IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.53
Volume 4, Issue 4, June 2024

Curcumin (Nanocurcumin) – A Unique Approach to Treat Human Cancer

Tanmay Gharat[*2], Vidya Walunj[2], Ms. Sana Maniyar[1], Utkarsha Ghanwat[2]
Assistant Professor, Department of Pharmaceutics[1]
Department of Pharmacy[2]
Samarth College of Pharmacy, Belhe, Pune, Maharashtra, India,
Corresponding author : Tanmay Gharat * tanmaygharat999@gmail.com

Abstract: *Since ancient times, herbal remedies have been used extensively around the world. Medical professionals as well as patients now recognise the superior therapeutic value of herbal drugs due to the fact that they have less side effects than modern medications. To improve the patient compliance and prevent the repetitive administration, phototherapeutics require a systemic approach to administer the components over time. Introducing novel drug delivery system (NDDS) for herbal ingredients can help achieve this. Nanotechnology is one such innovative strategy. Increasing the effectiveness and resolving concerns with plant medicines may be possible in the future using nano-sized drug delivery systems for herbal medications. In order to treat more chronic diseases including asthma, diabetes, cancer and others, nanocarriers must be introduced into traditional treatment as NDDS. Formulating nano dosage forms (Liposomes, Proliposomes, Solid Polymeric Nanoparticles [Nanospheres and Nanocapsules], Liposomes, SolidLipid nanoparticles [SLNs], Nano emulsion, etc.) have numerous benefits for herbal drugs, including improved solubility and bioavailability, protection from toxicity, increased pharmacological activity, increased stability, improved tissue macrophage distribution, sustained delivery, protection from physical and chemical deterioration, etc. Hence, nano-sized delivery systems for herbal medicines may one day be used to improve activity and address issues with plant-based treatments.*
Various herbal drugs such as Curcumin, Artemisinin, Vincristine, Vinblastine, Vicenin, Gossypol, Noscapine, Acetogenin, etc. Traditional Indian and Chinese medicine uses curcumin to treat a variety of illnesses. Numerous human cancer cell lines and animal carcinogenesis models have shown that curcumin, a yellow polyphenol derived from the rhizome of turmeric (Curcuma longa), has strong anti-cancer activities.By enabling ready aqueous dispersion, nanocurcumin offers a chance to increase the clinical versatility of this effective drug..

Keywords: Novel Drug Delivery System, Nanotechnology, Nanoparticles, Nano-sized delivery, Nanocurcumin

I. INTRODUCTION

Nanotechnology in Herbal Drug Technology:

Natural items and herbal medicines have been utilised to treat illnesses since the dawn of time. Contrary to the prevalent allopathic approach, herbal treatments include thousands of active ingredients that all cure disease concurrently.[2]In order to improve patient compliance and prevent repetitive administration, phototherapeutics require a systematic approach to administer the components over time. The process of developing novel drug delivery systems (NDDSs) for herbal ingredients can be used to accomplish this. The therapeutic benefit of NDDSs is increased by reducing toxicity, enhancing bioavailability, and other factors, in addition to reducing the need for recurrent administration to prevent noncompliance.[1,3] The goal of nanotechnology, a field of applied science and technology, is to create device and dosage form between 1 and 100 nm. Recently, the term "nanomedicines" has been used to describe the use of nanotechnology in biological systems for treatment, diagnosis, monitoring, and control. The synthetic biodegradable polymers, lipids, and polysaccharides used to create the nanocarriers are all harmless substances.[4]

Due to the following qualities, herbal medicines were chosen as a potential medicinal option for nano delivery:

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1. There are effective extracts of acetone, chloroform, petrol, and methanol that may not be appropriate for distribution in that form.
2. Because these medications are in bulk, dose reduction is intended.
3. Target specificity for a number of chronic illnesses is lacking in currently available formulations.
4. Currently available formulations include a few other adverse effects.
5. Patient non-compliance as a result of excessive dosages and inadequate efficacy of the formulations available.

II. A NOVEL DRUGS DELIVERY SYSTEM USING NANOTECHNOLOGY

Drug delivery system produced NDDS, a creative solution to the problems of conventional drug administration systems.

The following factors led to the choice of a nano-sized delivery system:

• Due to their special shape and large loading capacity, they seem to be able to deliver high medication concentrations to disease locations.[2]

• The concentration appears to remain at the sites for longer periods of time; • The medication is delivered in small particle size, which increases the total surface area of the drug thus allotting speedier blood breakdown.[2]

Nanoparticles:

Nanoparticles are sub-nanosized colloidal entities made of synthetic or natural polymers with sizes ranging from 1 to 1000 nm. The medication is dissolved, trapped, enclosed, or joined to a nanoparticle matrix. Nanoparticles might be nanospheres or nanocapsules, depending on the technique of manufacture. Nanospheres are matrix systems in which the drug is physically and uniformly spread, while nanocapsules are systems in which the drug is constrained to a cavity surrounded by a specific polymer membrane. The nanocarriers are made of secure substances such lipids, polysaccharides, and synthetic biodegradable polymers.[17]

Nanocarriers:

A nanocarrier is a type of nanomaterial primarily employed as a drug or other substance's delivery module. Various substances, such as micelles, polymers, carbon-based compounds, liposomes, and others, are frequently utilised as nanocarriers. Currently, nanocarriers are employed for medication transport, and chemotherapy may benefit from their special properties. Dendrimers, carbon nanotubes, gold nanoparticles, polymer conjugates, lipid-based carriers, polymeric nanoparticles, and gold nanoparticles are examples of nanocarriers. Both liposomes and micelles are lipid-based transporters.Unwanted toxicity caused by the usage of particular nanomaterials is one potential issue with nanocarriers. Inorganic nanomaterial can potentially be harmful to the body if it builds up in specific cell organelles. Due to its natural occurrence and generally lower cytotoxicity than manufactured compounds, protein-based nanocarriers are one of the potential medication and gene delivery systems.[17]

Nanoparticles' role in the development of herbal treatments:

- By using nanoparticles to direct herbal medicine to specific organs, selectivity, medication delivery, efficacy, and safety are improved.
- Nanoparticles can be used to make herbal drugs more soluble and to localise the medicine at a specific spot, which improves effectiveness.
- Because of their distinct size and high loading capabilities, nanoparticles can deliver high doses of medications to disease regions.
- Giving the medication in small granules increases its surface area overall, accelerate its absorption into the circulation.
- Demonstrates improved permeation and retention effects, i.e., enhanced penetration across barriers due to small size and retention due to inadequate lymphatic drainage.
- Does not require the inclusion of any specific ligand moiety and exhibits passive targeting to the disease site of action.
- Reduces adverse effects.

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Formulations	Active Ingredients	Biological Activity	Method of Preparation
Curcuminoids solid lipid nanoparticles	Curcuminoids	Anticancer and antioxidant	Micro emulsion technique[2,5]
Glycyrrhizic acid loaded nanoparticles	Glycerrhizic acid	Anti-inflammatory, antihypertensive	Rotary evaporated film ultrasonication method[2,6]
Nanoparticles of cuscuta chinensis	Flavonoids and lignans	Hepatoprotective and antioxidant	Nanosuspension method[2,7]
Taxel loaded nanoparticles	Taxel	Anticancer	Emulsion solvent evaporation method[2,8]
Artemisinin nano capsules	Artemisinin	Anticancer	Self-assembly procedure[2,9]
CPT encapsulated nanoparticles	Camptothecin	Anticancer	Dialysis method[2,10]
Berberine loaded nanoparticles	Berberine	Anticancer	Ionic gelatine method[2,11]

Table 1: Some herbal drug nanoparticles

Curcumin: Background

Curcumin, also known as diferuloyl methane (C21H20O6), is a yellow polyphenolic compound that is extracted from the rhizome of the Zingiberaceae plant species curcuma longa. Turmeric's yellow colour is primarily derived from the polyphenolic pigment and fat-soluble compound known as curcuminoids.[12]The main active component in turmeric is called a curcuminoid; other types of curcuminoids include bisdemethoxycurcumin and demethoxycurcumin. It is mostly used as a spice and food colour in India.[13]Turmeric's yellow colour is mostly caused by polyphenols and curcuminoids, while its tautomeric forms, enol and keto, are also important.[14] Curcumin was extracted from turmeric in 1815, and diferuloylmethane was established as the structure in 1910.[15] Turmeric organically grows and is used for many different purposes in Southeast Asia and other tropical nations.

Curcumin is utilised in traditional Chinese and Indian medicine to treat a variety of illnesses as well as a wound healing agent. Curcumin has recently been studied as part of multiple studies that have demonstrated its ability to inhibit the growth of cancer cells and to trigger cell death by activating a variety of signalling pathways.Curcumin has therefore evolved into a chemo preventive and anti-cancer agent as a result of its ability to promote cell death. This can be demonstrated by doing various in vitro experiments and preclinical research using animal models.[16]

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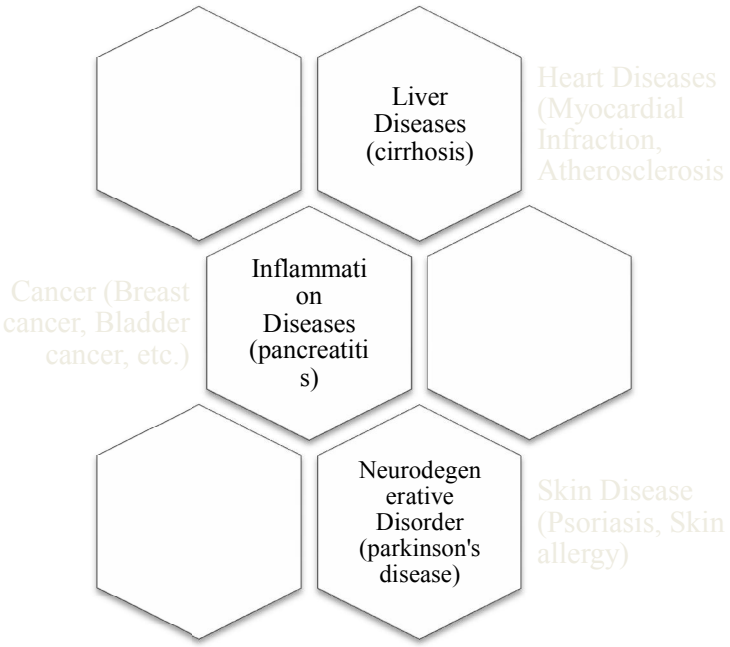
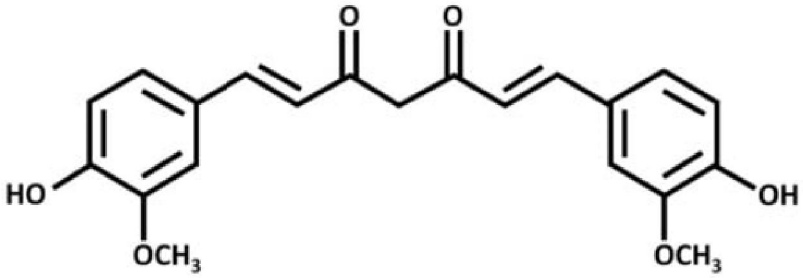


Table 2: Medicinal Uses of Curcumin in Various Diseases

Turmeric: as a source of Curcumin



Structure of Curcumin

Nanocurcumin: Nano formulation Techniques

Many different methods have been devised to create nanocurcumin. The most widely used processes are nanoprecipitation, single emulsion, microemulsion, spray drying, emulsion polymerization, solvent evaporation, antisolvent precipitation, ultrasonication, coacervation technique, ionic gelation, wet milling, solid dispersion, thin-film

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hydration, and the Fessi method. Each technique has unique benefits and qualities that have been examined by numerous researchers.[18]

The powerful phytochemical curcumin, a hydrophobic polyphenol (diferuloyl methane) found in turmeric (Curcuma longa, Family: Zingiberaceae), has a variety of biological effects, including anticancer, anti-inflammatory, antioxidant, antiviral, antibacterial, and antifungal ones. However, due to its brief half-life, poor water solubility, fast metabolism, and rapid elimination, which eventually results in poor bioavailability upon oral administration, its clinical applicability was restricted. Curcumin's hydrophobic characteristics could be lost using medication delivery methods based on nanoparticles. Using a wet milling approach, curcumin nanoparticles have been created. Nanocurcumin is easily dissolved in water, unlike curcumin.

Curcumin Nano formulations	Description	Models Used	Major Outcomes
Liposomes	Liposomes are the spherical vesicles consisted of single or multiple phospholipid bilayers surrounding aqueous units that very closely resemble the cell membrane structure. It solubilizes curcumin in the phospholipidic bilayer and allows curcumin to be distributed in aqueous medium and increases the effect ofcurcumin.	Malaria, melanoma, renal ischemia, colorectal cancer, and lung cancer	Increased the antimalarial and antimelanoma effects, greater encapsulation efficiency, excellent bioactivity, and anticancer activity.
Polymers	Polymers are another widely usedeffective drug delivery system forcurcumin. It can able to improve theoral bioavailability and solubility of Curcumin.	Wound healing and colorectal cancer	Exhibited strong wound healing andlong blood circulation, suppression of tumour growth, higher growth inhibition in cancer cells than free curcumin, and increased the cellular uptake and better anticancer activity.
Nanoparticles (Gold)	Gold nanoparticles have own unique physical and chemical properties and various surface functionalities. It offers versatility platform in drug delivery (curcumin).	Prostate and colorectal cancer cells.	Improved antioxidant activity, extended blood circulation, better solubility and stability, enhanced biocompatibility, and considerable anticancer activity.
Magnetic Nanoparticles	Magnetic nanoparticles used for multiple purposes including drug delivery (curcumin), hyperthermia, and quality imaging.	Cancer and inflammatory cells	Improved cellular uptake, potent targeting capability of curcumin, magnetic resonance imaging,effective protection against inflammatory agent, controlled curcumin delivery, excellent bio-compatibility, and anticancer activity.
Solid Lipid Nanoparticles (SLNs)	SLNs possess a lipid core matrix thatcan solubilize drug (curcumin) and thelipid core is steadied through emulsifiers. Normally SLN is	Allergy, colitis andcerebral ischemia, and breast cancer lines	Extended circulation of blood, increased anti-inflammatory effects, targeted andenhanced drug release in brain, andbetter anticancer activity.

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	spherical in shape.		
Conjugates	The complex formed from the joining together of two or more molecules, especially by covalent bond is referred as conjugates. Curcumin conjugation with small molecules and hydrophilic polymers increase its solubility and oral bioavailability.	Fibroblast cells, breast cancer, and amyloid fragments	Increased the solubility, stability and bioavailability, strong anti-cancer activity, higher stability and bioavailability, and anti-amyloid effects.
Cyclodextrins	Cyclodextrins are the bucket shapedoligosaccharides and well-knownsolubilizing and stabilizing agent. It can solubilize the curcumin in a lipophiliccavity, and the outer hydrophilic surface assists in greater dispersion of the formulation.	Bowel disease, lung, pancreatic, breast, colorectal cancer, and prostate cancer cells	Developed bioavailability and increased solubility, improved antiproliferation, anticancer and anti-inflammatory effects, increased the solubility, and formulated as eye drops.
Solid Dispersion	Solid dispersions are referred as one ormore active component in anappropriate matrix. It can improve thebio availability of poor water soluble drugs like curcumin.	Breast tumour, rat pawoedema, and woundhealing	Prolonged survival, anti-tumour and anti-metastasis activity and prolonged survival, enhanced stability, bioavailability and anti-inflammatory, anti-bacterial and improvement of vaginal wound healing.
Micelles	Micelles (20–100 nm) are normallycolloidal dispersions made fromamphiphilic molecule. It assists better solubilization and targeted delivery tocurcumin.	Lung tumour and colorectal cancer	Bioavailability and solubility improved, prolonged life, targeted drug delivery,great chemical stability, and betterantitumor and anticancer effects.
Nanospheres	Nanospheres are known as solid matrixparticles where in the main component(drug) is mixed, but microcapsulecontains internal core and outer polymeric shell.	Escherichia coli, Staphylococcus aureus,Vibrio vulnificus, and Candida albicans. Breast cancer cells,melanoma cells, and Alzheimer's	Exhibited strong antimicrobial and anti-cancer effects, effective target delivery and anti-amyloid effect.
Nanogels	A nanogel is a nanoparticle composed of a hydrogel synthesized by either physical or chemical cross-	Pancreatic cancer, colorectal cancer andskin cancer cells	Targeted and controlled drug release, Prolongcirculation, enhanced bio availability, and better anticancer activity.

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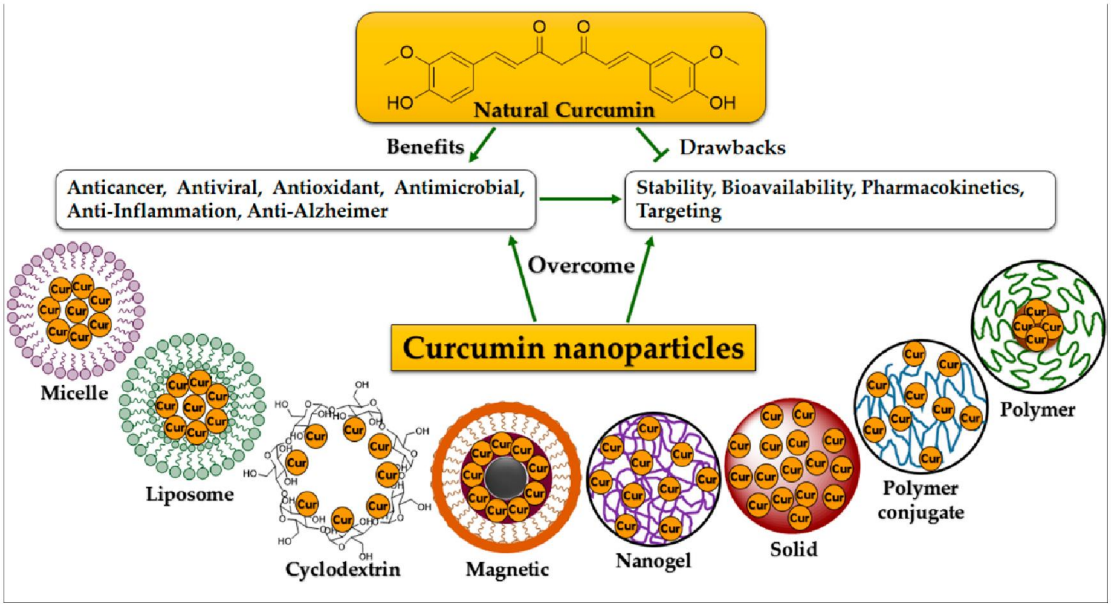
	linking ofpolymers under controlled conditions. Cross linked structure of nanogels offera strong base for drug storage andrelease. It is a possible technique toprepare and release active types of drugs like curcumin to cells for remaining activity, improving stability, and prevent drug immunogenicity.		
Nano discs	Nano disks are disk-shaped bilayers, apolipoprotein-stabilized and self-assembled. They boost the solubility and targeted release of curcumin.	Mantle cell lymphoma	Improved biological activity and apoptosis to mantle cell lymphoma and anticancer activity.



Molecules for Curcumin Nano formulation

Anticancer Effect of Nanocurcumin:

The anticancer properties of curcumin on humans have been proven by numerous investigations. It acts as a possible agent against human lung, breast, prostate, colorectal, liver, carcinoma, pancreatic, myeloma, and melanoma cancers because it has the ability to induce apoptosis, stop the proliferation of cancer cells, and suppress cell cycle development.

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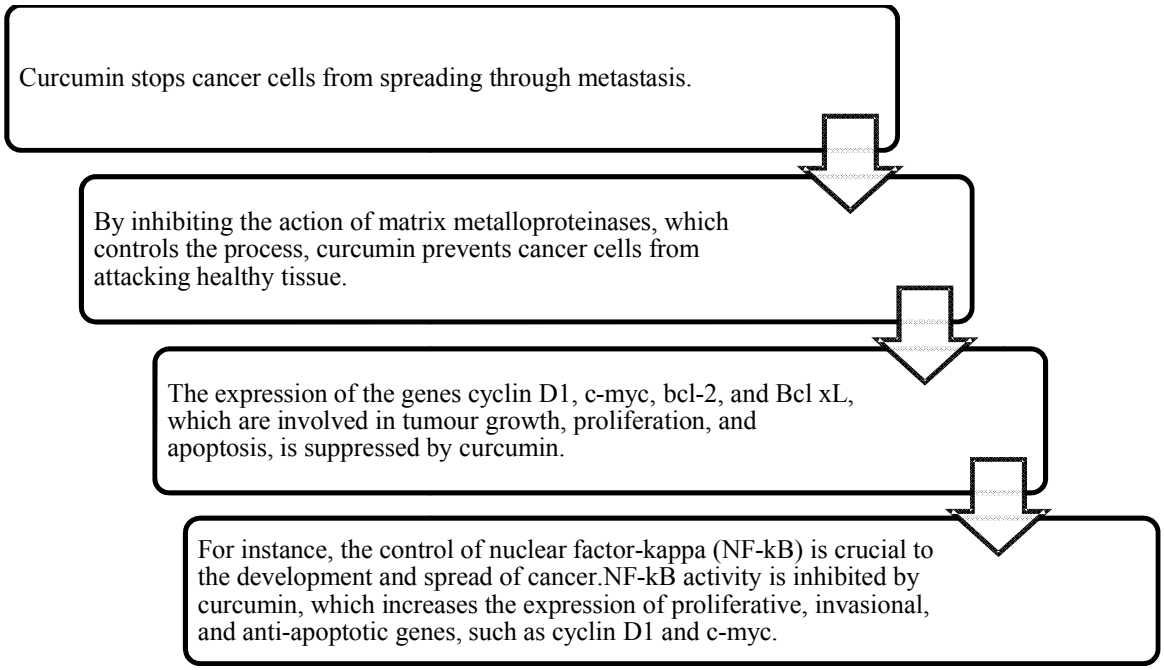

In contrast to native curcumin, curcumin encapsulated within monomethoxy poly (ethylene glycol)-poly(3-caprolactone) (MPEG-PCL) micelles reduced the growth of 26 colon cancer under in vivo conditions.

After synthesis, curcumin-loaded liposome nanoparticles (CLNP) were tested on B16BL6 melanoma cells to see if they had any anticancer properties. It became clear that CLNP greatly restricted the B16BL6 melanoma cells' ability to proliferate.

It was primarily brought about by improved medication delivery made possible by the fusing of lipid particles and intracellular cell membranes. Additionally, it blocks the primary player in the development of skin cancer, the PI3 K/AKT pathway.

Curcumin nanoparticles' anticancer effects were investigated in lung (A549), liver (HepG2), and skin (A431) cancer cell lines. When used in aqueous settings, curcumin nanoparticles were found to have a far stronger impact on cancer cells than native curcumin.

In another investigation, it was shown that PLGA-curcumin nanoparticles improved the lysosomal activity, apoptosis, blockage of the androgen receptor (AR), and nuclear b-catenin activity that came about as a result of a growth obstruction in prostate cancer cells.

One of the most significant breast cancers with a metastatic phenotypic histological subtype is triple-negative breast cancer (TNBC). It has been shown that the combination of exogenous p53 and dendrosomal nanocurcumin can inhibit TNBC cell growth.[18]

III. CONCLUSION

The field of “nanotechnology” has created promising pharmacological cures that will improve peoples’ health in the near future. It is expected that the effective and significant relevance of natural goods and herbal remedies used with the nanocarriers would increase the significance of current drug delivery systems.

Curcumin solubility in aqueous media was significantly improved by the incorporation of curcumin into chitosan nanoparticles. A novel curcumin nanoparticle system (CURN), guanidine functionalized PEGylated mesoporous silica nanoparticles as a novel and effective drug delivery system (DDS), loading CUR into the functionalized surface of the pores of nanocarriers, and nanoCurcTM – The predistilled monomers of NIPAAM, VP, and AA are prepared and evaluated which are beneficial in various purposes. Nanocurcumin is very beneficial in treatment of various types of cancers such as skin cancer, breast cancer, bladder cancer, prostate cancer, etc.

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