxy curcumin and Demethoxy curcumin also have antioxidant activities. An *in vitro* study was done for inducible stress protein effect, endothelial heme oxygenase 1, incubation with curcumin resulted in enhanced cellular resistance to oxidative damage. Curcumin is only the anti-mutagenic against mutagens which require metabolic activation (Tiwari et al., 2006). Curcumin was found to block cyclosporine A- resistant phorbol myristate acetate + anti- CD28 pathway of T-cell proliferation. In addition, it shows the properties of intrinsic anti-oxidative abilities of Curcumin such as reduction in testicular damage caused by exposure to di-n-butylphthalate (DBP), by increase in Glutathion (GSH), testosterone levels and glucose-6-phosphate dehydrogenase (G6PD) activity and decrease in malondialdehyde (MDA) levels.

Further research shows to determine the role of lipid peroxidation in pain and other symptomology associated with pancreatitis (Labban 2014; Durgaprasad *et al*., 2005).

2.6.5 Antimicrobial Activity:

Volatile oil and extract of *Curcuma longa* inhibit the growth of various organisms like bacteria, parasites and pathogenic fungi. The chicks infected with caecal parasite *Eimera maxima* when fed with diets supplemented with turmeric resulted in reduction in small intestinal lesion scores and improved weight gain were reported (Nasri *et al*., 2014). It was reported in another animal study that, turmeric oil inhibited dermatophytes and pathogenic fungal infections in guinea pigs at a 7 days post-turmeric applications. The turmeric oil was extracted by using ether, chloroform and also crude ethanol extract having antifungal activity. Turmeric oil has been shown to be active against *Aspergillus flavus, A. parasiticus, Fusarium moniliforme* and *Penicillium digitatum* (Verma et al., 2018). The turmeric extract of curcuminoid and oil showed antibacterial activity against pathogenic bacteria and they showed large inhibition zone against *Bacillus subtilis*. The varying degrees of the sensitivity of the bacterial test organisms are due to the intrinsic tolerance of microorganisms (Naz et al., 2010). The researchers have reported that, in *in vitro* studies the curcumin prevents the growth of *Helicobacter pylori* CagA+ strains. Both curcumin and oil fractions of Turmeric extract suppressed the growth of many bacteria such as *Streptococcus, Staphylococcus, Lactobacillus* etc., (Verma *et al*., 2018). Curcumin is shown to have antiviral activity. It acts as an inhibitor of Epstein-Barr virus (EBV). It also shows anti-HIV activity by inhibiting the viral replication by HIV-1 integrase and also inhibits UV light induced HIV gene 127 expression. Thus, the extract of curcumin and essential oil may be used as novel drug against pathogenic organisms (Araujo and Leon 2001).

2.6.6 Anticancer Activity:

Several animal studies have been reported that turmeric influence on the carcinogenesis. Various studies have demonstrated that curcumin is able to inhibit carcinogenesis in three stages: angiogenesis, tumour promotion, and tumour growth. During initiation and promotion, curcumin modulates transcription factors controlling phase I and II detoxification of carcinogenesis in a variety of cell types in both *in vitro* and *in vivo* studies (Nasri *et al*., 2014; Garg *et al*., 2008). Turmeric and curcumin are able to suppress the activity of mutagens and carcinogens. In a study on colon and prostate cancer the curcumin was shown to inhibit cell proliferation and tumour growth (Kwon and Magnuson 2009). The effects of turmeric and curcumin have been related to direct antioxidant and free-radical scavenging effects, and their ability to indirectly increase glutathione levels and also inhibit nitrosamine formation. Curcumin has been shown to inhibit the mutagenic induction effect of UV rays. The benefit of curcumin or turmeric extract to reducing the chemically induced tumours was studied in many reports. Applications of both the extract in carcinogenesis and promotion resulted in less production of papilloma cells, compared to control. Thus, they specify to produce best properties during the tumour promotion.

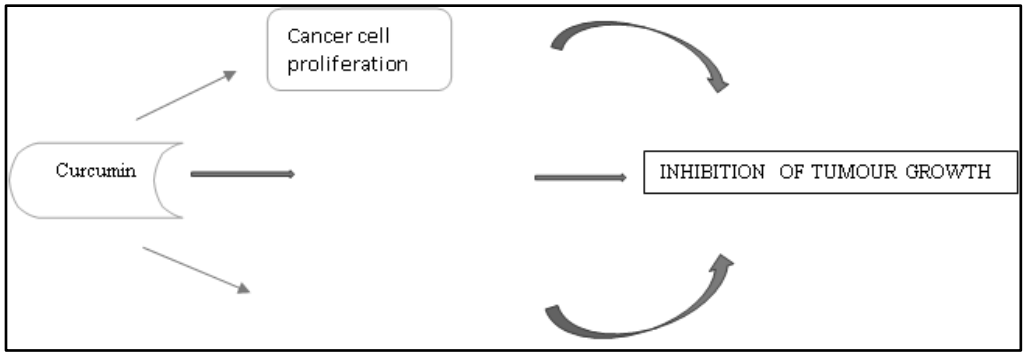

Figure 2.5: Mechanism of action of turmeric on cancer cells: turmeric inhibits the growth of tumours by blocking proliferation and inducing the senescence and apoptosis of cancer cells

The proliferation of many different cancer cell lines and cancer cell growth are suppressed by Curcumin via inducing apoptosis by inhibiting transcription factors. These factors include NF-KB, activator protein 1 (AP-1), cyclooxygenase II (COX-2), nitric oxide synthase, matrix metalloproteinase-9 (MMP-9), and STAT3 (Allegra et al., 2017). Thus Curcuma longa exhibits various health beneficial effects and serve as an important part in the human life.

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