

# Carbon nanotubes in delivery of curcumin: An overview

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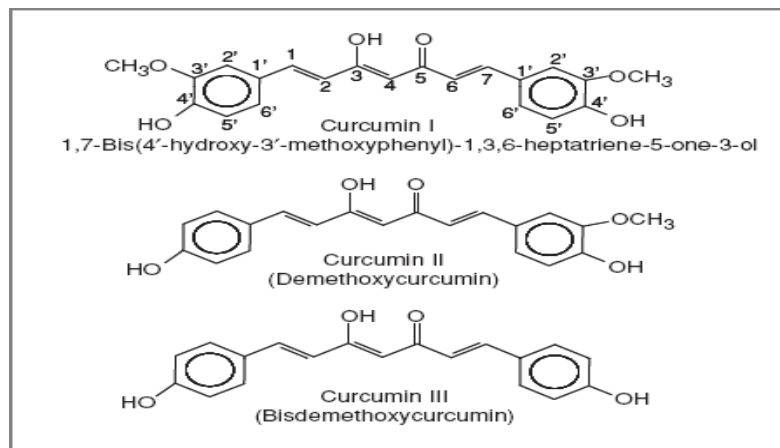
## **Abstract**

From the hour of Ayurveda Curcumin (diferuloylmethane) got from the *Curcuma longa* plant, generally known as turmeric is outstanding for its nontoxic and restorative properties including against oxidant, pain-relieving, calming germ-free action and hostile to malignant growth. Clinically confine the utilization because of its poor water dissolvability, fast digestion and quick end which bring about poor oral bioavailability. To upgrade the bioavailability curcumin will be conveyed via carbon nanotubes. Carbon nanotubes (CNTs) have risen as enamoring assets, promising to focus on tranquilizing conveyance inferable from their one of kind physicochemical properties like cell layer entrance, high surface territory and medication payload, biocompatibility, simple surface adjustment. It was first proved a splendid vehicle for the transmission of sedates into cells without digestion by the body. In this way utilization of CNTs gives diverse methodology towards expanded bioavailability of curcumin.

**Keywords:** Carbon nanotubes, Curcumin, Targeted drug delivery, Bioavailability.

## 1. Introduction

Curcumin (otherwise called curcumin-I) [1], is the standard curcuminoid which is the part of Indian species that is turmeric (*Curcuma longa*) of Family-Zingiberaceae. The different types of curcuminoids identified in turmeric are demethoxycurcumin (curcumin-III), late cyclocurcumin and bisdemethoxycurcumin (curcumin-III) [2-4]. Curcumin is a powerful Phyto molecule with a wide range of natural drugs [5]. Curcumin is a general nutraceutical component, mainly utilized by nutraceutical and pharmaceuticals industries alongside other curcuminoids [6]. Its clinical implementation is greatly restricted by poor dissolvability and rapid digestion, which leads to poor bioavailability. Curcumin is reported with extremely low solvency and remarkable pre-systemic biotransformation, mostly occur by the process of glucuronide and sulfate conjugation. The largest 8 g/day oral portion of curcumin has not been shown any lethal effects [7]. In order to improve penetration ability, minimize dose recurrence, reduce mortality and improve corrections adequacy, today nanoparticles are produced that are non-toxic, cost-effective, biocompatible and biodegradable with various colloid measurements.



**Fig.1: Structures of 3 curcuminoids as components of curcumin [8]**

## 2. Carbon nanotube: Emerging nanocarrier

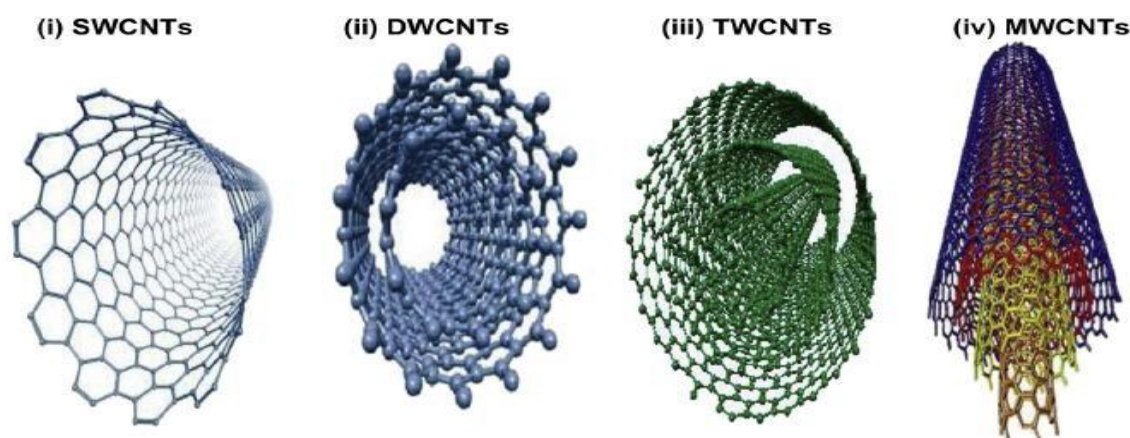
Different innovative procedures are accounted for in the writing including solid lipid nanoparticles, liposomes, magnetic nanoparticles, polymeric nanoparticles, polymeric micelles, nanogels, silver nanoparticles, gold nanoparticles, and various advancements of drug delivery frameworks of curcumin. Nowadays among different methodologies Carbon nanotubes (CNTs) as a drug delivery system have increased more consideration because of

upgraded oral bio-accessibility and significant compensation load adequacy and very little more investigate for a home remedy.

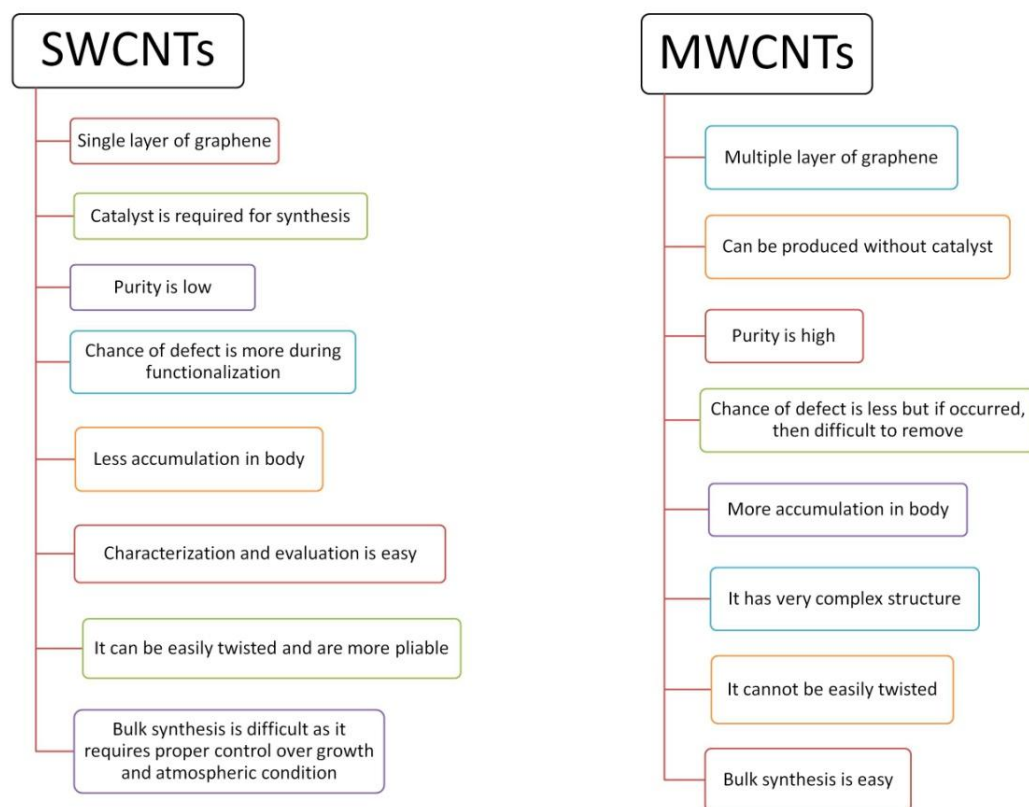
The CNTs, found by Japanese researcher Iijima in 1991 are currently viewed as a top-class subject in academics looks into just as indifferent mechanical zones [9]. Such nanomaterials are carbon allotropes which are made up of graphite and have been developed in nanometer-sized barrel cylinders with a width and length of several millimeters [10,11]. Their basic electronic features were first used as substitutes for different auxiliary materials in the fields of telecommunications, optics, plastics, and other nanotechnological materials owing to their size, economic properties, detailed mechanical properties, strong electrical and heat conductivity [12,13]. Due to their high density, extraordinary concoction capacity and rich polyaromatic electronic structure, CNTs may be retained or combined with various therapeutic agents (drugs, antibodies, proteins, DNA, compounds, etc.). It has proved to be an important tool for transmitting drugs by directly entering cell and retaining the ability to carry drugs in the body [10-13] and many studies have shown that these atoms are carried in cells more efficiently than typical CNT-associated strategies [11-13].

### 3. Types and structures of carbon nanotubes

In addition to diamond and graphite, this nanomaterial is crammed with the group of fullerenes, the three allotropic type of carbon, although both are  $sp^3$  (cubic) and regular  $sp^2$  (planar) structures, respectively [2, 3, 7, 14]. CNTs are generally categorized according to their distances, sizes, and dividers' proximity into four classes (Fig. 2) i.e. Single-, Double-, Triple- and Multi-walled carbon nanotubes, SWCNTs, DWCNTs, TWCNTs, and MWCNTs, respectively [15-22]. Widely explored SWCNTs and MWCNTs have unique properties, which are represented in Fig. 3 [10].



**Fig. 2 Types of carbon nanotubes**



**Fig. 3. Properties of SWCNTs and MWCNTs [10]**

### 3.1 Single-walled carbon nanotubes

SWCNTs consist of a continuous graphic sheet enclosed in a round, hollow cylinder with a diameter between 0.4 to 2.5 nm, and SWCNTs have a diameter of about 1 nm. According to their simplified structure as shown in the Fig. 2, a cylinder's size is several million times longer [12,16,17].

### 3.2 Double-walled carbon nanotubes

Because of significant structural and properties, DWCNT's are similar to SWCNT. DWCNTs contain precisely double aligned graphene layers, which are coaxial nanostructures. This is a form of a hybrid structure of SWCNT and MWCNT. The outer wall can only be altered while the internal cylinders remain unchanged and its inner features can be retained [23].

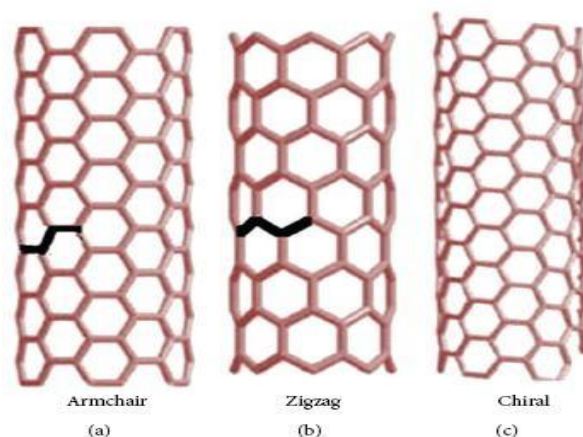
### 3.3 Triple-walled carbon nanotubes

The presence of three graphene sheet layers indicates a triple-walled nanotube

(TWCNTs) [22].

### 3.4 Multi-walled carbon nanotubes

Multi-walled carbon nanotubes (MWCNTs), composed of several graph condensed pipes, usually consist of two variants (Fig. 4), and designs such as parching and Russian doll are used, are more than a single atomic layer with a diameter larger than 10 nm. graphite sheets are arranged in a concentrated cylinder and are surrounded by a solo graphite sheet as a rolling paper in a Parchment model. The diameter and angle of chiral vary. CNTs have electrical properties, such as metals. Zigzags and chiral CNT have electrical properties similar to those of semiconductors [15]. The CNT substructure ('armchair', 'zigzag') is obtained from the kind of method applied during the synthesis process.



**Fig. 4 Different CNTs structures**

## 4. Fabrication techniques of CNTs

### 4.1 Laser ablation method

Thess et al. also obtained impressive CNTs (> 70%) at medium Co and Ni concentrations at 1200 °C through laser ablation methods of graphite rods. In this procedure, the purpose of graphite is blocked by laser light. The pipe is shaped at the end of the nanotube until such a large number of catalysts molecules are created; massive particles either reposition themselves or are coated with enough carbon to destroy the catalysis [24].

### 4.2 Arc Discharge Method

Another tubular-shaped structure, which is currently called as CNTs, was announced in Iijima in 1991. The tubes have been produced using a strategy for arc discharge. Carbon dioxide evaporations in an argon-fill vessel (100 torrs) needles with lengths of up to 1 mm

are carried out with the cathode of a carbon electrode using direct current (DC) methods [9].

The major synthesis of the MWCNTs was reported by Ebbesen and Ajayan in 1992 through this technique [25]. Bethune et al. used the thin bored anodes filled with unadulterated powdered metals and graphite (Fe, Ni, or Co). The electrode was vaporized at 100-500 torr in the helium atmosphere with a moderately low current of 95-105 A [26].

#### **4.3 Method of chemical vapors deposition**

Catalyst is applied on the product in two phases and the catalytic nucleation is ultimately transferred by chemicals or by heat regeneration where ammonia is used as a grafting device, the metal catalysts used are Fe, Co and Ni, where carbon sources are then put in the reaction chamber at the gas level. Then the carbon molecules switch in the atomic level by using power sources like plasma or a heated spiral and then carbohydrate into a substratum protected by a catalyst, creating nanotubes over this metal catalyst, the origin of carbon being acetylene, monoxide or methane. The temperature of the nanotube synthesis is 650-900 ° C. The average production was 30% [ 27].

#### **4.4 Flame synthesis method**

The SWCNTs are formed by hydrocarbon fuel and vaporized metal catalysts in controlled flame conditions. The SWCNTs have been shown at 50 Torr in the post-flame region of a premixed argon / oxygen-acetylene flame used as a metal catalyst source with iron pent carbonyl vapor [28].

### **5. Purification techniques of CNTs**

Carbon nanotubes typically have several impurities, including amorphous carbon and metal fragments. There are various techniques for CNT purification [29].

#### **5.1 Air oxidation**

The proportion of unknown carbon and metal catalyst is appropriate to reduce by the air oxidation process. Ideal oxidation is seen for 40 min at 673 K.

#### **5.2 Acid refluxing**

High-Acid reflux may decrease the concentrations of carbon amorphous and metal. Various acids such as HNO<sub>3</sub>, HCl and H<sub>2</sub>SO<sub>4</sub>, however, HCl is the ultimate reflux acid.

#### **5.3 Surfactant aided filtration, annealing, and sonication**

Acid reflux made the CNTs purer, but CNTs can capture catalysts and carbon particles which are difficult to eliminate by filtration. Sodium dodecylbenzenic sulphonate (SDBS) favored facilitated ethanol (or methanol) sonification since it took more time for the CNT to

create a good degree of suspension. Then the specimen was filtered in N<sub>2</sub>, at 1273 K with an ultra filtration system for 4 hours. Annealing will strengthen CNTs structures.

## **6. Properties of carbon nanotubes**

CNTs are tube-shaped cylinders with nanoscopic measurements. The average diameter of SWCNTs is approximately 5-30 nm and the average length is within a few millimeters. The thermal and electrical properties of CNTs are far better than conventional materials. [30].

Another feature of nanotubes is that membranes such as cell walls can easily penetrate by them. Nanotube long, narrow-shaped act like diminutive needles, so it tends to make sense to work on a cellular level like a needle. Medical researchers use this property by attaching nanotubes to molecules attracted by cancer cells to deliver drugs to the target site of the action [30].

## **7. Applications of CNTs**

The special aggregates of CNTs with irregular horns are carbon nanohorns (CNHs). Different reports have shown CNTs as a potential framework for drug delivery. Amphotericin B is used to target cells in functional CNTs. Cisplatin containing SWNHs suggested the mild aqueous release of Cisplatin. The release was demonstrated to be effective to inhibit human lung cancer cell growth while SWNH itself showed no action against cancer [31]. Nanotubes administered polyphosphazene platinum has improved penetration, distribution and maintenance in the brain owing to the lipophilic controls of the CNTs [11].

Doxorubicin is connected to the carbon nanotube, resulting in increased intracellular penetration. The gelatin-based CNT hydrogel was used as a bioactive lucrative delivery framework. The successful oral alternative administrators for Erythropoietin (EPO) could provide a CNT-based distribution system that is still not feasible because of gastric conditions and EPO denaturation of enzymes [32]. Glidant and lubricants can be used in the formulations of tablets because of the nano-size and slipping features of the graphite surfaces [11].

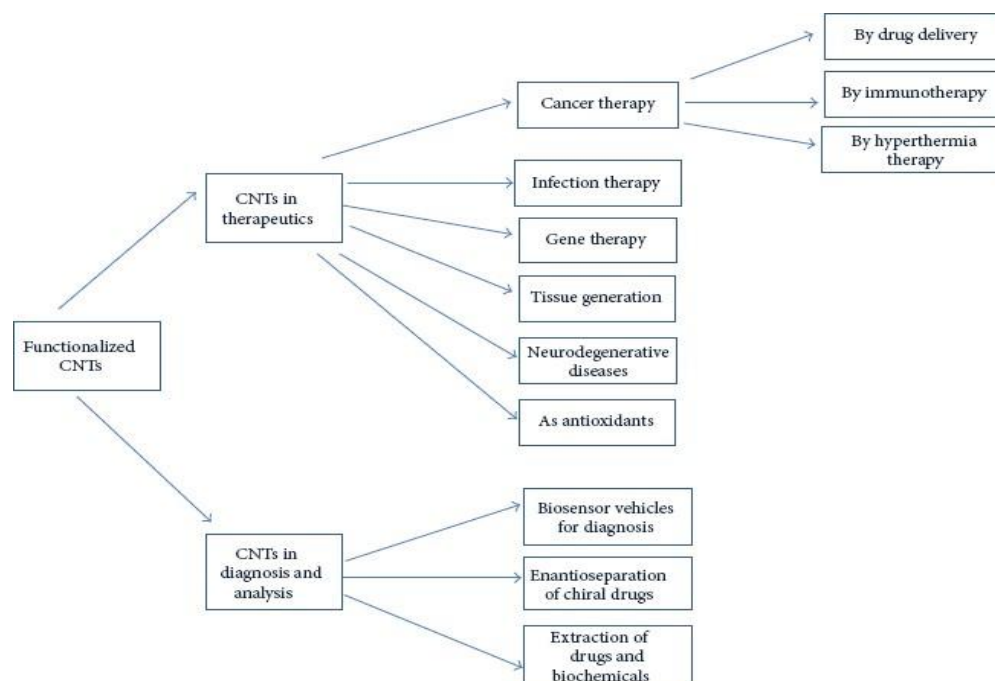


Fig. 5 Applications of CNTs [15]

## 8. CNTs in curcumin delivery

Curcumin, a generally utilized natural compound for antitumor treatment, can not accomplish maximum capacity because of poor bioavailability. In this regard, Li et al. developed curcumin (cur)-stacked SWCNTs formulation for using the anticancer potential of curcumin by bypassing traditional impediments of stability and very low aqueous solubility under physiological conditions. After functionalization SWCNTs and the corresponding SWCNT-Cur conjugates displayed zeta potential and size -12.5 mV and 170.4 nm, respectively with enhanced curcumin stability and aqueous solubility in PC-3 cells as compared to curcumin alone. Improved inhibition capacity was demonstrated in PC-3 cells [33].

Recently Li et al. created a novel delivery framework for curcumin utilizing polyvinylpyrrolidone and phosphatidylcholine (SWCNT-Cur) with functionalized SWCNTs and demonstrated significantly greater tumor growth inhibition up to 18 times in mice. No toxicity of main organs in a murine S 180 tumor model in mice was exhibited by SWCNT-Cur [34].

## 9. The obstacle in curcumin delivery and remedy

The oral absorption of curcumin is low and is thought to happen predominantly by trans-epithelial diffusion. Curcumin first undergoes rapid digestion of the bowels to form

curcumin glucuronide and curcumin sulfate by O-conjugation. Tetrahydrocurcumin, hexahydrocurcumin, and hexahydrocurcuminol are incorporated by means of reduction into different metabolites. Curcumin may also undergo extensive secondary metabolism in the liver where the essential metabolites are tetrahydro curcumin glucuronides and hexahydro curcumin, with dihydro ferulic acid and ferulic acid traces as additional metabolites that are considerably less than 1 percent usable in oral bioavailability.

Roughly 40% of new natural drug molecules have low aqueous solubility, which prompts poor bioavailability and absence of dose proportionality. Various advances are accessible to improve solubility and disintegration rate, for example, solid dispersion, micronization, complexation with cyclodextrin, however, these techniques have a certain drawback. In the present situation, various institutions and researchers from all over the world are attempting to build up a promising CNTs based formulation to improve the bioavailability of the hydrophobic drug, curcumin.

## **10. Conclusion**

Curcumin is strongly unsterilized and alkalized in the acidic pH of the stomach and has metabolized many components before reaching the body. Therefore, the optimal amount of curcumin cannot reach the blood without showing any therapeutic effect. CNTs related to curcumin will transfer the optimal amount of drugs at their site of action which crosses boundaries, such as the acidic pH of the liver digestion, stomach and the reduced blood flow of the drug. So CNTs based drug delivery framework can be investigated to improve the solubility, upgrade of bioavailability, decrease of dose, targeted site of activity and controlled release of curcumin.

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