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Review on: Carbon Nanotubes

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HUMAN

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ABSTRACT

Carbon Nanotubes (CNTs) are nanostructures derived from the graphene planes having one or several layers of graphenes discovered by Iijima in 1991. CNTs synthesized for the drug delivery system using controlled composition, shape, size and morphology, can be increased solubility, immune compatibility, and cellular uptake by manipulating surface properties for the targeted area of drug delivery. CNTs exist the Single-walled carbon nanotubes (SWCNTs) and Multi-walled carbon nanotubes (MWCNTs) structures having several properties such as ultra-lightweight, high-aspect-ratio, electronic properties including metallic and semiconducting, high thermal properties, mechanical properties (tensile strength and elastic strength), optical properties and chemical properties. Techniques for the development of CNT are the arc discharge method, laser ablation method, and chemical vapor deposition (CVD). After production CNTs can be purified by using various techniques such as oxidative treatment, acid treatment, magnetic treatment, ultra-sonication, filtration, centrifugation, and microwave purification. Functionalized CNTs can be conjugated with the drugs, nucleic acid, proteins which are used in several biomedical applications and diagnosis. Functionalized CNTs make them use a wide range of applications in different areas includes, including cancer treatment, infection therapy, gene therapy, tissue generation, neurodegenerative disease, as antioxidants, a biosensor for diagnosis. This review regarding CNTs has shown a promising glimpse in the field of pharmacy due to their surface area, strength, stiffness, and resilience.

INTRODUCTION:

Nanotechnology is the latest and advanced manufacturing technology and it has a wide area of research rising worldwide. Dimensions of the nanostructured material are below 100 nm. This nanomaterial access to various properties such as magnetic, electronic, mechanical, and optical properties. In nanotubes, nanomaterials are the promising group. Many nanotubes based on boron and molybdenum have been stated worldwide, but carbon nanotubes are a current vital group in nanotechnology. [1]Carbon nanotubes (CNTs) derived from rolled graphene planes having one or several layers of concentric graphite with diameter 0.4 to 10 nm(Figure No. 1) Carbon nanotubes discovered by Japanese scientist Iijima in 1991 by stimulated intense experimental and theoretical studies on carbon nanotubes using High-Resolution Electron Microscopy (HREM). For the characterization of microstructure and study of structural features of nanotubes, HREM is the robust approach and it should be pointed out the two-dimensional and three-dimensional image of the object. Carbon nanotubes allotropes of carbon molecules that having nanostructure arranged in 60 atoms arranged in stuffed tubes. [1, 2, 4]

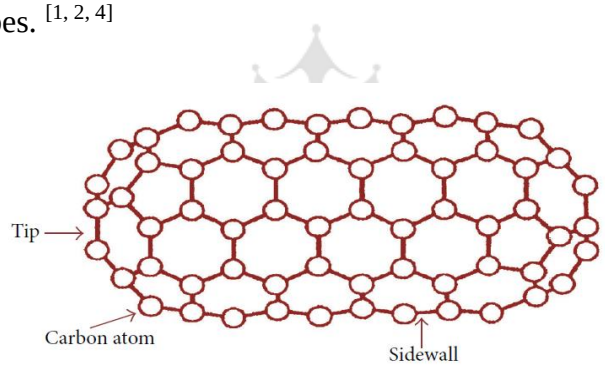


Figure No. 1: Structure of carbon nanotubes

In carbon nanotubes (CNTs), a drug delivery system synthesized using controlled composition, shape, size, and morphology. These can be increased the solubility, immune compatibility, and cellular uptake by manipulating surface properties that match the requirements of the target area of delivery. CNTs having tremendous application in Nanobiotechnology and Biomedicine Field because these exhibits less toxicity and are not immunogenic after functionalization. [2]

The structure of CNTs exists in two types as Single-Walled Nanotubes (SWCNTs) and Multi-Walled Nanotubes (MWCNTs) (Figure No. 2). They possess several intrinsic properties such as ultra-lightweight, high thermal conductivity, high aspect ratio, tremendous strength, and remarkable electronic properties ranging from metallic to semiconducting.

SWCNTs having photoluminescence property that can be effectively applied in diagnosis and MWCNTs having wider surface area allows more efficient internal encapsulation and external functionalization with active molecules. CNTs can be conjugated with various biological molecules such as drugs, proteins, and nucleic acid to improve bio-functionalities. CNT exists an aromatic network on the surface that allows efficient loading of aromatic molecules such as chemotherapeutic drugs. Carbon nanotubes having versatile chemistry that can enable a wide range of applications in biomedicine. SWCNTs and MWCNTs have been used for biosensors, field-effect transistors, and scanning probe elements.[3]

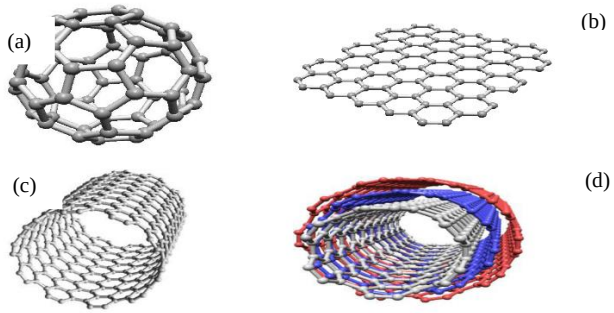


Figure No. 2: Nano Allotropes of carbon (a) Fullerene C60 (b) Graphite sheet (c) SWCNTs (d) and MWCNTs

ADVANTAGES OF CARBON NANOTUBES:

- CNTs having a Biocompatible, Non-biodegradable, and Non-immunogenic nature.
- The highly elastic nature gives the possibility of intracellular delivery.
- Minimum cytotoxicity.
- Excretion of CNTs by urine is 96 % and the remaining 4 % by feces.
- Do not break down during processing due to ultra-lightweight.
- Access to the inner surface and subsequent incorporation of species within nanotubes is easy because both ends of nanotubes are opened.
- Longer inner volume relative to the diameter of nanotubes
- Tubular and nanoneedle shape structure of CNTs able to enter cells by spontaneous mechanism.

- Differentially modified for chemical and biochemical functionalization due to distinct and inner surface.

LIMITATIONS OF CARBON NANOTUBES:

- Difficulty in production of structurally and chemically reproducible batches of CNTs with identical characteristics.
- Maintenance of high quality and minimal impurities is a challenging approach.
- Lack of solubility in most solvents.

TYPES OF CARBON NANOTUBES:

Carbon nanotubes are hollow tubular structures consist of carbon atoms arranged in series of a condensed benzene rings. CNTs contain artificial nanomaterial which belongs to the family of fullerenes is the third allotropic form of carbon along with graphite and diamond this both are natural sp^2(planer) and sp^3(cubic) forms (Table No.1). [5]CNTs can be classified into two types based on the number of layers and structure:

1. Single-walled carbon nanotubes (SWCNTs)
2. Multiple-walled carbon nanotubes (MWCNTs)

Table No. 1: Comparison between SWCNTs and MWCNTs

Characteristics	**SWCNTs**	**MWCNTs**
Layer of graphenes	Single	Multiple
Catalyst for Synthesis	Required for synthesis	Without catalyst can be produced
Bulk synthesis	difficult	Easy
Purity	Poor	High
Accumulation in the body	Less	More
Characterization and evaluation	Easy	Difficult
Twisting	Easy	Difficult
Defection during functionalization	More	Less, but difficult to improve

1. Single-walled carbon nanotubes (SWCNTs): It consists of a single layer or sheet of carbon benzene ring which is wrapped into the shape of a cylinder. The diameter of SWCNTs is 0.4-2 nm and the length ranges from 50 nm up to 1cm as short as. Diameter of SWCNTs based on the temperature i.e. higher the growth temperature larger is the diameter of CNTs. The structure of the SWCNTs based on the arrangement of carbon atoms may be an armchair, zigzag, chiral, or helical arrangement (Figure No. 3). This classification of the SWCNTs is based on the variation in the angle of graphite planes that make up the bulk of single-walled nanotubes. In the nanotubes, the way of graphene sheets wraps this is represented by pair that indicates n and m called the chiral vector. The structure of SWCNTs is found in curled and curved strands rather than straight lines.

a) In **"Armchair"** nanotubes, the graphene sheet rolls up at an angle that is perpendicular in the form of a hexagonal lattice armchair that is n=m and chiral angle=30^0.

b) In **"Zigzag"** nanotubes, the angle of graphene sheet is rolled up, which makes parallel to the row of zigzag bonds in the hexagonal structure that is n=0 or m=0 and chiral angle= 0^0.

c) In **"Chiral"** nanotubes, graphene sheets are aligned as cylindrical at some chiral angle other than armchair and zigzag that is the value of n and m and chiral angle lie between 0 and 30^0.

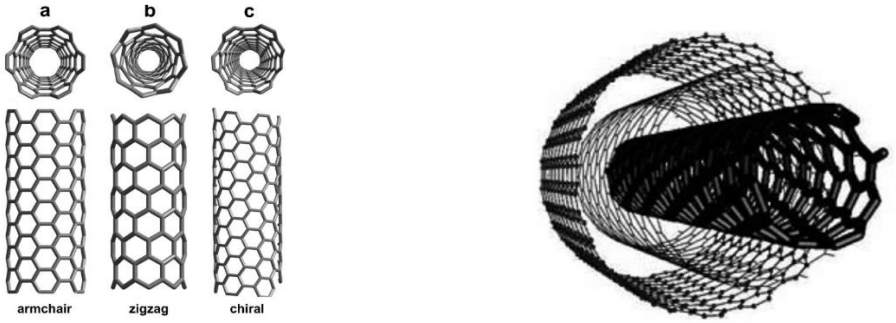
SWCNTs are more efficient for drug delivery than MWCNTs, this is due to SWCNTs have an ultra-high surface area as large as 1300 m^2/g and efficient drug loading capacity. SWCNTs anticancer drug complex found that longer blood circulation time than own anticancer drugs. SWCNTs give the more prolonged and sustained uptake of the drug by tumor cells by enhancing the permeability and retention effect. After functionalization of SWCNTs, releases the drug into a specific area and it is excreted from the body via the biliary pathway and finally in the feces. SWCNTs are suitable for drug delivery and promising nanoplatform for cancer therapeutics. (Figure No. 3)[6]

2. Multi-walled Carbon nanotubes: It consists of several coaxial cylinders each layer made up of graphene sheets surrounding the hollow core to form tube shape cylinder. The outer diameter of the nanotube ranges from 2-100 nm, and the inner diameter is in the range of 1-3 nm, and their length is several micrometers (Figure No. 3). The structure of MWCNTs is categorized into two types based on the arrangement of graphite layers such as parchment-like structure and Russian doll model.

a) In **"Parchment-like"** structure consisting of a single sheet of graphite rolled around itself.

b) The **"Russian doll model"** consists layer of graphite sheets are arranged in a concentric structure.

MWCNTs have several applications in catalysis, biosensors, biomedical, magnetic data storage, and electronic device. This can be done by depositing nanoparticles on the wall or ends of MWCNTs bonded by physical interaction.[5]



(A) **(B)**

Figure No. 3: Models of CNTs (A) structure SWCNTs (a) armchair configuration (b) zigzag arrangement (c)chiral configuration (B) Structure of MWCNT

PROPERTIES OF CARBON NANOTUBES:

The properties of CNTs are based on the formation of the networks of carbon molecules which takes high advantage of the aspect ratio in between the length and diameter of the tube. This can enhance the electric and thermal properties of the nanotube as compared to the conventional material used.

Another property of carbon nanotube is the structure that is a long and narrow structure of CNTs looks like a miniature needle so their function as a needle at the cellular level. This property of CNTs used for the medical application for the treatment of cancer by attaching molecules that are attracted by cancer cells and delivering the drug directly to the affected cells.[5,11]

1. **Mechanical properties:** High flexibility and high strength with high stiffness due to the small diameter of carbon nanotubes give an important effect on the mechanical properties as compared with micron-size graphite fibers.

a) **Tensile strength**: SWCNTs are 100 times stronger than steel and one-sixth weight of steel, copper, and half weight of aluminium and hallow structure and chicken wire-like structure make it very light. Reported tensile strength of SWCNTs ranging from 13 to 52 GPa and MWCNTs found that only the outermost layer breaks during the loading process. In the CNTs strong carbon-to-carbon bond that holds together its fullerene lattice, each carbon atom covalently bonded to the other three carbon atoms. This strong binding mechanism gives the stability of the geometric structure of nanotubes and makes them strong and it gives the remarkably tensile strength. [6, 7, 8]

b) **Elastic strength**: The young's module of CNTs is directly related to the cohesion of the solid and chemical bonding of constituent atoms. In CNTs, it can be related to sp2 bond strength and equal to that of graphene sheets. This is applicable when the diameter is not too small to distort the C-C bond significantly. Young's modulus of SWCNTs 2.8-3.6 TPa and MWCNTs is 1.4-2.4 TPa reported by Lourie and Wagner. Nanotubes show bending, twisting, kink, and finally buckle when exposed to axial compressive force. This tube does not break under compressive force. [6, 9]

2. Electrical properties: Carbon nanotubes are not extremely strong, higher strength, flexible but they are having good electrical properties. The electrical property of the CNTs is due to the rolling up of graphene sheets. A single flat graphene sheet is semimetal that is it possesses properties of both metals like copper wire and semiconductors like silicon chips. [6]

a) The diameter and chirality of the carbon nanotubes are most important because they can influence their electrical properties.

b) The conductivity of CNTs is eight times higher than copper.

c) CNTs behave like a metallic conductor when a graphite sheet is rolled up like a sheet of paper with edges of top and bottom evenly lined up and it efficiently carrying the electricity. Its electrical property changes to the silicon-like semiconductor where current can be switched on and off when nanotube rolled up a skew or like misbuttoned of a shirt.

d) The electrical properties of CNTs can be effectively affected due to the structure of nanotubes and symmetry and the electronic structure of graphenes.

e) In theory, the Electrical current density of carbon nanotubes is 48109 A/cm^2 which is 1000 times greater than metal such as copper. [6,9]

3. Thermal properties: Carbon nanotubes exhibit the 'ballistic conductance' property, so all nanotubes are expected to be a very good thermal conductor. Hence all nanotubes are extremely stable at high temperatures. Small size, quantum effects low temperature that thermal conductivity at room temperature is larger than graphite or diamond. Measurements show the thermal conductivity at room temperature of bulk samples of SWCNTs is over 200 W/mk and individual MWCNTs is 3000 W/mk. The addition of epoxy resins in carbon nanotubes can double the thermal conductivity for only loading 1% and it may be useful for thermal management application. Carbon nanotubes can stable at 2800^0C in a vacuum and up to 750^0C at normal atmospheric pressure. These all thermal characteristics and other factors that make nanotubes serve as well-suited electrical conductors. Typical metallic conductors melt at temperatures 600^0C to 1000^0C.

4. Chemical properties: The chemical reactivity of CNTs can be enhanced as compared with graphene sheets due to the curvature of the CNT surface. Hybridization between the orbitals due to mixing of π and σ orbital because curvature surface of CNT. Larger the degree of hybridization, the smaller the diameter of SWCNT. Hence reactivity of carbon nanotubes is related to the π-orbital mismatch which is caused due to the increased curvature. Therefore, the distinction between sidewalls and the end cap of the nanotube is most important. For the increasing the reactivity, smaller the diameter of nanotubes. Solubility of CNT in the different solvents can be controlled by covalent chemical modification of sidewalls and end caps of a nanotube. Attachment of molecular species to sp2 bonded carbon atoms to sidewalls of a nanotube is very difficult. Therefore, nanotubes are considered chemically inert.

5. Optical properties: SWCNT's optical properties contribute to quasi-existence. Theoretical experimental have shown that as the nanotubes grow larger, the optical property of chiral nanotubes disappears and other physical properties are to be improved by these parameters too. Optical properties of CNTs; nanotubes having metallic property (for n, m: n-m is divisible by 3 shows 0eV and nanotubes having semi-conducting property (for n, m: n-m is not divisible by 3) shows ~0.5eV.

METHODS TO PRODUCTION OF CNTS:

Production of Carbon Nanotubes, a high-temperature preparation technique first used to produce CNT's such as arc discharge and laser ablation method. Nowadays these methods have been replaced by low temperature (<800^0C) i.e. chemical vapor deposition (CVD) techniques. In this technique orientation, nanotube length, diameter, alignment, density, and

purity of carbon nanotubes can be precisely controlled. These methods require supporting gases and vacuum. The gas-phase method is volumetric and they are suitable for the production of large quantities of nanotubes and make economically feasible for industrial-scale synthesis. The disadvantages of this method are low catalyst yield, a small percentage of catalysts from nanotubes, short catalyst lifetime, and low catalyst density.[3, 14]Mechanism of production of Carbon Nanotubes is shown in Table No. 2.

Table No. 2: Mechanism of production CNTs

Arc discharge method	**Laser ablation method**	**The chemical vapor deposition method**
Electric discharge from one electrode to another ➡ electrode. (In gaseous environment) nonconductive gas converts conductive gas. Carbon substrates get vaporized get reassembles to form CNTs on the cathode. ➡	An intense pulse of laser light. ⬇ Directed on On a small amount of carbon substrate and transition metals in the stream of helium gas. ⬇ Carbon substrate gets evaporates and this evaporated carbon deposited and assembles to form CNTs	Decomposition of volatile carbon precursor at high temperature (700^0-900^0C). ⬇ Hydrocarbon molecules dissociation. ⬇ Precipitation of carbon atoms from saturated metal particles. ⬇ Formation of CNT's.

1. Arc Discharge Method: For the Production of carbon nanotubes, the arc discharge method is based on a high temperature (above 1700^0C) process. This method is based on the mass production of fullerenes using arc discharge.

In the arc discharge method, ignition of the arc between two electrodes of the graphite in a gaseous state as background generally hydrogen/ argon gas is used.

When the process of evaporation carbon meanwhile it's cooled and condensed itself and that some product forms the filamentous carbon on the cathode.

The purity of MWCNT nanotubes and yield depended sensitivity depends on the gas pressure in the reaction vessel. Final morphology of CNT's influenced by the different gaseous atmospheres. They used DC Arc Discharge of Graphite electrodes helium and methane. Under a methane gas pressure of 50 Torr and arc current of 20A for anode forms the thin and long MWCNT having 6 mm diameter. Evaporation of carbon atom under high pressured methane gas and high arc current, formation of thick nanotubes with many carbon nanoparticles were obtained. It is found that the variation in the morphology of carbon nanotubes was more marked in the evaporation of carbon atoms in methane gas than in helium gas.

The SWCNT was produced by using the transition metal catalyst. The process of production of SWCNT by Arc Discharge utilizes composite anode in hydrogen or argon gaseous atmosphere. The anode contains graphite and metals such as Ni, Co, Pd, Ag, Pt, etc. Or the mixture of metals with the other elements such as Co-Ni, Fe-Ni, Fe-No, Co-Cu, Ni-Cu. In the process of production, the metal catalyst plays a significant role. The constant gap distance between the electrodes, stable current density, and anode consumption rate ensures the high efficiency of the process. In this process, the unwanted product is also produced such as MWCNT and fullerenes too.[3,12, 13]

2. Laser Ablation Method: The mechanism of the laser ablation method is based on the pulsed and continuous laser to vaporize graphite in the oven, which is filled with argon or helium gas to keep constant pressure. The process of laser ablation and arc discharge method is similar such as they both taking high temperature and similar optimum gaseous background and catalyst mixed where observed.[14]

SWCNTs are produced by continuous wave CO_2 laser ablation without applying additional heat. They found that the average diameter nanotubes were produced by increasing the power of the CO_2 laser.

This method produced primarily SWCNTs with controlled diameter, this can be determined by the reaction temperature and yield of nanotubes around 70%.

The laser ablation method is more expensive than the arc discharge and chemical vapor deposition method.[3, 5, 13]

3. Chemical vapor deposition (CVD): In this method nanotubes synthesized by putting a carbon source in the gas phase and using plasma and heating coil continuously heated to heat gaseous carbon-containing molecules. Heat is used for the "crack" the molecule into reactive atomic carbon.

This method is also known as Catalytic CVD because this method used the catalyst in the synthesis of CNT's. Most frequently catalyst is transition method such as Fe, Co, Ni. But sometimes catalysts are further doped with other methods such as with Au.

The most preferred Carbon sources in CVD are hydrocarbons such as methane, ethane, acetylene, xylene, ethylene, or their mixture with isobutene or ethanol. In the case of gaseous carbon sources, the growth efficiency of CNTs is strongly dependent on the reactivity and concentration of gas-phase intermediates produced as a result of hydrocarbon decomposition along with reactive species and free radicles.

These studies showed that the growth efficiency of CNTs strongly depends on the intermediate complex gas-phase reaction which is produced from the reactivity and concentration of the gas phase. The most efficient intermediates, which have the potential to initiates CNT growth should be produced in the gas phase by physisorption or chemisorption catalyst surface reaction. The overall kinetics of the growth process of CNTs by CVD depends on the composition of the gas phase, interaction, and surface reaction.[5, 14, 15]

Types of CVD are: 1) Methane CVD, 2) High-pressure Catalytic CVD, 3) plasma-enhanced CVD, 4) Plasma enhanced CVD, 5) CO CVD (Figure No. 4). [16]

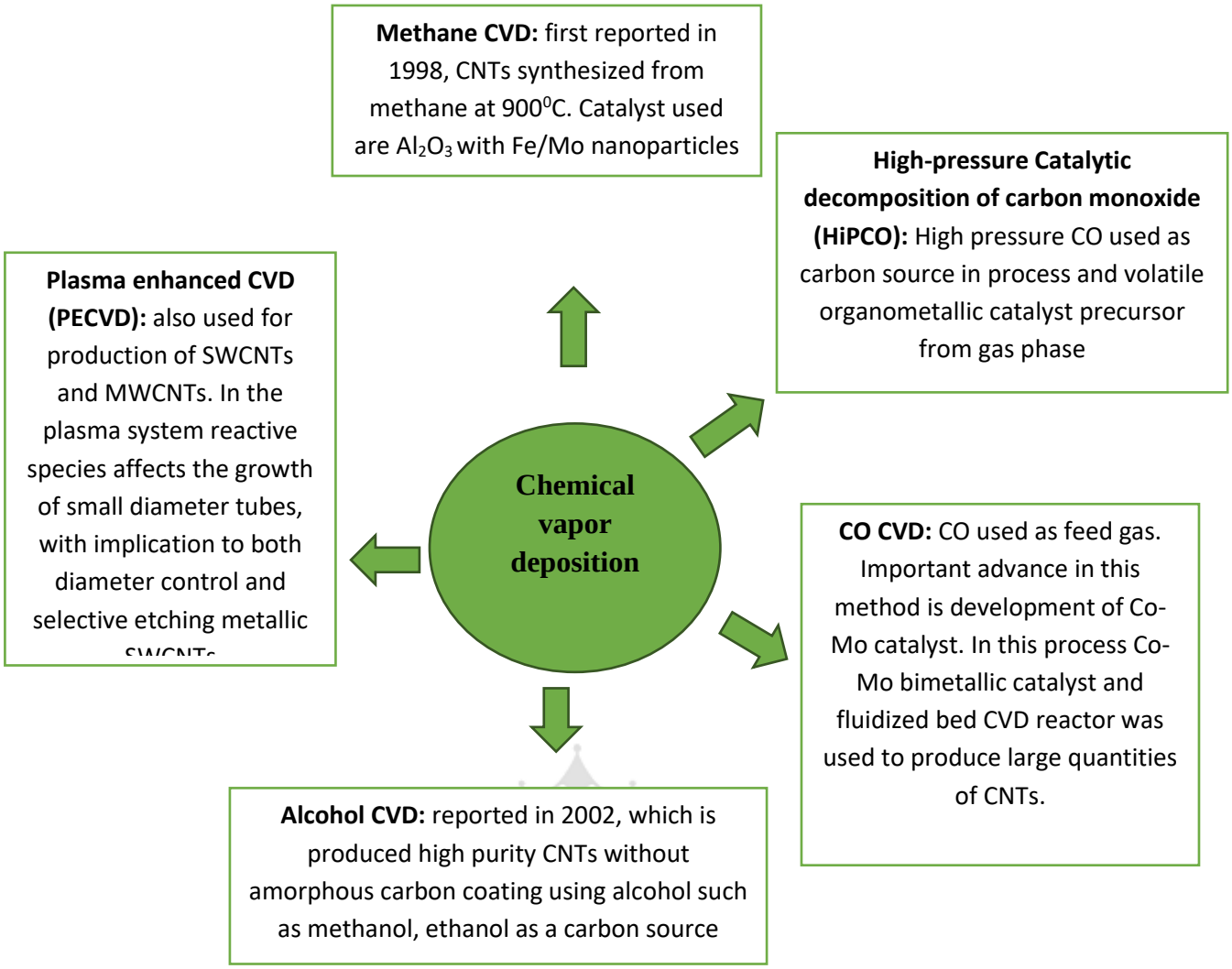


Figure No 4: Types of Chemical Vapor Decomposition

Summary of the major production method and their efficiency shown in Table No. 3.

Table No. 3: summary of the major production method and their efficiency

Method	**Arc Discharge**	**Chemical Vapor Deposition**	**Laser Ablation**
Who	Ebbesen and Ajayan, NEC, Japan 1992	Endo, Shinshu University, Nagano, Japan.	Smally, Rice, 1995
Process	Connect two graphite rods to a power supply, place them a few mm apart, and throw the	Substrate placed in an oven at 600^{0}C and slowly add a carbon-bearing gas such as methane. As gas	Graphite blasts with intense laser pulses: use of the laser pulses rather than electricity to

	switch. At 100 amps carbon vaporizes and form hot plasma	methane. As gas decomposes it free up carbon atoms, which recombine in the form of nanotubes.	generate carbon gas.
Gas-phase condition	Helium low-pressure inert gas	High temperature within 500 to 1000^{0}C at atmospheric pressure.	Argon or Nitrogen gas: at 50 Torr
Yield	30-90 %	20-100 %	Up to 70 %
SWCNT	Short tube Diameter:0.6-.4 nm	Long tubes Diameter: 0.6-4 nm	Long bundles of tubes: 5-20 microns. Diameter 1-2 nm
MWCNT	Short tube Inner diameter: 1-3 nm Outer diameter: approx.10nm	Long tubes Diameter: 10-240 nm	Not very much interested in this technique because it is too expensive but the synthesis of MWCNT is possible.
Carbon source	Pure graphite	Fossil based hydrocarbon and botanical hydrocarbon	Graphite
Cost	High	Low	High
Advantage	Can easily produce SWCNT and MWCNTs, less expensive, open-air synthesis possible.	Easiest scale up to industrial production, SWCNT has a long length, controllable diameter, simple process, and quite pure.	Good quality, higher yield.
Limitation	Needs a lot of purification.	Often riddled with defects.	The costly technique requires an expensive laser and high power requirements but improvement.

FUNCTIONALIZATION:

The surface of raw carbon nanotubes having highly hydrophobic and these CNT's are not soluble in an aqueous solution and pristine CNT's are unable to soluble in any solution. Functionalization of CNT's is the chemical synthesis process where the desired functional group can be attached to the wall of CNT's. These functionalized CNT are produced for several applications. Functionalized CNT's used for Cancer treatment, can be enhancement of biocompatibility within the body, multi-model drug delivery, enhancement of encapsulation tendency, and solubility.[17, 18]Functionalization of CNT's divided into two categories:

1. Covalent functionalization
2. Noncovalent functionalization

1. Covalent Functionalization: In the process of covalent functionalization chemical reactions are carried out to form bonds with sidewalls of nanotubes.

In covalent functionalization, the chemical bonding of the polymer chain to the sidewalls of nanotubes forms the strong chemical bond between nanotubes and attached molecules.

Three main methods used for covalent bonding are

– Molecules or polymer chain reacting with the surface of pristine
– Pre-functionalized
– Oxidized CNTs

The strategy of the covalent functionalization is based on oxidation and carboxyl-based coupling.

The oxidation process of CNTs represents the modification using an oxidizing agent. In this method opening of the tube cap and created the holes created the holes in the sidewall of the tube by an oxidation process by using strong acids e.g. nitric acid. Concentrated nitric acid to form carboxyl group at the most reactive site i.e. end of the tube, which are more reactive site and on any defect on the walls such as 5-membered rings. Through this method, CNTs can be conjugated with various functional groups, by bonding with a suitable group the nanotubes can be easily soluble in aqueous and organic solvents. It can be reduced van der wall

interactions between tubes by bonding with a carboxylic group on sidewalls of tubes represents the separation of nanotube bundles into individual separated tubes.[17, 18,19]

2. Noncovalent functionalization: Noncovalent bonding of molecules to the nanotubes is a more widely used method of drug delivery. Ideal properties of the non-covalently functionalized CNT are the more closely matched, greater usefulness in biological roles. This can be carried out using amphiphilic molecules to create the micelle-type structure that is coated to the nanotubes.

Another method for the functionalization is π-π bonding carried out by stacking of pyrene molecules on the surface of nanotubes. This type of bonding is applied to single strands of DNA by the aromatic DNA base units. This can be shown the unstable because it is cleaved by nucleases and consequently biological application also limited.

Non-covalent functionalization does not interrupt the π- network but the shortening of length and physical properties of CNTs are preserved and show great promise for imaging and photothermal ablation.[17, 19]

PURIFICATION OF CARBON NANOTUBES:

The production of carbon nanotubes generally contains a large number of impurities such as amorphous carbon, metal particles, and multishell. The different purification stages are Oxidative treatment, Acid treatment, Magnetic purification, and Ultrasonication.[5, 16]

1. Oxidative treatment: Oxidative treatment of the CNTs is a good process to remove impurities such as carbonaceous material, metal particles and clear the metal surface.

The main disadvantage of oxidative treatment is, in this process not only impurities are oxidized, but also the CNTs. But the damage of CNTs is very less than the damage of the impurities. Oxidative treatment for removing impurities is the most preferred method because impurities are commonly attached to the metal catalyst, which also acts as an oxidizing catalyst or these impurities have a more open structure.[5, 11]

The yield of procedure and efficiency is highly dependent on lots of factors such as oxidation time, oxidizing agent, temperature, metal content, and environment.

The fact of this process is that the metal acts as an oxidizing agent, the metal content should be taken into consideration. The temperature and time are also important factors for the

oxidative treatment e.g. when the temperature is raised above 60^0C, CNTs themselves oxidized, even without oxidizing catalyst.[20, 21]

2. Acid treatment: Acid treatment will remove the metal impurities. The first step of acid treatment is, the surface of the metal exposed to sonication or oxidation, then the metal catalyst exposed to acid and solvated. For the acid treatment, HNO_3 and HCl are used. Treatment with HNO_3 does not affect CNTs or other carbon material only removes the metal impurities. If treatment with HCl, it gives a considerable effect on CNTs and other carbon materials. Therefore HCl is considered the ideal refluxing acid.[5, 11,16]

3. Magnetic purification: In this method catalytic ferromagnetic particles are mechanically removed from their graphite shell. In this process, the CNTs are suspended with inorganic nanoparticles mainly ZrO_2, then subjected to ultrasonication to remove the ferromagnetic particles. After that particles are trapped with permanent magnetic poles. This subsequent chemical treatment gives highly pure CNTs. The main advantage of this process is, this process does not require large equipment and produces laboratory-sized quantities of CNTs containing no magnetic impurities.[21]

4. Ultrasonication: Due to ultrasonic vibration particles are separated. Due to vibration, agglomerates of different nanoparticles will be forced to vibrate and will get dispersed. Surfactants, reagents, and solvents used in this process are the highly dependent factor for the separation of particles. The solvents may influence the stability of dispersed nanotubes in the system. CNTs are more stable in poor solvents if they are still attached to the metal. Monodispersed particles are relatively stable in some solvents such as alcohol. When acids are used for ultrasonication as a solvent, the purity of nanotubes depends on the exposure time. When the nanotubes are exposed to longer time in acidic solvents the tubes are chemically cut but exposed for short time it only dissolves metal impurities.[5,16,22]

5. Centrifugation: CNTs are centrifuged at 7000 rpm or more for 30 min to 3 hrs, after that supernatant is removed and centrifuged again. This removes nanospheres, metal nanoparticles, and other carbon particles. [16, 22]

6. Filtration: This technique is used in conjugation with oxidation. The impurities are separated from acid treatment (acid decomposition products) are highly soluble in basic solution and CNTs are not, they can be separated using a basic solution of pH11 and filtered using 3-5 µm under vacuum. This process removes the metal particles, fullerenes, nanospheres, and polyatomic carbon. [16]

7. Microwave purification: CNTs are sonicated and then, diluted in nitric acid or other acids. Microwave at 100-200W at ramped up to ~200^{0}C over 30min. then, the microwave was held at a temperature of 200^{0}C for 30 to 90 min. This removes amorphous carbon, metal, and other nanoparticles. [16,21]

APPLICATIONS OF CARBON NANOTUBES: Functionalization of CNTs makes them useful in a wide range of applications in different areas. Structure of CNTs that the tubes have an inner and outer core which can be modified by different functional groups. The CNTs can be designed for a very specific purpose. The main application of CNTs in the biomedicine area is investigating especially four main fields: drug delivery, biomedical imaging, biosensors, and tissue engineering.[3, 25]

1. Cancer treatment:

1.1 By Drug Delivery: CNTs can be used as drug carriers to treat the tumors in cancer. The efficiency of anticancer drugs, when used alone is restrained by their systemic toxicity, narrow therapeutic window, drug resistance, and limited cellular penetration. The action of CNTs in the tumor cell will be than an alone drug administered by traditional therapy because CNTs easily cross the cytoplasmic membrane and nuclear membrane. After all, this anticancer drug is transported by the vehicle and it will be liberated in situ with intact concentration. The development of an efficient drug delivery system with the ability to enhance cellular uptake of an existing potent drug. CNTs have a wide range of applications in cancer treatment over existing drug delivery therapy because the high surface area of CNTs provides multiple sites for attachment of drugs. Many anticancer drugs have been conjugated with functionalized CNTs such as epirubicin, doxorubicin, cisplatin, methotrexate, quercetin, paclitaxel (Table No. 4). [17, 25]

Table No. 4: List of Anticancer drugs delivered using CNTs

Sr. No.	Name of drug	Functionalization	Type	Advantages
1.	Doxorubicin	PEG conjugation	SWCNT	Reduced toxicity
2.	Mitoxantrone	PEG conjugation	SWCNT	
3.	Paclitaxel	PEG conjugation	SWCNT	Reduced toxicity
4.	Cisplatin	-	SWCNT	Increased circulation period
5.	Carboplatin	Not functionalized	SWCNT	Decreased toxicity
6.	Doxorubicin	Conjugate with folate	MWCNT	
7.	Paclitaxel	Conjugate with folate	MWCNT	Active targeting
8.	Methotrexate	PEGlyted	MWCNT	Increased circulation period
9.	Quercitin	PEGlyted	SWCNT	Reduced side effects
10	Folic acid	-	MWCNT	Longer circulation period, active period

1.2 By Immunotherapy: CNTs are used as a carrier for the treatment of cancer and can be effectively applied in antitumor immunotherapy. This can attack the malignant cells by stimulating the patient's immune system. This stimulation can be achieved by the administration of a therapeutic antibody or a cancer vaccine as a drug.[25]

1.3 By Hypothermia Therapy: Hypothermia therapy using CNTs has been an efficient strategy for cancer treatment. SWCNTs are considered as potential candidates for hypothermal therapy because it exhibits strong absorbance in near-infrared (NIR)700-1100 nm, therefore they generate a significant amount of heat upon excitation with NIR light. Due to excessive heating of SWCNTs, the photothermal effect can induce the local thermal ablation of tumor cells and SWCNTs shackled in tumor cells such as pancreatic cancer. This technique is shown feasibility in clinical application.[25]

- **Blood Cancer:** Leukemia is cancer that begins in the bone marrow i.e. the soft and inner part of some bones, but it moves into the blood. Then it can be spread to other parts of the body such as organs and tissues. Acute lymphoblastic leukemia (ALL), is a slow-growing blood cancer that starts in bone marrow cells called lymphocytes and white blood cells, when

these blood cells are affected by leukemia then they do not go through their normal process of maturing.

The targeted delivery of daunorubicin to acute lymphoblastic leukemia developed the tertiary complex of Sgc8c aptamer this aptamer targets the protein tyrosine kinase-7 biomarker of leukemia. Daunorubicin and SWCNT are named Dau-aptamer SWCNTs. This tertiary complex was internalized effectively into the human T cell, leukemia cell (MOLT-4) but not to the U266 myeloma cell. The release of the drug in Dau-loaded nanotubes was pH-dependent. Dau was released from a complex in a slightly acidic solution in 72 h at 37^0C, while the tertiary complex of Dau-aptamer-SWCNTs was stable after the same incubation at pH 7.4 (Figure No. 5).

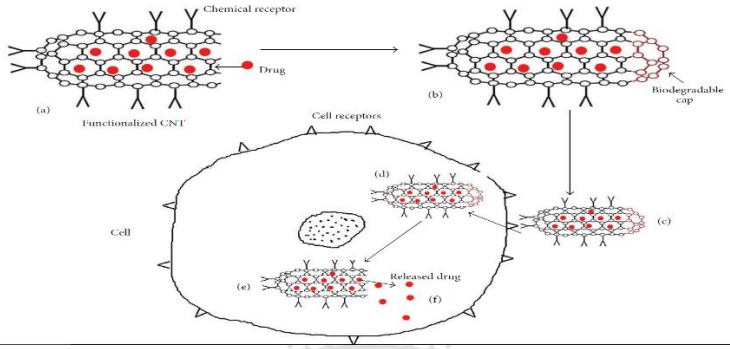


Figure No. 5: Schematic illustration of the drug delivery process. (a) CNT surface is linked with a chemical receptor (Y) and drug are loaded inside, (b) open end of CNT capped, (c) drug-CNT barrier is introduced in the body and reaches the target cell due to chemical receptor on CNT surface, (d) cell internalizes CNT by cell receptor (V) via endocytosis pathway € cap is removed or biodegrades inside the cell drug are released. **[25]**

- **Breast cancer:** SWCNTs functionalized PEGylated conjugation with introducing drug paclitaxel (PTX) showed higher water solubility and maintain the toxicity to cancer cell-like as Taxol. Blood circulation time of PTX in SWCNT-PTX much longer than Taxol. PEGylated PTX has high tumor uptake of the drug through the EPR effect. SWCNT-PTX can slow down tumor growth even at a lower dose of a drug due to its strong therapeutic efficiency.[3,13]

- **Liver cancer:** Polyamidoamine dendrimer CNTs i.e.dMWCNTs were fabricated for the efficiently delivered antisense c-myc oligonucleotide (ODN) into liver cancer cell line HepG2cell. This complex (ODN-dMWCNT) was incubated with HepG2 cell and enter into

tumor cell within 15 min by laser confocal microscopy. This inhibited the cell growth within time. This complex shows maximum inhibition effect of tumor cell and transfection efficiencies as compared to drug alone.[3,13]

- **Brain cancer:** Functionalized SWCNTs synthesized using phospholipid bearing polyethylene glycol (PL-PEG) and conjugated in protein A, and then it was coupled with fluorescein-labeled integrin monoclonal antibody to form a complex of SWCNT-integrin monoclonal antibody (SWCNT-PEG-mAb). SWCNT-PEG-mAb shows much higher fluorescence on integrin positive U87MG cells and presented low cellular toxicity, with high targeting efficiency, this is revealed by Confocal Microscopy. Integrin negative MCF-7 cell has fluorescence was not observed. This is revealed that the efficiency of the functionalized SWCNTs demonstrating the specific targeting of integrin positive U87MG which is caused by the specific recognition on the cellular membrane by the monoclonal antibody.[3, 24]

- **Cervical cancer:** Novel approach in the development of CNTs, utilizing the naturally biocompatible polymer chitosan for imaging the tumor cell. SWCNT was modified by using chitosan (CHIT), fluorescein isothiocyanate (FITC). Further, this was conjugated with folic acid (FA), as cancer cells overexpress the folic acid receptor, to construct the functionalized conjugate FITC-CHIT-SWCNT-FA. This novel functionalized SWCNT was found that, soluble and stable in phosphate buffer saline and easily transported inside the human cervical carcinoma HeLa cells. Combining the properties of CNTs, folic acid, and versatility of chitosan can be used as a potent device targeting the drug into the tumor cell and its imaging.[3,13,24]

2. Infection therapy: Carbon nanotubes applicable to treat the infection using antiviral, antibacterial drugs, and vaccines. Functionalized CNTs have been able to act as carriers for antimicrobial agents such as Amphotericin B. CNT-Amphotericin B conjugates transport into mammalian cells which reduced the antifungal toxicity by about 40% as compared to the alone drug. Functionalized CNTs also applicable for vaccine delivery procedures by linking the bacterial or viral antigen with CNTs, which permits keeping intact antigen conformation, therefore with the right specificity induced antibody response. The fixation of B and T cell peptide epitopes on functionalized CNTs can generate a multivalent system that can strengthen immune response, therefore, the becomes a good candidate for vaccine delivery.[2,25]

3. Gene therapy by DNA delivery: To correct the defective gene which is caused by some chronic or hereditary disease introducing DNA molecules into cell nucleus by Gene therapy. CNTs used as a delivery system to transfer DNA include liposome, cationic lipids, and nanoparticles. The use of CNTs as gene therapy vectors has effectively transported the genes inside mammalian cells and keep them intact because the complex of CNT-gene can express a protein. SWCNT bonded DNA conjugates protected from interference from nucleic acid binding protein and enzymatic cleavage. DNA-SWCNT complex has superior biostability and self-delivery capability of DNA as compared to DNA used alone.[19, 22,25]

4. Tissue Regeneration and Artificial Implants: Carbon nanotubes are the best candidates for tissue engineering by bonding regenerative medicines such as natural and synthetic polymers for tissue scaffold, this nanomaterial is resistant to biodegradation, biocompatible, and can be functionalized using biomolecules for enhancing organ regeneration. By incorporating the host's body, CNTs can be used as additives to reinforce the conductivity and mechanical strength of tissue scaffolding. Carboxylated SWCNTs have successfully conjugated with polymer or collagen such as poly-1-lactic or poly-D and lactic-co-glycolide to form composite nanomaterial used as tissue regenerative scaffold. Other applications in tissue engineering such as sensing cellular behavior, cell tracking, and labeling and enhancing tissue matrices.[11, 18, 25]

5. Neurodegenerative Disease and Alzheimer's syndrome: CNTs are used in neuroscience because structure CNTs having tiny dimensions and accessible external modification which can cross the blood-brain barrier by targeting mechanism for an effective delivery carrier for the target brain. SWCNTs successfully delivers acetylcholine for the treatment of Alzheimer's disease. Many other functionalized CNTs i.e. SWCNT and MWCNTs are successfully used as a delivery system for the treatment of neurodegenerative disease or brain tumors.[23, 25]

6. As Antioxidants: CNTs as free radical scavengers is a potential role in the emerging area of research. CNTs and carboxylated SWCNTs have antioxidant properties and useful in biomedical applications for the prevention of aging, chronic alignments, and food preservation. –COOH groups increase the free radical scavenging activity of SWCNTs. Carboxylated SWCNTs better for free radical scavengers than their non-functionalized partners. Due to their antioxidant property, they can be used as sunscreen creams to protect skin against free radicals formed by UV sunlight or body and anti-aging cosmetics.[25]

7. Biosensor: Biosensors are used for the diagnosis, biological process, for recognition of biomolecules. Biosensors are differing from the other sensor because they have a sensing element consisting of biological material such as proteins, oligonucleotides, polynucleotides, or microorganisms. CNT-based biosensor enzymatic catalysis reaction that produces or consumes electrons by incorporating enzymes and produced for detection of glucose other biomolecules. The most popular type's biosensors are the electrochemical biosensor, Piezoelectric sensor, and Gas sensor. The electrochemical sensor is used for the detection of molecules in the solution. Piezoelectric sensor and Gas sensor used for diagnosis purpose.[2,6,25]

CONCLUSION

Carbon nanotubes as a nanoparticulate drug delivery system are designed to improve the therapeutic and pharmacological properties of the conventional drug by increasing their solubility, biocompatibility, immune compatibility. Incorporation of the drug in the CNTs as nanocarrier, can protect the drug from degradation and makes them applicable for targeting and controlled release system. Functionalized Carbon nanotubes containing nanocarrier-drug conjugates, reduce the toxicity and adverse effects of drugs in target sides; and they are more effective and selective as compared to the traditional form of drug delivery system. In the field of Carbon nanotubes, we concluded that they have a wide range of applications as targeted drug delivery in various cancer treatments, Alzheimer's disease, gene therapy, neurological disorders, and antioxidants.

Functionalization of CNTs, conjugation with a biodegradable polymer which makes them compatible with biological system. Due to their availability of various sites for attachment, both covalently or non-covalently functionalization with a therapeutically active molecule such as proteins, nucleic acid, or other small drug molecules can be attached to the CNTs as a nanocarrier for the delivery of site-specific therapeutic agents for targeting of cancer cells, tumors, tissues, organs, and genes.

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