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Curcumin and Cancer: Recent Developments

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ABSTRACT:

Cancer is a malignant disease with high mortality rates affecting millions. Although chemotherapeutic agents are employed largely in cancer management, they often result in toxicity and side effects and may lead to resistance. These draw backs of the conventional chemotherapeutic agents have lead to the urging need for development of safer, biocompatible, nontoxic compounds from natural sources and their application in cancer management. Products from natural sources are being exploited in cancer research worldwide due to its less toxicity. Of the several natural products tested, curcumin, well known for its chemopreventive, cytoprotective and immune suppressive properties holds great promise for cancer research. Curcumin has been reported to affect different signaling pathways either in a direct or indirect manner in a wide range of cancers. Despite the therapeutic effectiveness of curcumin, its application is largely restricted due to its poor absorption, lipophilic nature and low bioavailability. Thus newer and effective formulations for curcumin in cancer treatment are being continuously exploited. In this review we highlighted (i) recent developments of application of natural products in cancer research (ii) role of curcumin in different cancers (iii) curcumin formulations and their application in cancer research. The future scope of this review lies in the effective employment of curcumin and its formulations, in the eradication of cancer.

Keywords:
Curcumin, cancer, anticancer therapy.

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INTRODUCTION

Despite ongoing progress of the chemotherapeutic agents in cancer management, it still remains to be a major killer. The main challenge in cancer therapeutics revolves around specific killing of cancer cells within a milieu of the normal ones, overcome resistance to chemotherapeutic drugs called as Multi Drug Resistance (MDRs) and prevention of metastasis, targeting clinical relapse and augmentation of chemotoxicity. The conventional anticancer agents employed in cancer management are mostly toxic that lead to life threatening complications of neurotoxicity and cognitive changes (Dutta *et al.,* 2011; Fardell *et al.,* 2011). Therefore the need for safer, nontoxic products remains in targeting cancer. Different types of natural products are being continuously exploited in cancer research (Ulbricht *et al.,* 2010; Dai *et al.,* 2010) due to the tested advantage of being less toxic than synthesized chemical compounds.

Curcumin, a major curcuminoid derivative, is a main component of turmeric obtained from the roots of *Curcuma longa* and forms an important component of the South Asian cushine. **(Fig-1).** It is chemically formulated as diferuloylmethane ($C_{21}H_{20}O_6$), a polyphenol in its properties, curcumin has been reported to affect the biological system immensely by its antiinflammatory, antitumorigenic, antioxidant, antiseptic, anti-toxic, cancer chemopreventive, chemo sensitization, radio sensitization epigenetic change inducer, and potentially chemotherapeutic properties (Aggarwal *et al.,* 2007, Basnet *et al.,* 2011) and thus finds wide application in health research.

Several classes of bio-molecules are selectively regulated by curcumin thereby affecting diverse signaling pathways (Arora *et al.,* 1973; Srimal *et al.,* 1973; Jobin *et al.,* 1999; Sharma *et al.,* 2005 and Shanmugam *et al.,* 2011) in the biological system.

The hall mark property of targeted cell killing by curcumin (Shanmugam *et al.,* 2011; Syng-Ai *et al.,* 2004), through different signaling pathways portray it as a promising chemotherapeutic molecule. The exact molecular mechanism of curcumin in different cancer cells is being determined. However some of the target molecules that curcumin effect in different cancers include nuclear factor-κB, activator protein-1, nitric oxide synthase, receptor tyrosine kinases, cell cycle regulators like cyclins, matrix metalloproteinases, pro-apoptotic markers and inhibits angiogenesis (Syng-Ai *et al.,* 2004; Aggarwal *et al.,* 2007; Bierhaus *et al.,* 1997; Brouet *et al.,* 1995; Hahm *et al.,* 2004; Korutla *et al.,* 1994; Singh *et al.,* 1995). Curcumin is currently in clinical trials for treatment of various cancers, including multiple myeloma, pancreatic cancer, and colon cancer (Aggarwal *et al.,* 2003).

In this review we focus our attention to (a) mortality rates in different cancer (b) recent references to natural products applied in cancer research (c) how curcumin inhibits cancer through different pathways (d) recent developments in curcumin formulations and applications in cancer research.

Fig 1A: Plant

Fig 1C: Rhizome

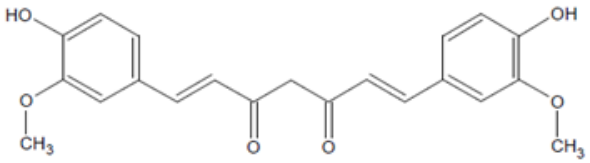

Fig 1B: Chemical Structure of curcumin

Fig 1: Curcumin: 1A. Plant, 1B. Chemical Structure of curcumin, 1C. Rhizome

Mortality rates in different types of cancer

Cancer remains to be a leading cause of death worldwide accounting for 7.6 million deaths (around 13% of all deaths) in 2008, as determined by statistics on Cancer Incidence and Mortality Worldwide by GLOBOCAN, Cancer Fact Sheet conducted by WHO (http://www.globocon.iarc.fr/) **(Fig-2).** The statistics summarized the mortality rate in cancer and was represented by an Age-standardized rate (W) including the number of new cases or deaths per 100,000 persons per year. In India the most frequent cancers reported were cervix and uteri, breast, oral and lips, lungs and oesophagus while lung, breast, colorectal and prostrate were the five most frequent occurring ones in the world. Hence the need for suitable molecules to fight the disease is urgent.

Recent references of Natural products applied in cancer research

A whole range of natural products obtained from bacterial, algal, fungal and higher plant sources (Kinghorn *et al.,* 2011) are being exploited for obtaining active molecules to combat cancer **(Table-1).**

Curcumin: Molecular Pathways and Inhibition of Cancer

Cancer is a disease with major manifestations like uncontrolled cell proliferation and metastasis. Research in the field of cancer chemotherapy broadly revolves around the control by the following mechanisms

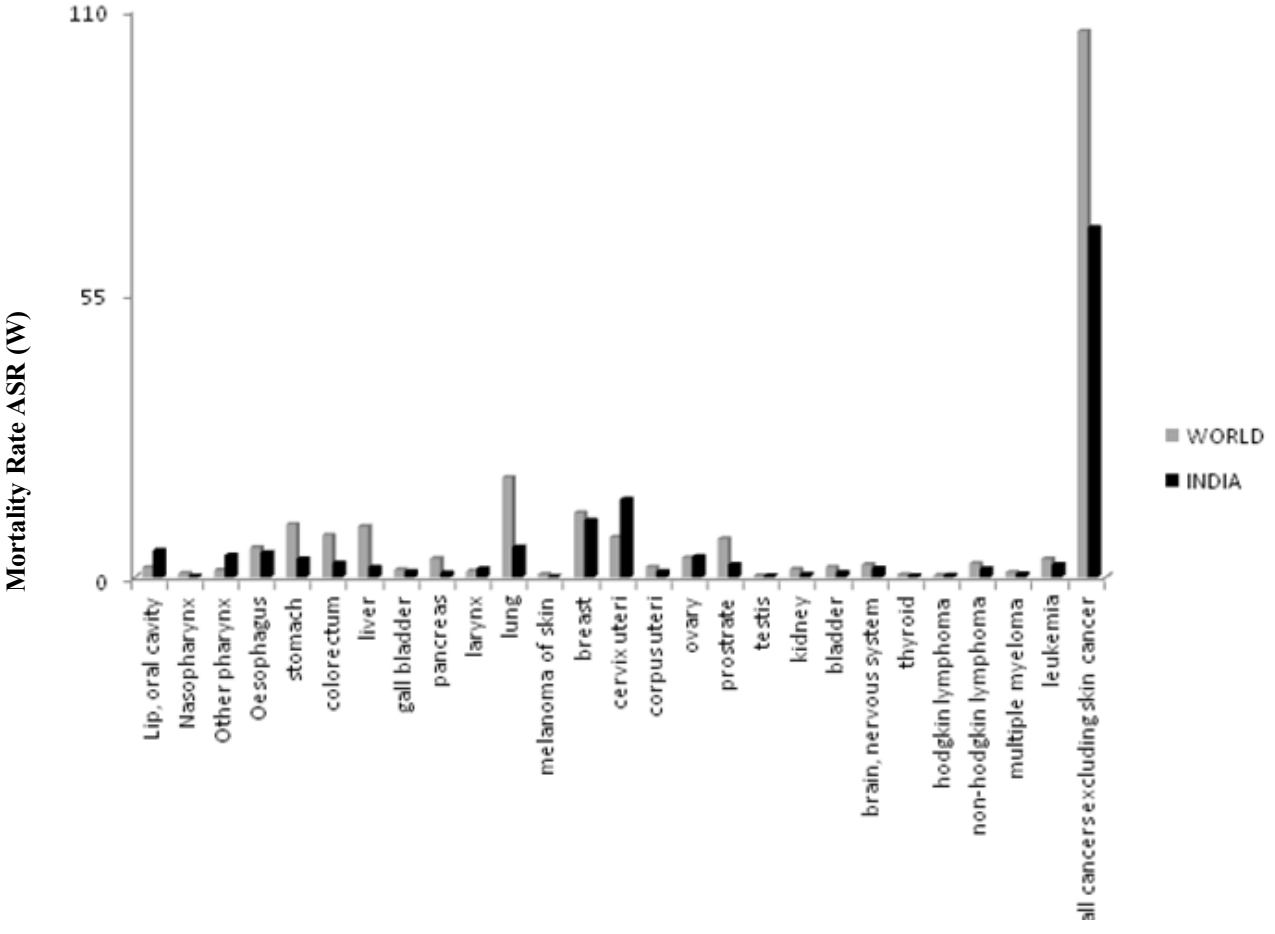

Fig 2: Cancer Statistics: World and India: The statistics is based on Mortality in most frequent cancers. The data is based on Age-standardized rate (W): A rate is the number of new cases or deaths per 100, 000 persons per year. An age-standardized rate is the rate that a population would have if it had a standard age structure. (Globocon, WHO 2008, Cancer Facts Sheet).

(i) Inhibition of cell proliferation and metastasis (ii) Induced apoptosis (iii) Overcoming MDRs, (iv) Tumour suppression. The effects of curcumin, in inducing the above roles both by direct and indirect effect on molecules have been extensively studied in different cancer and cell lines **(Fig-3).** Curcumin has been reported to play a dominant role in the prevention of different types of cancer by promoting apoptosis or by inhibiting cell proliferation.

In pituitary cancer, curcumin has been reported to inhibit cell proliferation (Schaaf *et al.,* 2009; Schaaf *et al.,* 2010) by decreased cyclin D3 expression thus affecting cell cycle G_1 to S transition and suppressed growth hormone (GH) levels like chymothypsin prolactins and enhanced the growth-inhibitory effect of low concentrations of bromocriptine. It is also known to induce apoptosis by decreased phosphorylation of retinoblastoma protein (Rb), and block clonogenicity of tumor cells (Miller *et al.,* 2008) thus enabling cancer prevention.

In colon carcinoma, curcumin inhibits tumor growth by increased apoptosis through the expression of cyclooxygenase-2 (COX-2) and inhibition of proteasomal chymothypsin-like activity thereby leading to accumulation of ubiquitinated proteins and proteasome target proteins IκB-α, p27, and p21/Bax leading to apoptosis (Milacic *et al*., 2008), activation of Reactive Oxygen Species (ROS) (Lee YJ *et al.,* 2011) and, suppression of mitochondrial NADP(+)-dependent isocitrate dehydrogenase activity (Jung KH *et al*., 2011). Curcumin also inhibits tumor cell proliferation by promoting cell cycle arrest in the G1 phase manifested by decreased levels of PCNA, Cyclin D1, C-Myc, and Bcl-2, Nuclear Factor kappa B, NF-kB-regulated

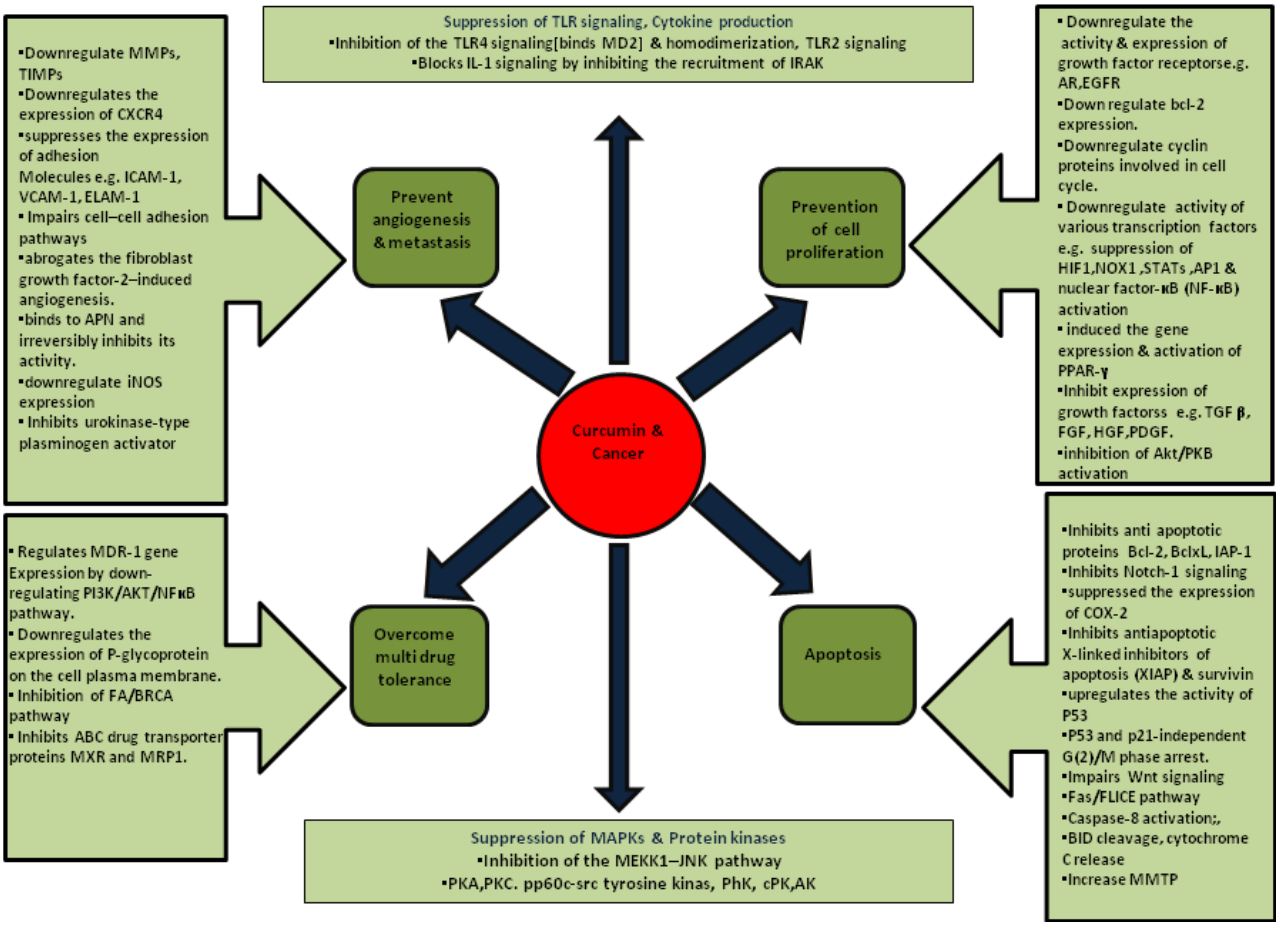

Fig 3: Curcumin and Cancer: Biomolecules and Pathways

Table 1: Natural Products and Cancer Research: Recent Developments

Major source of Natural Product	Examples and References
Bacteria	Bacterial products (Wang C *et al.,* 2011), Largazole, from the marine cyanobacterium *Symploca* species (Li S *et al.,* 2011), Marine cyanobacterium *Lyngbya majuscule (*Tripathi *et al.,* 2011).
Algae	Red sea weeds (Ahmed *et al.,* 2011), Alga (Shalaby *et al.,* 2011)
Fungus	Endophytic fungal strain(Wang XN *et al.*, 2011), Halophilic actinomycete *Actinopolyspora erythraea* YIM 90600(Zhao *et al.*, 2011), Mushroom(Jiang *et al.,* 2010).
Herbs	Chinese herbs (Eichhorn *et al.,* 2011), Thunder god vine or *Tripterygium wilfordii* Hook. F. (Liu Z *et al.,* 2011), Herbal flavenoids(Liu PX *et al.,* 2011), lipid-soluble ginseng extract (LSGE)(Kang *et al,* 2011), *Phyllanthus urinaria (*Huang ST *et al.,* 2010).
Higher plants	Curcumin(Aggarwal *et al.,* 2007; Basnet *et al.,* 2011), Rhizome of *Cnidium officinale(*Bae *et al.,* 2011), *Hypoestes forskaolii*, *Withania somnifera*, *Solanum glabratum, Adenium obesum, Pistacia vera oleoresin*, *Caralluma quadrangula, Eulophia petersii, Phragmanthera austroarabica*, and *Asparagus officinalis(*Almehdar *et al.,* 2011), Terpenoids(Kuttan *et al.,* 2011), *Salvia officinalis L.* (sage) essential oil(Sertel *et al.,* 2011) Xanthone V(1) and 2-acetylfuro-1,4-naphthoquinone(Kuete *et al.*, 2011), Pomegranate extract(Nair *et al.,* 2011), Tea polyphenols(Singh M *et al.,* 2011; Chen D *et al.,* 2011), green tea extract (Chen D *et al.,* 2011; Cross *et al.,* 2011; Vu *et al.,* 2010; Lopez-Lazaro *et al.,* 2011; Liu X *et al.*, 2011), catechins from green tea(Shimizu *et al.*, 2011), methanolic leaf extract of *Indigofera cassioides* (MEIC)(Kumar *et al.*, 2011), phenolic compound from the wood of *Millettia leucantha(*Rayanil *et al.*, 2011), triterpenoid from the leaves of *Sinojackia sarcocarpa(*Wang O *et al.,* 2011), Phytochemicals green tea polyphenols (epigallocatechin gallate)(Wahl *et al.*, 2011), isoflavins from soy bean(Szliszka *et al.*, 2011; Jung *et al.*, 2011), biflavonoid amentoflavone(Lee S *et al.*, 2011), flesh of avocado fruits(D'Ambrosio *et al.*, 2011), polyphenolic compounds isolated from the leaves of *Leucenia leucocephala (*Haggag *et al.*, 2011), extracts of *Xanthium strumarium* (Cocklebur)(Takeda *et al.*, 2011), extracts from root bark of *Juglans Regia L.* (RBJR) (Hasan *et al.*, 2011), red beetroot (*Beta vulgaris L.*) extract(Kapadia *et al.*, 2011), Moringa oleifera leaf extract(Sreelatha *et al.*, 2011), Solvent extracts from the aerial and root parts and seed oil from E. sativa (rocket salad)(Khoobchandani *et al.*, 2011), *Toona sinensis* (leaf extracts)(Hseu *et al.*, 2011), water extract from *Mahonia bealei* (Fort.) Carr. Leaves (Hu *et al.*, 2011), Palm tocotrienols(Selvaduray *et al.*, 2010), Gugulipid (GL), extract from medicinal plant *Commiphora mukul (*Xiao D *et al.*, 2011), Methanol extracts of leaves of *Alnus sieboldiana(*Ludwiczuk *et al.*, 2011), ginger (*Zingiber officinale Roscoe*) (Tuntiwechapikul *et al.*, 2010), extract from black rice(Hui *et al.*, 2010), Cacao (*Theobroma cacao L.*)(Preza *et al.*, 2010), Periwinkle (*Catharanthus roseus*)(Liscombe *et al.*, 2010), *Panax stipuleanatus* rhizomes(Liang *et al.*, 2010), root extract of *Polygala senega(*Paul *et al.*, 2010), Black pepper (*Piper nigrum*) (Liu Y *et al.*, 2010), organic extracts of mulberry (*Morus alba L.*) leaves(Naowaratwattana *et al.*, 2010), *Phyllanthus emblica L.(*Ngamkitidechakul *et al.*, 2010), dry olive leaf extract(Mijatovic *et al.*, 2011), Cedrus deodara lignins(Saxena *et al.*, 2010).

(Chen C *et al.*, 2011). It is known to induce DNA damage and cause S and G2/M arrest in the cell cycle (Lu JJ *et al.*, 2012) .

In breast cancer, curcumin is reported to prevent tumor growth by causing cell cycle arrest by inhibiting cyclin-dependent kinase (cdk) activity, suppressing cyclin D1 and cyclin E expression (Mukhopadhyay *et al.*, 2002), increasing levels of cdk inhibitors p21 and p27, inducing p53 transcriptional activity (Aggarwal *et al.*, 2007; Sen *et al.*, 2011), inhibition of matrix metalloproteinase-3 secretion (Boonrao *et al.*, 2010) and induce apoptosis by induction of Bax pathway (Choudhuri *et al.*, 2002). It is also reported to cause DNA damage and apoptosis in association with increased expression, phosphorylation, and cytoplasmic retention of the Breast cancer protein BRCA1 protein- a tumor suppressor protein which is a critical mediator of DNA repair in response to double-strand breaks (Rowe *et al.*, 2009).

In bladder cancer, curcumin has been reported to prevent tumor cell growth and induces apoptosis (Saini *et al.*, 2011) via decreased expression of the proapoptotic protein survivin and the angiogenic proteins vascular endothelial growth factor (VEGF) and VEGF receptor 1 (VEGFR1) (Chadalapaka *et al.*, 2008). In Acute Myeloid Leukemia (AML), curcumin promotes apoptosis and inhibit cell proliferation (Rao *et al.*, 2011) and is reported to inhibit telomerase activity in human leukemia cell HL-60 (Mukherjee *et al.*, 2007). In skin cancer, curcumin inhibits tumor progression by inhibiting the mammalian target for rapamycin or mTOR pathway (Phillips *et al.*, 2011).

In gastric cancer, curcumin suppresses cancer cell proliferation and invasion via down-regulation of P 21 activated kinase 1(PAK1) activity and cyclin D1 expression (Cai *et al.*, 2009) and overcome MDR (Tang *et al.*, 2005) and inhibits proliferation by affecting the cell cycle (Moragoda *et al.*, 2001). In ovarian carcinoma curcumin has been reported to inhibit tumor growth and angiogenesis via nuclear factor-kappa B pathway (Lin *et al.*, 2007). Curcumin has been reported to induce apoptosis in nasopharyngeal cancers by activation of Reactive Oxygen Species (ROS), mitochondrial depolarization and caspase 3 dependant pathways and prevents tumor cell growth and alters the phenotype of migratory cells (Kuo *et al.*, 2011; Wang *et al.*, 2011a; Wang *et al.*, 2011b; Wong *et al.*, 2010).

In liver cancer, curcumin has been reported to cause cell death and promote mitochondria mediated apoptosis (Qian *et al.*, 2011) and inhibits tumor cell growth (Cheng *et al.*, 2010; Ning *et al.*, 2009). Curcumin has been reported to induce apoptosis in pancreatic cancer (Sahu *et al.*, 2009). to inhibit matrix metalloproteinase protein-2, MMP-2 in human laryngeal squamous carcinoma cells (Mitra *et al.*, 2006) promote apoptosis in human lung adenocarcinoma cells (Zhang J *et al.*, 2010) by DNA damage (Saha *et al.*, 2010), caspase pathways and ER Stress mechanisms (Wu *et al.*, 2010). Curcumin has been reported to inhibit growth of uterine (Tsuiji *et al.*, 2011), ovarian cancer (Saydmohammed *et al.*, 2010; Watson *et al.*, 2010; Seo *et al.*, 2010), brain and nervous system cancer (Zanotto-Filho *et al.*, 2011; Spiller *et al.*, 2011). It is known to cause apoptosis and prevent cell growth in Hodgekins lymphoma (Mackenzie *et al.*, 2008), lymphoma (Vishvakarma *et al.*, 2011; Zhang *et al.*, 2010; Li *et al.*, 2009; Xiao *et al.*, 2010; Zhongguo *et al.*, 2008) and esophageal cancers (O'Sullivan-Coyne *et al.*, 2009; Tian *et al.*, 2008). It is reported to participate in mechanisms aiding in overcoming MDR in multiple myeloma (Xiao *et al.*, 2010). The overall effect of curcumin in different cancer has been summarized in **Table-2.**

Curcumin formulations and recent developments

Although curcumin offers promise to cancer research over the conventional toxic chemotherapeutic drugs, the main disadvantage of applicability of curcumin in disease therapy is its lipophilic nature and poor aqueous solubility, minimum bioavailability and

Table 2: Major effects of Curcumin and its derivatives in different Cancers

Role of curcumin	Target molecules/pathways		Cancer
	Direct	Indirect	
Overcome drug resistance	ABC transporter TLR4 dimerization IκBα kinase Cyclooxygenase-2 Protein kinase C Protein kinase A Phosphorylase kinase pp60c-src tyrosine kinase Ca2+-dependent protein kinase Xanthine oxidase Ca2+-ATPase of sarcoplasmic reticulum Inositol 1,4, 5-triphosphate receptor (Shrikanth *et al*,1994)	p53-p300 cross-talk leading to cell death pathway	Breast cancer(Sen *et al.*, 2011)
		Proteasome pathway	Multiple myeloma(Mujtaba *et al*., 2012)
		Down-regulating the activity of NF-κB	Gastric cancer cells (Tang *et al.*, 2005; Yu LL *et al*., 2011)
		Decrease of pro-caspase 3 pro-caspase 9, increase of PARP cleavage and the ratio of Bax/Bcl-xL	K562/A02(Lu JJ *et al.*, 2012)
Epigenetic		Demethylation of the Neurog1 gene and restored the expression of this cancer-related CpG-methylation epigenome marker gene	Prostate cancer(Shu *et al.*, 2011)
		Down Regulation of histone deacetylases, histone acetyltransferases, DNA methyltransferase I, and miRNAs	Cancer(Reuter *et al.*, 2011)
Apoptosis		Activation of Apoptosis pathways	Prostate cancer(Yallapu *et al.*, 2011b)
		Induce apoptosis by decreased phosphorylation of Retinoblastoma (Rb).	Pituitary tumour(Schaaf *et al*, 2010)
		Activation of ROS pathway, DNA damage mitochondria-mediated and ER stress-dependent pathways.	Myelomonocytic leukemia (Huang *et al.*, 2011)
		Down Regulation of caspase cascade	Breast cancer cell line(Zong *et al.*, 2011)
		Down-regulation of Bcl-2 and procaspase-3 and increased production of reactive oxygen species (ROS) level	Adenocarcinoma cell line (Ibrahim *et al.*, 2008)
		Increasing Bax expression, decreasing the expression of Bcl-2 and Bcl-xL, decreasing mitochondrial membrane potential, increased ROS	Small Cell Lung Cancer (Yang *et al.*, 2011)
		ROS level Up regulation of Bax and down regulation of Bcl-2, mitochondrial dysfunction	Human nasopharyngeal carcinoma cells (Kuo *et al.*, 2011)
		Bcr-Abl suppression	Chronic myeloid leukemia (Acharya *et al*, 2011)
		Down regulation of NF-κB expression	Oesophageal cancer (Tian *et al.*, 2008)
		Proapoptotic via cytotoxicity of Cum-np	Rat C6 glioma cells (Shao *et al.*, 2011)
		FAS/caspase-8 (extrinsic) pathway and ER stress proteins, growth arrest- and DNA damage-inducible gene 153 (GADD153) and glucose-regulated protein 78 (GRP78)	Human non-small cell lung cancer cells (Wu *et al.*, 2010)
		Induction of apoptosis by cleavage of PARP, caspase-3, and reduction in Bcl-XL levels	Gastric and colon cancer (Moragoda *et al.*, 2001)
Inhibits invasion and metastasis		Down-regulating the NF-kB transcription factor	Human mammary epithelial carcinoma MCF-7 cells (Zong *et al.*, 2011)
		Down regulation of Matrix metalloproteinase-3 (MMP-3)	Human invasive breast carcinoma cells (Yallapu et al, 2010b)
Tumor suppression		Induces a tumor-suppressive miRNA, miR-203	Bladder cancer (Rejinold *et al.*, 2011c)
		Reduces SCC-4 cell invasion, leads to the recruitment of alpha-tubulin.	Human tongue squamous cell carcinoma (Chen JW *et al*,, 2011)
		Inhibits tumor growth by inhibiting angiogenesis	Colon cancer (Gou *et al.*, 2011)
		Inhibition of STAT3 signaling pathway via LLL12 and FLLL32, down regulation of cyclin D1, Bcl-xL	Human rhabdomyosarcoma cells (Wei *et al.*, 2011)
		Inhibits tumor cell proliferation	Jurkat cell lines (Yadav *et al.*, 2010)
		Inhibition of Activation of nuclear factor-kappaB	Pancreatic cancer (Bisht *et al.*, 2010)
		Disturbed mitotic spindle structure, activated mitotic check points	MCF-7 cells (Banerjee *et al.*, 2010)
		G1/S arrest	Drug resistant AML cell lines (Rao *et al.*, 2011)
		Inhibition of NF-kB signaling	Medulloblastoma (Spiller *et al.*, 2011)

targeted delivery to the transformed cell.

Different formulations and delivery devices are being tested to enable curcumin as an effective agent in cancer management. Biocompatible urithin polymers (PU) from polylactic acids and hexamethylene diamide (Selvaraj *et al*., 2011), liposomes coated with N-trimethyl chitosan chloride (TMC) (Chen H *et al.,* 2011) have been reported to function as efficient formulations. Cationic and anionic curcumin conjugates by anchoring curcumin (Cur) onto poly (vinylpyrroidone) (PVP-Cur) and onto hyaluronic acid (HA-Cur) (Manju *et al.,* 2011b) are also being exploited. Delivery through formulations like niosomes (Rungphanichkul *et al.,* 2011), amphiphilic polymers like Lauroyl sulphated chitosan (LSCS) (Shelma *et al.,* 2011) and carboxy methyl derivatives (Anitha *et al.,* 2011), fibrinogen nanoparticles (CRC-FNPs) (Rejinold *et al.,* 2011a), nanospheres (Mukerjee *et al*., 2009), 2-Hydroxypropyl-γ-cyclodextrin/curcumin-liposomal nanoparticles (Dhule *et al.,* 2011) have been reported to be effective. Nanoparticles (Li R *et al.,* 2011; Yallapu *et al.,* 2010a; Yallapu *et al.,* 2010b) reported for their biocompatible, non toxic, biodegradable nature and thermoresponsive properties (Rejinold *et al.,* 2011c) have shown positive results in curcumin delivery. Conjugated nanoparticle copolymers with Chitosan-g-poly (N-isopropylacrylamide) nanoparticles (Rejinold *et al*., 2011b), amphilic methoxy polyethylene glycol-poly (caprolactone) (mPEG-PCL) are being employed (Shao *et al*., 2011). Magnetic particles are being tested for controlled drug delivery (Koppolu *et al*., 2010; Chin *et al*., 2010; de-Souza *et al*., 2011).

Strategies to increase the solubility of analogues of curcumin (Zhang *et al*., 2011), lipid-based formulations (Thangapazham *et al.,* 2008; Yu *et al*., 2011; Setthacheewakul *et al.*, 2011; Xie *et al.*, 2011), nanosuspensions (Zhang H et al, 2011), liposomes (Chen H *et al.,* 2011; Dhule *et al.,* 2011; Li *et al.*, 2005; Mach *et al*, 2009; Pandelidou *et al.,* 2011; Agashe *et al.,* 2011), microemulsions (Liu CH *et al.,* 2011), polymer encapsulations (Mohanty *et al.,* 2010; Sahu *et al.,* 2011; Das *et al.,* 2010), aerosols (Selvam *et al.,* 2011), and nanodisks (Singh AT *et al*., 2011; Tadmor *et al.,* 2011; Ghosh *et al*., 2011) are being tested as delivery formulations of curcumin in different cancer.

Few reports on targeted delivery (Thamake *et al.,* 2011) of curcumin exists. Tissue specific targeting are being tested like curcumin loaded Eudragit® S100 coated calcium pectinate microsphere in colon cancer (Zhang L *et al*., 2011). Reports on the use of Gelatin microspheres (C-GMS) in lung cancer (Cao *et al.,* 2011) and Gelucire44/14 in eyes (Liu R *et al*., 2011) have shown promising results. The application of different formulations of curcumin in different cancer is summarized in **Table-3**.

DISCUSSIONS

Curcumin has shown strong reports in its anti-cancerous activities in different malignancies including brain, skin, lung, prostate, breast, ovarian, liver, nasopharyngeal, gastrointestinal, pancreatic and colorectal cancers. Synergistic effects of curcumin with agents like decetaxel has also been reported in lung cancer (Yin *et al.,* 2011). However, because of its both pro and anti-oxidant effect, it has been reported to behave like a "double edged sword". (Kawanishi *et al*., 2005) and its safety as a chemopreventive agent remains yet to be exploited. The future scope of this review remains in potential applications of targeted cancer cell killing by a natural product like curcumin.

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Table 3: Curcumin and Formulations : Cancer Research

Cancer	Delivery Systems
Lung adenocarcinoma H441 cells and nude rats bearing xenograft H441 tumors	Cyclodextrin entrapped curcuminoid derivative(Agashe *et al*., 2011)
Skin cancer	Micro emulsions for transdermal delivery(Liu *et al.*, 2011)
Non small cell lung cancer	Intravenous synergistic with Docetaxel(Yin *et al.*, 2011)
Lung cancer cells	Matrix of Urethane polymers (PU) prepared from low-molecular weight polylactic acid (PLA) and hexamethylene diisocyanate (HMDI) curcumin-containing PU membranes(Selvaraj *et al*., 2011)
Glioma cells and Caco-2 cells	Magnetic nanoparticles (MNPs) (Manju *et al.*, 2011a)
L929 (mouse fibroblast), PC3 (prostate) and MCF7 (breast) cancer cell lines	Fibrinogen nanoparticles (Rejinold *et al.*, 2011b)
Tumor mice model	Curcuminoids-loaded solid lipid nanoparticles (curcuminoids-SLNs) and curcumin-loaded solid lipid nanoparticles (curcumin-SLNs)(Li *et al.*, 2005)
Osteosarcoma	Liposomal nanoparticles(Dhule *et al.*, 2011)
Cancer cells	N,O-Carboxymethyl Chitosan Nanoparticles(Anitha *et al.*, 2011)
Bcr-Abl + leukemia cells	Nanoparticles(Acharya et al, 2011)
PC3, L929 cells	Biocompatible thermoresponsive polymeric chitosan-g-poly (N-vinylcaprolactam) nanoparticles (TRC-NPs)(Rejinold *et al.*, 2011c)
Colorectal cell lines	Lyophilised egg PC liposomes (Pandelidou *et al.*, 2011)
C6 Glioma cells	Methoxy polyethylene glycol-poly (caprolactone) nanoparticles (Shao et al, 2011)
3T3-L1 preadipocytes and adipocytes	Conjugated with Polyethylene glycol (Kim *et al.*, 2011)
Breast cells	Surface functionalized polymeric PLGA nanoparticles by non-covalent insertion of a homo-bifunctional chemical crosslinker, bis(sulfosuccinimidyl) suberate (BS3) for targeted cancer therapy (Thamake *et al.*, 2011)
L929 cells	Hollow microcapsules (Manju *et al.*, 2011 b)
Cisplatin resistant A2780CP ovarian and metastatic MDA-MB-231 breast cancer cells	Encapsulated PGLA formulation (Yallapu *et al.*, 2010a)
Prostrate cancer	Poly(β-cyclodextrin)/curcumin self-assembly (Yallapu *et al*., 2010b), Nanoparticles (Thangapazham et al, 2008), cellulose nanoparticles (Yallapu *et al*.,, 2011a), PGLA nanospheres (Mukerjee *et al.*, 2009)
Sub cutaneous injection in mice	A biodegradable and biocompatible polymer, poly (d,l-lactide-co-glycolide), was used to fabricate curcumin microparticles (Shahani *et al*., 2010)
Pancreatic cell lines MIA PaCa-2 and PANC-1	Encapsulated methoxy poly (ethylene glycol) (MePEG)/poly-epsilon-caprolactone (PCL) diblock copolymeric micelle (Mohanty *et al*., 2010)
Hela cells	Micelles of Pluronic encapsulated curcumin (Sahu *et al.*, 2011), Alginate-chitosan-pluronic composite nanoparticles (Das *et al.*, 2010)
Pancreatic cancer	Liposome mediated (Li *et al.*, 2005)

REFERENCES

Acharya S, Sahoo SK. 2011. Sustained targeting of Bcr-Abl + leukemia cells by synergistic action of dual drug loaded nanoparticles and its implication for leukemia therapy. Biomaterials., 32:5643-5662.

Agashe H, Sahoo K, Lagisetty P, Awasthi V. 2011. Cyclodextrin-mediated entrapment of curcuminoid 4-[3,5-bis(2-chlorobenzylidene-4-oxo-piperidine-1-yl)-4-oxo-2-butenoic acid] or CLEFMA in liposomes for treatment of xenograft lung tumor in rats. Colloids Surf B Biointerfaces., 84:329-337.

Aggarwal BB, Banerjee S, Bharadwaj U, Sung B, Shishodia S, Sethi G. 2007. Curcumin induces the degradation of cyclin E expression through ubiquitin-dependent pathway and up-regulates cyclin-dependent kinase inhibitors p21 and p27 in multiple human tumor cell lines. Biochem Pharmacol., 73:1024-1032.

Aggarwal BB, Kumar A, Bharti AC. 2003. Anticancer potential of curcumin: preclinical and clinical studies. Anticancer Res., 23:363-398.

Aggarwal Bharat B, Surh Young-Joon, Shishodia Shishir. 2007. The molecular targets and therapeutic uses of curcumin in health and disease. Springer Science pub., 1-47.

Ahmed HH, Hegazi MM, Abd-Alla HI, Eskander EF, Ellithey MS. Z. 2011. Antitumour and antioxidant activity of some Red Sea seaweeds in Ehrlich ascites carcinoma in vivo. Z Naturforsch C., 66:367-376.

Almehdar H, Abdallah HM, Osman AM, Abdel-Sattar EA. 2011. In vitro cytotoxic screening of selected Saudi medicinal plants. J Nat Med., Sep 28.

Anitha A, Maya S, Deepa N, Chennazhi KP, Nair SV, Jayakumar R. 2011. Curcumin-Loaded N,O-Carboxymethyl Chitosan Nanoparticles for Cancer Drug Delivery, J Biomater Sci Polym Ed. Jun 28.

Arora RB, Kapoor V, Basu N, and Jain AP. 1973. Anti-inflammatory studies on Curcuma longa (turmeric). Indian J Med Res., 59:1289-1295.

Bae KE, Choi YW, Kim ST, Kim YK. 2011. Components of Rhizome Extract of Cnidium officinale Makino and Their In vitro Biological Effects. Molecules., 16:8833-8847.

Banerjee M, Singh P, and Panda D. 2010. Curcumin suppresses the dynamic instability of microtubules, activates the mitotic checkpoint and induces apoptosis in MCF-7 cells. FEBS J., 277(16):3437-3448.

Basnet P, Skalko-Basnet N. 2011. Curcumin: An anti-inflammatory molecule from a curry spice on the path to cancer treatment. Molecules., 16:4567-4598.

Bierhaus A, Zhang Y, Quehenberger P, Luther T, Haase M, Müller M, Mackman N, Ziegler R, Nawroth PP. 1997. The dietary pigment curcumin reduces endothelial tissue factor gene expression by inhibiting binding of AP-1 to the DNA and activation of NF-kappa B. Thromb Haemost., 77:772-782.

Bisht S, Mizuma M, Feldmann G, Ottenhof NA, Hong SM, Pramanik D, Chenna V, Karikari C, Sharma R, Goggins MG, Rudek MA, Ravi R, Maitra A, Maitra A. 2010. Systemic administration of polymeric nanoparticle-encapsulated curcumin (NanoCurc) blocks tumor growth and metastases in preclinical models of pancreatic cancer. Mol Cancer Ther., 9:2255-2264.

Boonrao M, Yodkeeree S, Ampasavate C, Anuchapreeda S, Limtrakul P. 2010. The inhibitory effect of turmeric curcuminoids on matrix metalloproteinase-3 secretion in human invasive breast carcinoma cells. Arch Pharm Res., 33:989-998.

Brouet I, Ohshima H. 1995. Curcumin, an anti-tumour promoter and anti-inflammatory agent, inhibits induction of nitric oxide synthase in activated macrophages,

Biochem Biophys Res Commun., 206:533-540.

Cai XZ, Wang J, Li XD, Wang GL, Liu FN, Cheng MS, and Li F. 2009. Curcumin suppresses proliferation and invasion in human gastric cancer cells by downregulation of PAK1 activity and cyclin D1 expression. Cancer Biol Ther., 8:1360-1368.

Cao F, Ding B, Sun M, Guo C, Zhang L, Zhai G. 2011. Lung-targeted delivery system of curcumin loaded gelatin microspheres. Drug Deliv 18:545-554.

Chadalapaka G, Jutooru I, Chintharlapalli S, Papineni S, Smith R , Li X, Safe S**. 2008.** Curcumin decreases specificity protein expression in bladder cancer cells. Cancer Res 68:5345-5354.

Chen C, Liu Y, Chen Y, Xu J. 2011. C086, a novel analog of curcumin, induces growth inhibition and down -regulation of NFκB in colon cancer cells and xenograft tumors. Cancer Biol Ther.,12:797-807.

Chen D, Wan SB, Yang H, Yuan J, Chan TH, Dou QP. 2011. EGCG, green tea polyphenols and their synthetic analogs and prodrugs for human cancer prevention and treatment. Adv Clin Chem., 53:155-177.

Chen H, Wu J, Sun M, Guo C, Yu A, Cao F, Zhao L, Tan Q, Zhai G. 2011. N-trimethyl chitosan chloride-coated liposomes for the oral delivery of curcumin. J Liposome Res., Oct 18.

Chen JW, Tang YL, Liu H, Zhu ZY, Lü D, Geng N, Chen Y. 2011. [Anti-proliferative and anti-metastatic effects of curcumin on oral cancer cells]. [Article in Chinese] Hua Xi Kou Qiang Yi Xue Za Zhi., 29:83-86.

Cheng CY, Lin YH, Su CC. 2010. Curcumin inhibits the proliferation of human hepatocellular carcinoma J5 cells by inducing endoplasmic reticulum stress and mitochondrial dysfunction. Int J Mol Med., 26:673-678.

Chin SF, Iyer KS, Saunders M, St Pierre TG, Buckley C, Paskevicius M, Raston CL. 2010. Encapsulation and sustained release of curcumin using superparamagnetic silica reservoirs. Chemistry., 15:5661 -5665.

Choudhuri T, Pal S, Agwarwal ML, Das T and Sa G. 2002. Curcumin induces apoptosis in human breast cancer cells through p53-dependent Bax induction. FEBS Lett., 512:334-340.

Cross SE, Jin YS, Lu QY, Rao J, Gimzewski JK. 2011. Green tea extract selectively targets nanomechanics of live metastatic cancer cells. Nanotechnology., 22:215101.

Dai J, Mumper RJ. 2010. Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. Molecules., 15:7313-7352.

D'Ambrosio SM, Han C, Pan L, Kinghorn AD, Ding H. 2011. Aliphatic acetogenin constituents of avocado fruits inhibit human oral cancer cell proliferation by targeting the EGFR/RAS/RAF/MEK/ERK1/2 pathway. Biochem Biophys Res Commun., 409:465-469.

Das RK, Kasoju N, Bora U. 2011. Encapsulation of curcumin in alginate-chitosan-pluronic composite nanoparticles for delivery to cancer cells. Nanomedicine., 6:153-160.

De Souza FF, dos Santos MC, dos Passos DC, Lima EC, Guillo LA. 2011. Curcumin associated magnetite nanoparticles inhibit in vitro melanoma cell growth. J Nanosci Nanotechnol., 11:7603-7610.

Dhule SS, Penfornis P, Frazier T, Walker R, Feldman J, Tan G, He J, Alb A, John V, Pochampally R. 2011. Curcumin-loaded γ-cyclodextrin liposomal nanoparticles as delivery vehicles for osteosarcoma. Nanomedicine., Aug 10.

Dutta V. 2011. Chemotherapy, neurotoxicity, and cognitive changes in breast cancer J Cancer Res Ther., 7:264-269.

Eichhorn T, Efferth T. 2011. P-glycoprotein and its inhibition in tumors by phytochemicals derived from Chinese herbal medicine, J Ethnopharmacol.,

Fardell JE, Vardy J, Johnston IN, Winocur G. 2011. Chemotherapy and cognitive impairment: treatment options , Clin Pharmacol Ther., 90:366-376.

Ghosh M, Singh AT, Xu W, Sulchek T, Gordon LI, Ryan RO. 2011. Curcumin nanodisks: formulation and characterization, Nanomedicine., 7:162-167.

Gou M, Men K, Shi H, Xiang M, Zhang J, Song J, Long J, Wan Y, Luo F, Zhao X, Qian Z. 2011. Curcumin-loaded biodegradable polymeric micelles for colon cancer therapy in vitro and in vivo. Nanoscale., 3:1558-1567.

Haggag EG, Kamal AM, Abdelhady MI, El-Sayed MM, El-Wakil EA, Abd-El-Hamed SS. 2011. Antioxidant and cytotoxic activity of polyphenolic compounds isolated from the leaves of Leucenia leucocephala. Pharm Biol., 49:1103-1113.

Hahm ER, Gho YS, Park S, Park C, Kim KW, Yang CH. 2004. Synthetic curcumin analogs inhibit activator protein-1 transcription and tumor-induced angiogenesis. Biochem Biophys Res Commun., 321:337-344.

Hasan TN, B LG, Shafi G, Al-Hazzani AA, Alshatwi AA. 2011. Anti-proliferative effects of organic extracts from root bark of Juglans Regia L. (RBJR) on MDA-MB -231 human breast cancer cells: role of Bcl-2/Bax, caspases and Tp53. Asian Pac J Cancer Prev., 12:525-530.

Hseu YC, Chen SC, Lin WH, Hung DZ, Lin MK, Kuo YH, Wang MT, Cho HJ, Wang L, Yang HL. 2011. Toona sinensis (leaf extracts) inhibit vascular endothelial growth factor (VEGF)-induced angiogenesis in vascular endothelial cells. J Ethnopharmacol., 134:111 -121. http://www.globocan.iarc.fr/.

Hu W, Yu L, and Wang MH. 2011. Antioxidant and antiproliferative properties of water extract from Mahonia bealei (Fort.) Carr. Leaves. Food Chem Toxicol., 49:799-806.

Huang AC, Chang CL, Yu CS, Chen PY, Yang JS, Ji BC, Lin TP, Chiu CF, Yeh SP, Huang YP, Lien JC, Chung JG. 2011. Induction of apoptosis by curcumin in murine myelomonocytic leukemia WEHI-3 cells is mediated via endoplasmic reticulum stress and mitochondria-dependent pathways, Environ Toxicol., Jul 26.

Huang ST, Pang JH, and Yang RC. 2010. Anti-cancer effects of Phyllanthus urinaria and relevant mechanisms. Chang Gung Med J., 3:477-487.

Hui C, Bin Y, Xiaoping Y, Long Y, Chunye C, Mantian M, Wenhua L. 2010. Anticancer activities of an anthocyanin-rich extract from black rice against breast cancer cells in vitro and in vivo. Nutr Cancer., 62:1128-1136.

Ibrahim A, El-Meligy A, Lungu G, Fetaih H, Dessouki A, Stoica G, Barhoumi R. 2008. Curcumin induces apoptosis in a murine mammary gland adenocarcinoma cell line through the mitochondrial pathway. Eur J Pharmacol., 668:127-132.

Jiang J, Sliva D. 2010. Novel medicinal mushroom blend suppresses growth and invasiveness of human breast cancer cells. Int J Oncol., 37:1529-1536.

Jobin C, Bradham CA, Russo MP, Juma B, Narula AS, Brenner DA, Sartor RB. 1999. Curcumin blocks cytokine-mediated NF-kappa B activation and proinflammatory gene expression by inhibiting inhibitory factor I-kappa B kinase activity. J Immunol., 163:3474-

3483.

Jung KH, Park JW. 2011. Suppression of mitochondrial NADP (+)-dependent isocitrate dehydrogenase activity enhances curcumin-induced apoptosis in HCT116 cells. Free Radic Res., 45:431-438.

Jung MY, Choi NJ, Oh CH, Shin HK, and Yoon SH. 2011. Selectively hydrogenated soybean oil exerts strong anti-prostate cancer activities. Lipids, 46:287-295.

Kang MR, Kim HM, Kang JS, Lee K, Lee SD, Hyun DH, In MJ, Park SK, Kim DC. 2011. Lipid-soluble ginseng extract induces apoptosis and G0/G1 cell cycle arrest in NCI-H460 human lung cancer cells. Plant Foods Hum Nutr., 66:101-106.

Kapadia GJ, Azuine MA, Rao GS, Arai T, Iida A, Tokuda H. 2011. Cytotoxic effect of the red beetroot (Beta vulgaris L.) extract compared to doxorubicin (Adriamycin) in the human prostate (PC-3) and breast (MCF-7) cancer cell lines. Anticancer Agents Med Chem., 11:280-284.

Kawanishi S, Oikawa S, Murata M. 2005. Evaluation for safety of antioxidant chemopreventive agents. Antioxid Redox Signal.7:1728-39.

Khoobchandani M, Ganesh N, Gabbanini S, Valgimigli L, Srivastava MM. 2011. Phytochemical potential of Eruca sativa for inhibition of melanoma tumor growth. Fitoterapia .,82:647-653.

Kim CY, Bordenave N, Ferruzzi MG, Safavy A, Kim KH. 2011. Modification of curcumin with polyethylene glycol enhances the delivery of curcumin in preadipocytes and its antiadipogenic property. J Agric Food Chem., 59:1012-1019.

Kinghorn AD, Pan L, Fletcher JN, Chai H. 2011. The relevance of higher plants in lead compound discovery programs V J Nat Prod .,74:1539-1555.

Koppolu B, Rahimi M, Nattama S, Wadajkar A, Nguyen KT. 2010. Development of multiple-layer polymeric particles for targeted and controlled drug delivery. Nanomedicine., 6:355-361.

Korutla L, Kumar R. 1994. Inhibitory effect of curcumin on epidermal growth factor receptor kinase activity in A431 cells. Biochim Biophys Acta., 1224:597 -600.

Kuete V, Wabo HK, Eyong KO, Feussi MT, Wiench B, Krusche B, Tane P, Folefoc GN, Efferth T. 2011. Anticancer activities of six selected natural compounds of some Cameroonian medicinal plants, PLoS One., 6:e21762.

Kumar RS, Rajkapoor B, Perumal P. 2011. In vitro and in vivo anticancer activity of Indigofera cassioides Rottl. Ex. DC. Asian Pac J Trop Med., 4:379-385.

Kuo CL, Wu SY, Ip SW, Wu PP, Yu CS, Yang JS, Chen PY, Wu SH, Chung JG. 2011. Apoptotic death in curcumin-treated NPC-TW 076 human nasopharyngeal carcinoma cells is mediated through the ROS, mitochondrial depolarization and caspase-3-dependent signaling responses. Int J Oncol., 39:319-328.

Kuttan G, Pratheesh kumar P, Manu KA, Kuttan R. 2011. Inhibition of tumor progression by naturally occurring terpenoids, Pharm Biol., 49:995-1007.

Lee S, Kim H, Kang JW, Kim JH, Lee DH, Kim MS, Yang Y, Woo ER, Kim YM, Hong J,Yoon DY. 2011. The biflavonoid amentoflavone induces apoptosis via suppressing E7 expression cell cycle arrest at sub-G_1 phase, and mitochondria-emanated intrinsic pathway in human cervical cancer cells. J Med Food., 14:808-816.

Lee YJ, Kim NY, Suh YA, Lee C. 2011. Involvement of ROS in Curcumin-induced Autophagic Cell Death. Korean J Physiol Pharmacol., 15:1-7.

Lee-Sherick AB, Linger RM, Gore L, Keating AK, Graham DK. 2010. Targeting paediatric acute lymphoblastic leukaemia: novel therapies currently in development. Br J Haematol., 151:295-311.

Li L, Braiteh FS, Kurzrock R. 2005. Liposome-encapsulated curcumin: in vitro and in vivo effects on proliferation, apoptosis, signaling, and angiogenesis. Cancer., 104:1322-1331.

Li R, Qiao X, Li Q, He R, Ye M, Xiang C, Lin X, Guo D. 2011. Metabolic and pharmacokinetic studies of curcumin, demethoxycurcumin and bisdemethoxycurcumin in mice tumor after intragastric administration of nanoparticle formulations by liquid chromatography coupled with tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci., 879:2751-2758.

Li S, Yao H, Xu J, Jiang S. 2011. Synthetic routes and biological evaluation of largazole and its analogues as potent histone deacetylase inhibitors, Molecules., 16:4681-4694.

Li ZX, Ouyang KQ, Jiang X, Wang D, Hu Y. 2009. Curcumin induces apoptosis and inhibits growth of human Burkitt's lymphoma in xenograft mouse model. Mol Cells., 27:283-289.

Liang C, Ding Y, Nguyen HT, Kim JA, Boo HJ, Kang HK, Nguyen MC, Kim YH. 2010. Oleanane-type triterpenoids from Panax stipuleanatus and their anticancer activities, Bioorg Med Chem Lett., 20:7110-7115.

Lin YG, Kunnumakkara AB, Nair A, Merritt WM, Han LY, Armaiz-Pena GN, Kamat AA, Spannuth WA, Gershenson DM, Lutgendorf SK, Aggarwal BB, Sood AK. 2007. Curcumin inhibits tumor growth and angiogenesis in ovarian carcinoma by targeting the nuclear factor-kappaB pathway. Clin Cancer Res., 13:3423-3430.

Liscombe DK, Usera AR, and O'Connor SE. 2010. Homolog of tocopherol C methyltransferases catalyzes N methylation in anticancer alkaloid biosynthesis. Proc Natl Acad Sci U S A., 107:18793-18798.

Liu CH, Chang FY. 2011. Development and characterization of eucalyptol microemulsions for topic delivery of curcumin, Chem Pharm Bull (Tokyo)., 59:172-178.

Liu PX, Gao J, Chen YJ, Long W, Shen X, Tang WS. 2011. Anticancer activity of total flavonoids isolated from Xianhe Yanling Recipe. Chin J Integr Med., 17:459-463.

Liu R, Liu Z, Zhang C, Zhang B. 2011. Gelucire44/14 as a novel absorption enhancer for drugs with different hydrophilicities: in vitro and in vivo improvement on transcorneal permeation. J Pharm Sci., 100:3186-3195.

Liu X, Zhang DY, Zhang W, Zhao X, Yuan C, Ye F. 2011. The effect of green tea extract and EGCG on the signaling network in squamous cell carcinoma. Nutr Cancer., 63:466-475.

Liu Y, Yadev VR, Aggarwal BB, Nair MG. 2010. Inhibitory effects of black pepper (Piper nigrum) extracts and compounds on human tumor cell proliferation, cyclooxygenase enzymes, lipid peroxidation and nuclear transcription factor-kappa-B. Nat Prod Commun., 5:1253-1257.

Liu Z, Ma L, and Zhou GB. 2011. The main anticancer bullets of the Chinese medicinal herb, thunder god vine, Molecules., 16:5283-5297.

López-Lázaro M, Calderón-Montaño JM, Burgos-Morón E, Austin CA. 2011. Green tea constituents (-) epigallocatechin-3-gallate (EGCG) and gallic acid induce topoisomerase I- and topoisomerase II-DNA complexes in cells mediated by pyrogallol-induced hydrogen peroxide, Mutagenesis., 26:489-498.

Lu JJ, Cai YJ, Ding J. 2012. The short-time treatment with curcumin sufficiently decreases cell viability, induces apoptosis and copper enhances these effects in multidrug-resistant K562/A02 cells. Mol Cell Biochem., 360:253-260.

Ludwiczuk A, Saha A, Kuzuhara T, Asakawa Y. 2011. Bioactivity guided isolation of anticancer constituents from leaves of Alnus sieboldiana (Betulaceae). Phytomedicine., 18:491-498.

Mach CM, Mathew L, Mosley SA, Kurzrock R, Smith JA. 2009. Determination of minimum effective dose and optimal dosing schedule for liposomal curcumin in a xenograft human pancreatic cancer model. Anticancer Res., 29:1895-1899.

Mackenzie GG, Queisser N, Wolfson ML, Fraga CG, Adamo AM, Oteiza PI. 2008. Curcumin induces cell-arrest and apoptosis in association with the inhibition of constitutively active NF-kappaB and STAT3 pathways in Hodgkin's lymphoma cells, Int J Cancer 123:56-65.

Manju S, Sreenivasan K. 2011a. Enhanced Drug Loading on Magnetic Nanoparticles by Layer-by-Layer Assembly Using Drug Conjugates: Blood Compatibility Evaluation and Targeted Drug Delivery in Cancer Cells. Langmuir., 27:14489-14496.

Manju S, Sreenivasan K. 2011b. Hollow microcapsules built by layer by layer assembly for the encapsulation and sustained release of curcumin, *Colloids* Surf B Biointerfaces., 82:588-593.

Mijatovic SA, Timotijevic GS, Miljkovic DM, Radovic JM, Maksimovic-Ivanic DD, Dekanski DP, Stosic-Grujicic SD. 2011. Multiple antimelanoma potential of dry olive leaf extract. Int J Cancer., 128:1955 -1965.

Milacic V, Banerjee S, Landis-Piwowar KR, Sarkar FH, Majumdar AP, Dou QP. 2008. Curcumin inhibits the proteasome activity in human colon cancer cells in vitro and in vivo. Cancer Res., 68:7283-7292.

Miller M, Chen S, Woodliff J, Kansra S. 2008. Curcumin (diferuloylmethane) inhibits cell proliferation, induces apoptosis, and decreases hormone levels and secretion in pituitary tumor cells. Endocrinology., 149:4158-4167.

Mitra A, Chakrabarti J, Banerji A, Chatterjee A and Das BR. 2006. Curcumin, a potential inhibitor of MMP-2 in human laryngeal squamous carcinoma cells HEp2. J Environ Pathol Toxicol Oncol., 25:679-690.

Mohanty C, Acharya S, Mohanty AK, Dilnawaz F, Sahoo SK. 2010. Curcumin-encapsulated MePEG/PCL diblock copolymeric micelles: a novel controlled delivery vehicle for cancer therapy. Nanomedicine (Lond)., 5:433-449.

Moragoda L, Jaszewski R, Majumdar AP. 2001. Curcumin induced modulation of cell cycle and apoptosis in gastric and colon cancer cells. Anticancer Res., 21:873-878.

Mujtaba T, Kanwar J, Wan SB, Chan TH, Dou QP. 2012. Sensitizing human multiple myeloma cells to the proteasome inhibitor bortezomib by novel curcumin analogs, Int J Mol Med., 29:102-106.

Mukerjee A, Vishwanatha JK. 2009. Formulation, characterization and evaluation of curcumin-loaded PLGA nanospheres for cancer therapy. Anticancer Res., 29:3867-3875.

Mukherjee Nee Chakraborty S, Ghosh U, Bhattacharyya NP, Bhattacharya RK, Dey S,Roy M. 2007. Curcumin-induced apoptosis in human leukemia cell HL-60 is associated with inhibition of telomerase activity. Mol Cell Biochem., 297:31-39.

Mukhopadhyay A, Banerjee S, Stafford LJ, Xia C, Liu M, Aggarwal BB. 2002. Curcumin-induced

suppression of cell proliferation correlates with down-regulation of cyclin D1 expression and CDK4-mediated retinoblastoma protein phosphorylation. Oncogene., 21:8852-8861.

Nair V, Dai Z, Khan M, Ciolino HP. 2011. Pomegranate extract induces cell cycle arrest and alters cellular phenotype of human pancreatic cancer cells, Anticancer Res 31:2699-2704.

Naowaratwattana W, De-Eknamkul W, De Mejia EG. 2010. Phenolic-containing organic extracts of mulberry (Morus alba L.) leaves inhibit HepG2 hepatoma cells through G2/M phase arrest, induction of apoptosis, and inhibition of topoisomerase IIα activity. J Med Food., 13:1045-1056.

Ngamkitidechakul C, Jaijoy K, Hansakul P, Soonthornchareonnon N, Sireeratawong S. 2010. Antitumour effects of Phyllanthus emblica L.: induction of cancer cell apoptosis and inhibition of in vivo tumour promotion and in vitro invasion of human cancer cells. Phytother Res., 24:1405-1413.

Ning L, Wentworth L, Chen H, Weber SM. 2009. Down-regulation of Notch1 signaling inhibits tumor growth in human hepatocellular carcinoma. Am J Transl Res., 1:358-366.

O'Sullivan-Coyne G, O'Sullivan GC, O'Donovan TR, Piwocka K, McKenna SL. 2009. Curcumin induces apoptosis-independent death in oesophageal cancer cells. Br J Cancer., 101:1585-1595.

Pandelidou M, Dimas K, Georgopoulos A, Hatziantoniou S, Demetzos C. 2011. Preparation and characterization of lyophilised egg PC liposomes incorporating curcumin and evaluation of its activity against colorectal cancer cell lines, J Nanosci Nanotechnol., 11:1259-1266.

Paul S, Mandal SK, Bhattacharyya SS, Boujedaini N, Khuda-Bukhsh AR. 2010. In vitro and in vivo studies demonstrate anticancer property of root extract of Polygala senega. J Acupunct Meridian Stud., 3:188-196.

Phillips JM, Clark C, Herman-Ferdinandez L, Moore -Medlin T, Rong X, Gill JR,Clifford JL, Abreo F, Nathan CO. 2011. Curcumin inhibits skin squamous cell carcinoma tumor growth in vivo. Otolaryngol Head Neck Surg., 145:58-63.

Preza AM, Jaramillo ME, Puebla AM, Mateos JC, Hernández R, Lugo E. 2010. Antitumor activity against murine lymphoma L5178Y model of proteins from cacao (Theobroma cacao L.) seeds in relation with in vitro antioxidant activity. BMC Complement Altern Med., 10:61.

Qian H, Yang Y and Wang X. 2011. Curcumin enhanced adriamycin-induced human liver-derived Hepatoma G2 cell death through activation of mitochondria-mediated apoptosis and autophagy. Eur J Pharm Sci., 43:125-131.

Rao J, Xu DR, Zheng FM, Long ZJ, Huang SS, Wu X, Zhou WH, Huang RW, Liu Q. 2011. Curcumin reduces expression of Bcl-2, leading to apoptosis in daunorubicin-insensitive CD34+ acute myeloid leukemia cell lines and primary sorted CD34+ acute myeloid leukemia cells, J Transl Med., 19; 9:71.

Rayanil KO, Bunchornmaspan P, Tuntiwachwuttikul P. 2011. A new phenolic compound with anticancer activity from the wood of Millettia leucantha. O. Arch Pharm Res., 34:881-886.

Rejinold NS, Muthunarayanan M, Chennazhi KP, Nair SV, Jayakumar R. 2011a. Curcumin loaded fibrinogen nanoparticles for cancer drug delivery. J Biomed Nanotechnol., 7:521-534.

Rejinold NS, Muthunarayanan M, Divyarani VV, Sreerekha PR, Chennazhi KP, Nair SV, Tamura H, Jayakumar R. 2011b. Curcumin-loaded biocompatible thermoresponsive polymeric nanoparticles for cancer drug delivery. J Colloid Interface Sci., 360:39-51.

Rejinold NS, Sreerekha PR, Chennazhi KP, Nair SV, Jayakumar R. 2011c. Biocompatible, biodegradable and thermo-sensitive chitosan-g-poly (N-isopropylacrylamide) nanocarrier for curcumin drug delivery. Int J Biol Macromol., 49:161-172.

Reuter S, Gupta SC, Park B, Goel A, Aggarwal BB. 2011. Epigenetic changes induced by curcumin and other natural compounds. Genes Nutr., 6:93-108.

Rowe DL, Ozbay T, O'Regan RM, Nahta R. 2009. Modulation of the BRCA1 Protein and Induction of Apoptosis in Triple Negative Breast Cancer Cell Lines by the Polyphenolic Compound Curcumin. Breast Cancer (Auckl)., 3:61-75.

Rungphanichkul N, Nimmannit U, Muangsiri W, Rojsitthisak P. 2011. Preparation of curcuminoid niosomes for enhancement of skin permeation. Pharmazie., 66:570-575.

Saha A, Kuzuhara T, Echigo N, Fujii A, Suganuma M, Fujiki H. 2010. Apoptosis of human lung cancer cells by curcumin mediated through up-regulation of "growth arrest and DNA damage inducible genes 45 and 153". Biol Pharm Bull 33:1291-1299.

Sahu A, Kasoju N, Goswami P, Bora U. 2011. Encapsulation of curcumin in Pluronic block copolymer micelles for drug delivery applications. J Biomater Appl., 25:619-639.

Sahu RP, Batra S, Srivastava SK. 2009. Activation of ATM/Chk1 by curcumin causes cell cycle arrest and apoptosis in human pancreatic cancer cells. Br. J. Cancer., 100:1425-1433.

Saini S, Arora S, Majid S, Shahryari V, Chen Y, Deng G, Yamamura S, Ueno K, Dahiya R. 2011. Curcumin Modulates MicroRNA-203-Mediated Regulation of the Src-Akt Axis in Bladder Cancer. Cancer Prev Res (Phila)., 4:1698-1709.

Saxena A, Saxena AK, Singh J, Bhushan S. 2010. Natural antioxidants synergistically enhance the anticancer potential of AP9-cd, a novel lignan composition from Cedrus deodara in human leukemia HL-60 cells. Chem Biol Interact., 188:580-590.

Saydmohammed M, Joseph D, Syed V. 2010. Curcumin suppresses constitutive activation of STAT-3 by up-regulating protein inhibitor of activated STAT-3 (PIAS-3) in ovarian and endometrial cancer cells. J Cell Biochem., 110:447-456.

Schaaf C, Shan B, Buchfelder M, Losa M, Kreutzer J, Rachinger W, Stalla GK, Schilling T, Arzt E, Perone MJ, Renner U. 2009. Curcumin acts as anti-tumorigenic and hormone-suppressive agent in murine and human pituitary tumour cells in vitro and in vivo. Endocr Relat Cancer., 16:1339-1350.

Schaaf C, Shan B, Onofri C, Stalla GK, Arzt E, Schilling T, Perone MJ, Renner U. 2010. Curcumin inhibits the growth, induces apoptosis and modulates the function of pituitary folliculostellate cells. Neuroendocrinology., 91:200-210.

Selvaduray KR, Radhakrishnan AK, Kutty MK, Nesaretnam K. 2010. Palm tocotrienols inhibit proliferation of murine mammary cancer cells and induce expression of interleukin-24 mRNA, J Interferon Cytokine Res., 30:909-916.

Selvam P, El-Sherbiny IM, Smyth HD. 2011. Swellable hydrogel particles for controlled release pulmonary administration using propellant-driven metered dose inhalers. J Aerosol Med Pulm Drug Deliv., 24:25-34.

Selvaraj Nagarajan, Bo Siva Rami Reddy, Jhon Tsibouklis. 2011. In vitro effect on cancer cells: Synthesis and preparation of polyurethane membranes for controlled delivery of curcumin Journal of biomedical materials research. Part A 12 99:410-417.

Sen GS, Mohanty S, Hossain DM, Bhattacharyya S, Banerjee S, Chakraborty J, Saha S, Ray P, Bhattacharjee P, Mandal D, Bhattacharya A, Chattopadhyay S, Das T, Sa G. 2011. Curcumin enhances the efficacy of chemotherapy by tailoring p65NF{kappa}B-p300 cross-talk in favor of p53-p300 in breast cancer. J Biol Chem., 286:42232-42247.

Seo JH, Jeong KJ, Oh WJ, Sul HJ, Sohn JS, Kim YK, Cho do Y, Kang JK, Park CG, Lee HY. 2010. Lysophosphatidic acid induces STAT3 phosphorylation and ovarian cancer cell motility: their inhibition by curcumin. Cancer Lett., 288:50-56.

Sertel S, Eichhorn T, Plinkert PK, Efferth T. 2011. Anticancer activity of Salvia officinalis essential oil against HNSCC cell line (UMSCC1). [Article in German] HNO.

Setthacheewakul S, Kedjinda W, Maneenuan D, Wiwattanapatapee R. 2011. Controlled release of oral tetrahydrocurcumin from a novel self-emulsifying floating drug delivery system (SEFDDS). AAPS PharmSciTech., 12:152-164.

Shahani K, Swaminathan SK, Freeman D, Blum A, Ma L, Panyam J. 2010. Injectable sustained release microparticles of curcumin: a new concept for cancer chemoprevention. Cancer Res., 70:4443-4452.

Shalaby E. 2011. Algae as promising organisms for environment and health. Plant Signal Behav., 6.

Shanmugam MK, Kannaiyan R, Sethi G. 2011. Targeting cell signaling and apoptotic pathways by dietary agents: role in the prevention and treatment of cancer. Nutr Cancer., 63:161-173.

Shao J, Zheng D, Jiang Z, Xu H, Hu Y, Li X, Lu X. 2011. Curcumin delivery by methoxy polyethylene glycol-poly(caprolactone) nanoparticles inhibits the growth of C6 glioma cells. Acta Biochim Biophys Sin (Shanghai)., 43:267-274.

Sharma RA, Gescher AJ, Steward WP. 2005. Curcumin: the story so far. Eur J Cancer., 41:1955-1968.

Shelma R, Sharma CP. 2011. Submicroparticles composed of amphiphilic chitosan derivative for oral insulin and curcumin release applications. Colloids Surf B Biointerfaces., 88:722-728.

Shimizu M, Adachi S, Masuda M, Kozawa O, Moriwaki H. 2011. Cancer chemoprevention with green tea catechins by targeting receptor tyrosine kinases. Mol Nutr Food Res., 55:832-843.

Shrikanth Reddy, Bharat B. Aggarwal. 1994. Curcumin is a non-competitive and selective inhibitor of phosphorylase kinase, FEBS Letters., 341:19-22.

Shu L, Khor TO, Lee JH, Boyanapalli SS, Huang Y, Wu TY, Saw CL, Cheung KL, Kong AN. 2011. Epigenetic CpG Demethylation of the Promoter and Reactivation of the Expression of Neurog1 by Curcumin in Prostate LNCaP Cells. AAPS J., Sep 22.

Singh AT, Ghosh M, Forte TM, Ryan RO, Gordon Li. 2011. Curcumin nanodisk-induced apoptosis in mantle cell lymphoma. Leuk Lymphoma., 52:1537-1543.

Singh M, Singh R, Bhui K, Tyagi S, Mahmood Z, Shukla Y. 2011. Tea polyphenols induce apoptosis through mitochondrial pathway and by inhibiting nuclear factor-kappaB and Akt activation in human cervical cancer cells. Oncol Res., 9:245-257.

Singh S, Aggarwal BB. 1995. Activation of transcription factor NF-kappa B is suppressed by

curcumin (diferuloylmethane). J Biol Chem., 270:24995-25000.

Spiller SE, Logsdon NJ, Deckard LA, Sontheimer H. 2011. Inhibition of nuclear factor kappa-B signaling reduces growth in medulloblastoma in vivo. BMC Cancer., 11:136

Sreelatha S, Jeyachitra A, Padma PR. 2011. Antiproliferation and induction of apoptosis by Moringa oleifera leaf extract on human cancer cells. Food Chem Toxicol., 49:1270-1275.

Srimal RC, Dhawan BN. 1973. Pharmacology of diferuloyl methane (curcumin), a non-steroidal anti-inflammatory agent. J Pharm Pharmacol., 25:447-452.

Syng-Ai C, Kumari AL, Khar A. 2004. Effect of curcumin on normal and tumor cells: role of glutathione and bcl-2. Mol Cancer Ther., 3:1101-1108.

Szliszka E, Krol W. 2011. Soy isoflavones augment the effect of TRAIL-mediated apoptotic death in prostate cancer cells. Oncol Rep., 26:533-541.

Tadmor T, Polliack A. 2011. Mantle cell lymphoma: curcumin nanodisks and possible new concepts on drug delivery for an incurable lymphoma. Leuk Lymphoma., 52:1418-1420.

Takeda S, Matsuo K, Yaji K, Okajima-Miyazaki S, Harada M, Miyoshi H, Okamoto Y, Amamoto T, Shindo M, Omiecinski CJ, Aramaki H. 2011. (--)-Xanthatin selectively induces GADD45γ and stimulates caspase-independent cell death in human breast cancer MDA-MB-231 cells. Chem Res Toxicol., 24:855-865.

Tang XQ, Bi H, Feng JQ, Cao JG. 2005. Effect of curcumin on multidrug resistance in resistant human gastric carcinoma cell line SGC7901/VCR. Acta Pharmacol Sin., 26:1009-1016.

Thamake SI, Raut SL, Ranjan AP, Gryczynski Z, Vishwanatha JK. 2011. Surface functionalization of PLGA nanoparticles by non-covalent insertion of a homo -bifunctional spacer for active targeting in cancer therapy. Nanotechnology., 22:035101.

Thangapazham RL, Puri A, Tele S, Blumenthal R, Maheshwari RK. 2008. Evaluation of a nanotechnology -based carrier for delivery of curcumin in prostate cancer cells. Int J Oncol., 32:1119-1123.

Tian F, Song M, Xu PR, Liu HT, Xue LX. 2008. Curcumin promotes apoptosis of esophageal squamous carcinoma cell lines through inhibition of NF-kappaB signaling pathway. [Article in Chinese]. Ai Zheng., 27:566-570.

Tripathi A, Puddick J, Prinsep MR, Rottmann M, Chan KP, Chen DY, Tan LT. 2011. Lagunamide C, a cytotoxic cyclodepsipeptide from the marine cyanobacterium Lyngbya majuscula., Phytochemistry 72:2369-2375.

Tsuiji K, Takeda T, Li B, Wakabayashi A, Kondo A, Kimura T, Yaegashi N. 2011. Inhibitory effect of curcumin on uterine leiomyoma cell proliferation. Gynecol Endocrinol., 27:512-517.

Tuntiwechapikul W, Taka T, Songsomboon C, Kaewtunjai N, Imsumran A, Makonkawkeyoon L, Pompimon W, and Lee TR. 2010. Ginger extract inhibits human telomerase reverse transcriptase and c-Myc expression in A549 lung cancer cells. J Med Food., 13:1347-1354.

Ulbricht CE, Chao W. 2010. Review. Phytochemicals in the oncology setting. Curr Treat Options Oncol., 11:95 -106.

Vilas-Zornoza A, Agirre X, Martín-Palanco V, Martín-Subero JI, San José-Eneriz E, Garate L, Álvarez S, Miranda E, Rodríguez-Otero P, Rifón J,

Torres A, Calasanz MJ, Cruz Cigudosa J, Román-Gómez J, Prósper F. 2011. Frequent and simultaneous epigenetic inactivation of TP53 pathway genes in acute lymphoblastic leukemia. PLoS One., 6:e17012.

Vishvakarma NK, Kumar A, Singh SM. 2011. Role of curcumin-dependent modulation of tumor microenvironment of a murine T cell lymphoma in altered regulation of tumor cell survival. Toxicol Appl Pharmacol., 252:298-306.

Vu HA, Beppu Y, Chi HT, Sasaki K, Yamamoto H, Xinh PT, Tanii T, Hara Y, Watanabe T, Sato Y, Ohdomari. I. 2010. Green tea epigallocatechin gallate exhibits anticancer effect in human pancreatic carcinoma cells via the inhibition of both focal adhesion kinase and insulin-like growth factor-I receptor, J Biomed Biotechnol., 2010:290516.

Wahl O, Oswald M, Tretzel L, Herres E, Arend J, Efferth T. 2011. Inhibition of tumor angiogenesis by antibodies, synthetic small molecules and natural products, Curr Med Chem., 18:3136-3155.

Wang C, Henkes LM, Doughty LB, He M, Wang D, Meyer-Almes FJ, Cheng YQ. 2011. Thailandepsins: bacterial products with potent histone deacetylase inhibitory activities and broad-spectrum antiproliferative activities. J Nat Prod., 74:2031-2038.

Wang O, Liu S, Zou J, Lu L, Chen L, Qiu S, Li H, Lu X. 2011. Anticancer activity of 2α, 3α, 19β, 23β-Tetrahydroxyurs-12-en-28-oic acid (THA), a novel triterpenoid isolated from Sinojackia sarcocarpa. PLoS One., 6:e21130.

Wang X, Xia X, Leung AW, Xiang J, Jiang Y, Wang P, Xu J, Yu H, Bai D, Xu C. 2011a. Ultrasound induces cellular destruction of nasopharyngeal carcinoma cells in the presence of curcumin. Ultrasonics., 51:165-170.

Wang X, Xia X, Xu C, Xu J, Wang P, Xiang J, Bai D, Leung AW. 2011b. Ultrasound-induced cell death of nasopharyngeal carcinoma cells in the presence of curcumin. Integr Cancer Ther., 10:70-76.

Wang XN, Bashyal BP, Wijeratne EM, U'ren JM, Liu MX, Gunatilaka MK, Arnold AE, Gunatilaka AA. 2011. Smardaesidins A-G, Isopimarane and 20-nor-Isopimarane Diterpenoids from Smardaea sp., a Fungal Endophyte of the Moss Ceratodon purpureus (1) J Nat Prod., 74:2052-2061.

Watson JL, Greenshields A, Hill R, Hilchie A, Lee PW, Giacomantonio CA, Hoskin DW. 2010. Curcumin -induced apoptosis in ovarian carcinoma cells is p53-independent and involves p38 mitogen-activated protein kinase activation and downregulation of Bcl-2 and survivin expression and Akt signaling. Mol Carcinog., 49:13-24.

Wei CC, Ball S, Lin L, Liu A, Fuchs JR, Li PK, Li C, Lin J. 2011. Two small molecule compounds, LLL12 and FLLL32, exhibit potent inhibitory activity on STAT3 in human rhabdomyosarcoma cells. Int J Oncol., 38:279-285.

Wong TS, Chan WS, Li CH, Liu RW, Tang WW, Tsao SW, Tsang RK, Ho WK, Wei WI, Chan JY. 2010. Curcumin alters the migratory phenotype of nasopharyngeal carcinoma cells through up-regulation of E-cadherin. Anticancer Res., 30(7):2851-2856.

Wu SH, Hang LW, Yang JS, Chen HY, Lin HY, Chiang JH, Lu CC, Yang JL, Lai TY, Ko YC, Chung JG. 2010. Curcumin induces apoptosis in human non-small cell lung cancer NCI-H460 cells through ER stress and caspase cascade- and mitochondria-dependent pathways. Anticancer Res., 30:2125-2133.

Xiao D, Zeng Y, Prakash L, Badmaev V, Majeed M, and Singh SV. 2011. Reactive oxygen species-dependent apoptosis by gugulipid extract of Ayurvedic

medicine plant Commiphora mukul in human prostate cancer cells is regulated by c-Jun N-terminal kinase. Mol Pharmacol., 79:499-507.

Xiao H, Xiao Q, Zhang K, Zuo X, Shrestha UK. 2010. Reversal of multidrug resistance by curcumin through FA/BRCA pathway in multiple myeloma cell line MOLP -2/R. Ann Hematol., 89:399-404.

Xie X, Tao Q, Zou Y, Zhang F, Guo M, Wang Y, Wang H, Zhou Q, Yu S. 2011. PLGA nanoparticles improve the oral bioavailability of curcumin in rats: characterizations and mechanisms J Agric Food Chem., 59:9280-9289.

Yadav VS, Mishra KP, and Singh DP. 2010. Curcumin inhibits Jurkat cell proliferation by inducing apoptosis via activation-induced cell death. Biomed Pharmacother., Sep 20.

Yallapu MM, Dobberpuhl MR, Maher DM, Jaggi M, Chauhan SC. 2011a. Design of Curcumin loaded Cellulose Nanoparticles for Prostate Cancer. Curr Drug Metab., Sep 5.

Yallapu MM, Gupta BK, Jaggi M, Chauhan SC. 2010a. Fabrication of curcumin encapsulated PLGA nanoparticles for improved therapeutic effects in metastatic cancer cells. J Colloid Interface Sci.,351:19-29.

Yallapu MM, Jaggi M, Chauhan SC. 2011b. Curcumin nanoformulations: a future nanomedicine for cancer. Drug Discov Today., Sep 18.

Yallapu MM, Jaggi M, Chauhan SC. 2010b. Poly (β-cyclodextrin)/curcumin self-assembly: a novel approach to improve curcumin delivery and its therapeutic efficacy in prostate cancer cells. Macromol Biosci., 10:1141-1151.

Yang CL, Ma YG, Xue YX, Liu YY, Xie H, Qiu GR. 2011. Curcumin Induces Small Cell Lung Cancer NCI-H446 Cell Apoptosis via the Reactive Oxygen Species-Mediated Mitochondrial Pathway and Not the Cell Death Receptor Pathway, DNA Cell Biol., Jun 28.

Yin H, Guo R, Xu Y, Zheng Y, Hou Z, Dai X, Zhang Z, Zheng D, Xu H. 2011. Synergistic antitumor efficiency of docetaxel and curcumin against lung cancer. Acta Biochim Biophys Sin (Shanghai).

Yu H, Huang Q. 2011. Investigation of the absorption mechanism of solubilized curcumin using Caco-2 cell monolayers. *J Agric Food Chem* 59(17):9120-9126, 2011.

Yu LL, Wu JG, Dai N, Yu HG and Si JM. 2011. Curcumin reverses chemoresistance of human gastric cancer cells by downregulating the NF-κB transcription factor. Oncol Rep., 26:1197-1203.

Zanotto-Filho A, Braganhol E, Edelweiss MI, Behr GA, Zanin R, Schröder R, Simões-Pires A, Battastini AM, Moreira JC. 2011. The curry spice curcumin selectively inhibits cancer cells growth in vitro and in preclinical model of glioblastoma. J Nutr Biochem.,

Zhang C, Li B, Zhang X, Hazarika P, Aggarwal BB, Duvic M. 2010. Curcumin selectively induces apoptosis in cutaneous T-cell lymphoma cell lines and patients' PBMCs: potential role for STAT-3 and NF-kappaB signaling. J Invest Dermatol., 130:2110-2119.

Zhang H, Zhang L, Yuan P, Wang C. 2011. Preparation and in vitro release characteristics of curcumin in nanosuspensions, Zhongguo Zhong Yao Za Zhi., 36:132-135.

Zhang J, Du Y, Wu C, Ren X, Ti X, Shi J, Zhao F, Yin H. 2010. Curcumin promotes apoptosis in human lung adenocarcinoma cells through miR-186* signaling pathway. Oncol Rep., 24:1217-1223.

Zhang L, Cao F, Ding B, Li Q, Xi Y, Zhai G. 2011. Eudragit® S100 coated calcium pectinate microspheres

of curcumin for colon targeting. J Microencapsul., 28:659-667.

Zhang Q, Zhong Y, Yan LN, Sun X, Gong T, Zhang ZR. 2011. Synthesis and preliminary evaluation of curcumin analogues as cytotoxic agents. Bioorg Med Chem Lett., 21:1010-1014.

Zhao LX, Huang SX, Tang SK, Jiang CL, Duan Y, Beutler JA, Henrich CJ, McMahon JB, Schmid T, Blees JS, Colburn NH, Rajski SR, Shen B. 2011. Actinopolysporins A-C and tubercidin as a Pdcd4 stabilizer from the halophilic actinomycete Actinopolyspora erythraea YIM 90600. J Nat Prod., 23;74:1990-1995.

Zhongguo Shi Yan Xue Ye Xue Za Zhi. Xiao H, Zhang KJ. 2008. Antiproliferative effect of curcumin combined with cyclophosmide on the growth of human lymphoma cell line HT/CTX with drug resistance and its relation with FA/BRCA pathway. [Article in Chinese] J Experimental hematology., 16:804-808.

Zong H, Wang F, Fan QX, and Wang LX. 2011. Curcumin inhibits metastatic progression of breast cancer cell through suppression of urokinase-type plasminogen activator by NF-kappa B signaling pathways. Mol Biol Rep.