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FULLERENESAS NOVEL DRUG CARRIER

Dr. (Mrs.) Rajashree
Hirlekar*, Sushant Gurav

Vivekanand Education Society's
college of pharmacy, HAMC,
Mumbai-400074, Maharashtra,
India

ABSTRACT

Higher therapeutic efficacy of a drug molecule can be achieved by target specific carriers. Application of nanotechnology for this purpose has great scope. The present article focuses on the research and development of carbon-based fullerene and carbon nanostructures. Carbon is a versatile element and can form various allotropes, including graphite, diamond, and fullerene-like structures. Nanomedicine of fullerene seems to be a beautiful platform to illustrate the synergetic of chemistry, biology and physics in fullerene science. The modern medicinal fullerene is a largely explored field, actively developing and enlarging. The fullerene family, and especially C60, has very appealing photo, electro, chemical and physical properties, which can be exploited in many and different biological fields.

KEY WORDS: Classification, Properties, Production, Functionalization, Characterization, Applications.

INTRODUCTION

An important area of research in modern material nanoscience concerns carbon-based materials, among which fullerene take one of the first places. Since their first detection and bulk production, they have gained prime role in scientific arena. In 1996 Nobel prize for Chemistry was awarded to Kroto, Curl and Smalley for their seminal discovery.^[1] The first member to be characterized was C₆₀, which features 12 pentagons separated by 20 fused hexagons. All the rings are fused and double bonds conjugated. In spite of their extreme conjugation, they behave chemically and physically as electron-deficient alkenes rather than electron rich aromatic system. It has full icosahedral symmetry and was given the name buckminsterfullerene in honour of the architect R. Buckminster Fuller whose buildings popularized the geodesic dome, which uses the same tectonic principle.^[2]

Classification:

Fullerenes can be classified into following ways,

A. Pure Fullerenes:

Depending on number of carbon atoms these are further classified as,

1. Fullerene C₆₀ or Buckminsterfullerene:

These have molecular wt about 720.66. These are granular, dark-brown powder. In sublimed form these appears as deep blue-black needle-like crystals. The diameter of a C₆₀ molecule is about 1 nanometer.

The C₆₀ molecule has two bond lengths. The 6:6 ring bonds (between two hexagons) can be considered "double bonds" and are shorter than the 6:5 bonds (between a hexagon and a pentagon) (Figure 1).

2. Fullerene C₇₀: Fullerenes with molecular wt. 840.77 are known as C₇₀. These are Granular, Sublimed black powder (Figure 2).

3. Fullerene C₇₆: C₇₆ has molecular wt. 912.84. These are granular, dark-brown powder.

4. Fullerene C₇₈: These have molecular wt. 936.86 and are granular, black powder in appearance (Figure 3).

5. Fullerene C₈₄: Fullerenes of molecular wt. 1008.92 are C₈₄ which are granular and brown-black in colour. (Figure 4).

B. Derived fullerenes:

As shown in figure 5, chemical groups can be attached to a fullerene carbon atom and this process is called functionalization, used for modifying the properties. The number of carbon atoms available to do this had led to the epithet "molecular pincushion", especially within the context of medical application. Ferrocenes are compounds containing iron and organic groups attached to fullerene cage. The hybrids might create vesicles for drug delivery.^[2]

C. Endohedrals fullerenes:

As shown in figure 6 putting atoms inside is one of the active functionalization and the results are called endohedral fullerenes. A huge number of elements have been encapsulated in fullerenes, including the noble gases, which have no desire to bond with surrounding carbon atoms but can be used in application such as magnetic resonance imaging (MRI).^[3]

D. Carbon Nanotubes (CNT's):

Cylindrical fullerenes are known as nanotubes. Figure 7 shows, these tubes of carbon are usually only a few nanometers wide, but they are ranges from less than a micrometer to several millimeters in length. CNTs are well-ordered, high aspect ratio allotropes of carbon. The two main types are single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs). MWCNTs are larger and consist of many single walled tubes stacked inside the other.^[4]

PHYSICAL CHARACTERISTICS:

Physically, fullerenes are extremely strong molecules, able to resist great pressure—they bounce back to the original shape after being subjected to over 3000 atmospheres. This gives fullerenes, graphite like potential as a lubricant. The same properties offer potential use in photo detectors for X-rays. The purified fullerenes have very attractive colors. Thin films of C₆₀ are mustard colored (dark brown in bulk) and solutions in aromatic hydrocarbons are a beautiful magenta. Thin films of C₇₀ are reddish brown (grayish-black in bulk) and solutions are port-wine red. C₇₆, C₇₈ and C₈₄ are yellow in color.^[5]

- **Solubility:**

Fullerenes are sparingly soluble in many solvents. Common solvents for the fullerenes include aromatics such as toluene and carbon disulfide. Solutions of pure Buckminsterfullerene have a deep purple color. Solutions of C₇₀ are reddish brown. The higher fullerenes C₇₆ to C₈₄ have a variety of colors.^[6] C₇₆ has two optical forms, while other higher fullerenes have several structural isomers. Fullerenes are the only known allotrope of carbon that can be dissolved in common solvents at room temperature.

- **Chemical stability:**

Fullerenes are stable and the characteristic reaction of fullerenes is electrophilic addition at 6, 6-double bonds, which reduces angle strain by changing sp²-hybridized carbons into sp³- hybridized ones. Other atoms can be trapped inside fullerenes to form inclusion compounds known as endohedral fullerenes.^[7]

- **Chemical reactions:**

Fullerenes undergo following chemical reactions: Hydrogenation, Addition, Functionalization, Oxidation and Reduction.^[8]

METHODS OF PRODUCTION:

- **Arc discharge method:**

Arc discharge technique is shown in figure 8; a vapor is created by an arc discharge between two carbon electrodes with or without catalyst. The carbon contained in the negative electrode sublimates because of the high temperatures caused by the discharge. Fullerene self-assembles from the resulting carbon vapour. Arc discharge methods generally produce large quantities of impure material. Methane, ethylene, ethanol, carbon monoxide and acetylene are the commonly used gaseous carbon source. If both electrodes are pure graphite, the main product will be MWCNTs. If SWCNTs are preferable, the anode has to be doped with metal catalyst, such as iron, cobalt or nickel. Tubes are easily produced (typical yields of 30–90%) and tend to be short with random sizes and directions. SWCNTs have diameters of 0.6–1.4nm while MWCNTs have inner diameter of 1–3nm and outer diameter of approximately 10 nm. Often they need a lot of purification.^[9]

- **Laser ablation methods:**

In the laser ablation technique, a high power laser beam impinges on a volume of carbon containing feedstock gas (such as methane or carbon monoxide) causing carbon atoms to ablate/evaporate. A carrier gas sweeps the carbon atoms from the high-temperature zone (1200 °C) to a cold copper collector on which they condense into carbon nanotubes as shown in figure 9. In order to generate SWCNTs using the laser ablation technique, it is necessary to impregnate the carbon source target with transition metal catalysts. Laser ablation produces a small amount of clean CNTs with typical yields of 70%. Furthermore it produces primarily SWCNTs which are long (5-20microns) and have diameters of 1-2nm. MWCNTs produced by this method have a number of layers varying from 4nm to 24nm and an inner diameter ranging between 1.5nm and 3.5nm.^[10]

- **Chemical Vapor Deposition:**

Chemical Vapor Deposition (CVD) generally involves reacting a carbon containing gas (such as acetylene, ethylene, and carbon dioxide) with a metal catalyst particle (usually cobalt, nickel, iron or a combination of these such as cobalt/iron or cobalt/molybdenum) at temperatures above 600°C. As the carbon source continuously and slowly passes through the reactor at high temperatures, the hydrocarbon decomposes into hydrogen and carbon. The carbon atoms dissolve and diffuse into the metal surface and rearrange themselves into a network containing hexagons of carbon atoms and finally precipitate out in the form of CNTs. Once the metal surface is covered by amorphous carbon and its surface is “poisoned,” the carbon atoms cannot come into contact with the metal catalyst, resulting in the termination of CNT growth. CVD has yields ranging from 20-100% and results in long tubes with diameters ranging from 0.6nm to 4nm for SWCNTs and 10 to 240nm for MWCNTs. The CNTs are usually MWCNTs and rarely SWCNTs. There are two different CVD configurations used widely today: horizontal furnace and vertical furnace. The advantages of the CVD method are that it can be scaled

up and produces high-quality production of CNTs at a relatively low cost. In addition, the growth of CNTs can be controlled by adjusting the reaction parameters such as the catalyst system, temperature, type of hydrocarbon, and the flow rate of the gases(Figure 10).^[9, 10]

SEPARATION OF PURE FULLERENE:

The methods of fullerene production that have been described all produce the macroscopic quantities of fullerene. However, the fullerene are produced as a crude mixture containing C₆₀ and other C_n (n>60), as well as conventional hydrocarbon species. In this crude soot state, fullerenes are unsuitable for material research. Individual fullerene must be isolated from the crude soot. ^[11]

The first in purification scheme involves extraction of soluble fullerene from the crude carbon soot. First soot can be extracted continuously using boiling toluene using Soxhlet extraction apparatus.

Figure 11 shows a second method used to extract fullerene from soot. It involves sonication of toluene-soot mixture at room temperature. In this procedure a flask containing toluene suspension of soot is placed in an ultrasonic cleaning bath and sonicated for 30 to 60 minutes. The insoluble carbon products are then removed from the toluene solution of fullerene by filtration. ^[12]

FUNCTIONALIZATION OF FULLERENE:

Fullerene can undergo chemical functionalization to produce novel materials and to enhance solubility in various solvents for further applications. The main approaches for the functionalization of CNTs can be grouped into three categories: (a) purification-oxidation; (b) the covalent attachment of chemical groups through reactions on the conjugated skeleton of CNT; (c) the non-covalent adsorption or wrapping of various functional molecules onto the walls. ^[9, 12]

- **Non-covalent functionalization of carbon nanotubes:**

Non-covalent methods of functionalizing fullerene increase their dispersion in most solvents and purify fullerene from amorphous carbon and metal impurities whilst preserving their aromatic structure and electronic properties unlike oxidative acid treatment. Wrapping of the fullerene is a general phenomenon, driven largely by a thermodynamic drive to eliminate the hydrophobic interface between the fullerene and their aqueous medium. The Fullerene-adsorbate conjugation is caused by π - π stacking interactions between the aromatic part of the adsorbate and the graphitic sidewall of fullerene. Methods include polymer, protein and DNA wrapping and surfactant adsorption. The dispersion methods involve ultra-sonication, centrifugation and /or filtration.

a) Surfactants:

Figure 12 shows adsorption of surfactants on the tube surface. A series of anionic, cationic and non-ionic surfactants have already been proposed to disperse fullerene. Sodium dodecyl sulphate (SDS) and Triton X-100 were used to obtain fullerene suspensions up to 0.1 and 0.5mg/mL, respectively,

study has been done on the non-covalent functionalization of fullerene via π - π interactions with 1-pyrenebutanoic acid activated succinimidyl ester. It immobilizes the proteins by promptly reacting with the amino groups present in the proteins like ferritin or streptavidin. The solubility of fullerene was between 0.1 and 0.7mg/mL, which is rather low but acceptable for biological use.

b) Polymers:

The mechanism of dispersion is based on polymers wrapping around the fullerene creating hydrophobic interactions which break the water-water interactions preventing the squeezing out of the insoluble fullerene-CNTs. The CNTs are covered by the hydrophobic backbone of the polymer whilst the hydrophilic groups are exposed to the surface to display water solubility. Studies have reported that SWCNTs had been reversibly solubilized in water in the g/l concentration range by non-covalently associating them with a variety of linear polymers such as polyvinyl pyrrolidone (PVP) and polystyrene sulfonate (PSS). They demonstrated that the association between the polymer and the SWCNT is robust, not dependent upon the presence of excess polymer in solution, and is uniform along the sides of the carbon nanotubes. It has been found that water-soluble SWCNTs with poly (ethylene glycol) (PEG) functionalization allowed for surprisingly high degrees of π - π stacking of aromatic molecules, with a cancer drug (doxorubicin) and a widely used fluorescent molecule. The strength of π - π stacking of aromatic molecules was dependent on the carbon nanotube diameter, leading to a method for controlling the release rate of molecules from CNTs by using carbon nanotubes with a suitable diameter.

c) Proteins and DNA:

Self-assembly processes similar to π - π stacking interactions typical of double strand DNA can be exploited to disperse carbon nanotubes. Researcher's sonicated the fullerene in the presence of single strand DNA to form a fullerene-DNA conjugate which was highly stable and soluble in the mg/ml range. A molecular modeling study was used to explain the formation of the hybrids exerted by DNA wrapping and subsequent fullerene debundling. Some possible wrapping arrangements are shown in figure 13. Amphiphilic and cyclic peptide sequences play a large role as water solubility enhancers. The peptides can be selected from phase display libraries or by design.

- **“Defect” Functionalization at the Tips and Sidewalls:**

Besides non-covalent procedures, CNTs can also be cut and functionalized simultaneously, becoming soluble in polar organic solvents, acids and water without the aid of sonication, surfactants, or any other means, by simply treating them with oxidizing agents such as strong acids (Li). This oxidizing procedure is usually known as “defect functionalization”, since it takes place at the ends or in correspondence of pre-existing defects of CNTs. After that, the carboxylic acid groups and the carboxylated fractions introduced by oxidization treatment, can further be functionalized by amidation, esterification or through the zwitterionic COO-NH_3^+ formation. This often requires activation of the carboxylic acids by thionyl chloride, N-hydroxysuccinimide (NHS), or carbodiimide (e.g. Diisopropyl carbodiimide) in order to get highly reactive intermediates. Drug can be successfully conjugated by amidation. Initially scientists directly coupled ethylene-diamine with the carboxylic groups to introduce amino groups via amide formation. Finally, these functionalized carbon nanotubes were conjugated to drug moiety. (E.g. Conjugation of Amphotericin B)

- **Covalent Functionalization on the External Sidewalls:**

Among the most powerful methodologies aimed to functionalize fullerene, a special kind of 1,3-dipolar cycloaddition represents a fascinating example of covalent bonding (as shown in figure 14): it is extremely versatile, since it requires only an α -amino acid (or correspondent ester) reacting with an aldehyde or ketone, to generate in situ azomethineylides that are very reactive and thus determine the formation of pyrrolidine rings on the sidewall of CNTs.

- **Encapsulation inside CNTs:**

Although many biomolecules, adsorbed or bound onto the surface of nanodevices have been mentioned to display an improved therapeutic activity, i.e. increased water dispersibility, a better bioavailability and a reduced toxicological profile, there are many other examples showing that the interaction with the carrier or the surrounding environment could determine inactivation or even degradation of these molecules. For this reason, the recent use of CNTs to encapsulate molecules has rendered these Nano systems particularly suitable for additional applications such as material storage and drug delivery. The advantage of this methodology lies on the ability of carbon nanotubes to provide protection and to control the release of loaded molecules, thus prolonging the effect of eventual drugs.

- **Nano-extraction:**

For this process to happen, the mutual interactions among graphene sheets, molecules and solvent must be accurately balanced, in the sense that both CNTs and guest molecules must have poor affinity to the solvent, but strong reciprocal attraction. If these conditions are ensured, the desired molecules can be deposited within the CNTs as the most stable site (e.g. anticancer drug, hexamethylmelamine).

- **Nano-condensation:**

It is difficult to understand the mechanism of Nano-condensation. Competing processes are the adsorption of solvent molecules onto the tube wall, evaporation of solvent molecules, segregation or self-crystallization of guest molecules, and deposition of guest molecules inside the tube walls. The following mechanism is suggested: the guest molecules-solvent remain adsorbed to the CNT surface via the Van der Waals force. The guest molecules then migrate through the thin solvent-layers and eventually depositing themselves at the most stable sites inside the carbon nanotubes. There should be strong affinities between the guest-molecule, solvent and CNTs otherwise the solvent-guest molecule solution will be unable to overcome the absorption force due to the filtration paper.

CHARACTERIZATION OF THE DRUG LOADED FULLERENE:

Characterization and analysis of drug-loaded fullerenes conjugate was carried out by a number of different techniques.^[9, 14]

- **Transmission electron microscopy:**

Transmission electron microscopy (TEM) was used to provide the visualization information on tube dimensions and level of aggregation. Samples were prepared for TEM by suspending ~0.02mg in 1ml of methanol. The solutions were sonicated for 10 minutes and 2 drops were placed on copper 400 mesh grids. TEM images were obtained on a Joel JEM 100S TEM operating at 80kV.^[13]

- **Thermogravimetric analysis:**

Information on the CNTs purity could be obtained from the TGA based on the extent of non-oxidizable residue at high temperature and on the difference between the burn temperature of amorphous carbon and that of the CNTs. The non oxidizable residue was taken to be residual metal catalysts. The thermogravimetric analysis was done in air at a rate of 5cm³/min from room temperature to 900°C. The following were monitored, 1) the weight loss of the CNTs and 2) the thermal stability of the purified fullerene-CNTs and drug loaded fullerene-CNTs.^[12]

- **UV-visible spectroscopy:**

Double beam spectrometer was used to estimate the amount of drug incorporated onto the acid fullerene-CNTs. A calibration curve of drug in suitable solvent at different concentration was prepared using the specific absorbance peak at specific λ_{max} value. The absorbance is correlated to the calibration curve and the amount of drug can be determined. The UV-vis spectrometer was also used to verify the presence of the fluorescence isothiocyanate (FITC) and the drug.^[13]

- **Fourier transform infrared spectroscopy:**

Fourier transform infrared (FTIR) spectrometer is also used to study the structural changes in the drug-fullerene conjugate. Drug-fullerene conjugate is mixed with potassium bromide (KBr) and then compressed with a hydraulic press into 1mm thick pellet discs. Perkin-Elmer spectrometer (Spectrum one) that enables KBr disc analysis was used. Four scans can be averaged with specific resolution. The formation of amide functionalities in the fullerene-drug conjugate can be verified by Fourier transform infrared spectrophotometer.^[12,13]

- **Raman Spectroscopy:**

Raman spectroscopy was used to provide the structural characteristics of the carbon nanotubes and an indication of the degree of functionalization. The D band intensity represented the existence of defects and other disorder-induced effects for any type of carbon. The D band can represent sp³ bonds while the G band can be attributed to a C-C stretching mode of well graphitized CNTs i.e. sp² bonds. The relative intensity ratio of the D and G bands is known to depend on the structural characteristics of CNTs and was used to measure the disorder in CNTs. The increase in the ratio of the D band

intensity to the G band intensity (I_D/I_G) is the key evidence for sidewall functionalization, due to the increased sp^3 -content in the sp^2 framework of the CNT sidewalls. In addition it shows an increase in the defect structure and a decrease in graphitization. [9,15]

- **BET Analyzer:**

At least about 0.2g of samples were degassed in N_2 at $150^\circ C$ overnight prior to analysis using a Micromeritics Flow Prep 060, sample degas system. The surface areas and pore size distributions were then obtained at $-196^\circ C$. The pore size distribution with specific surface areas of the samples, were determined via N_2 adsorption/desorption according to the BET method using a Micromeritics Tristar, surface area and porosity analyzer. In order to confirm the accuracy of the results, the analysis was repeated at least twice for all samples and the measurements were in good agreement.[9]

APPLICATIONS:

A. Biomedical Applications:

Fullerenes unique qualities have promise for certain type of drug design. The small size, spherical shape and hollow interior all provide therapeutic opportunities. Moreover, a cage of 60 carbon atoms has 60 places at which chemical groups can attach in almost any configuration. Such opportunity has led to the development of not only drug candidates for treating diseases including HIV, cancer and neurological conditions but also new diagnostic tools.[14]

B. Therapeutic Applications:

The relatively high tolerance of biological systems to carbon is one of the reasons for the potential of fullerenes in medical applications, in addition fullerenes are small enough to pass through kidneys and be excreted. The ability to chemically modify the sidewalls of fullerenes also leads to biomedical applications such as neuron growth and regeneration. [16]

- **Fullerenes for drug delivery:**

Tiny geodesic spheres that could be used for drug delivery and as containers for chemical reactions have been developed. About 70% of the volume of the DNA fullerene is hollow and drugs can be encapsulated in it to be carried into cells, where natural enzymes break down the DNA, releasing the drug. They might also be used as cages to study chemical reactions on the nanoscale.

- **Fullerenes to fight allergy:**

The fullerenes are able to interrupt the allergy/immune response by inhibiting a basic process in the cell that leads to release of an allergic mediator. Essentially, the fullerenes are able to prevent mast cells from releasing histamine. These findings advance the emerging field of medicine is also known as nanoimmunology.

- **Fullerenes as antioxidants:**

The unique structure of fullerene enables it to bind to free radicals dramatically better than any antioxidant currently available, such as vitamin E. Free radicals are molecules that cause oxidative stress, which is also may be the basis of aging therefore finds use in cosmetics.^[16]

- **Fullerenes as Passkey into Cancer cells:**

Drugs are far more effective if they are delivered through membrane, directly into the cells. The passkey developed contains a molecule called Bucky amino acid based on phenylalanines that are strung together like a beads on a necklace to build all proteins. The peptides were found effective at penetration the defenses both liver cancer cells and neuroblastoma cells.^[16,20,21]

- **Fullerenes as targeted antibiotic:**

A new variant of vancomycin that contains fullerene-- tiny cage-shaped molecules of pure carbon could become the world's first targeted antibiotic, creating a new line of defense against bioweapons like anthrax.^[18]

- **Fullerenes as HIV Protease (HIVP) Inhibitor:**

C60's drug targets the human immunodeficiency virus (HIV) that causes AIDS by latching onto the enzyme necessary for viral reproduction. The fullerenes deactivate both the HIV-1 and HIV-2 types of virus, and don't seem to harm cells or organs, which is a problem with some other HIV inhibitors. Since a C60 molecule has approximately the same radius as the cylinder that describes the active site of HIVP and since C60 and its derivatives are primarily hydrophobic, an opportunity exists for a strong hydrophobic Vander Waals interaction between the nonpolar active-site surface and the C60 surface. In addition, however, there is an opportunity for increasing binding energy by the introduction of specific electrostatic interactions. One obvious possibility involves salt bridges between the catalytic aspartic acids on the floor of the HIV-P active site and basic groups such as amines introduced on the C60 surface. The key to exploiting this promising system will be the development of organic synthetic methodology to derivatize the C60 surface in highly selective ways.^[16]

- **Fullerenes as Neuroprotectants:**

Fullerenes act as neuroprotectants-a drug that prevents or repair neurological damage. Diseases such as amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease and Parkinsonism are under trial.

- **Fullerenes as Cytoprotective agent:**

The water-soluble fullerenes derivative radical sponge exerts cytoprotective action against UV irradiation without visible light catalyzed cytotoxicity toward human skin keratinocytes.

- **Fullerene C60 α Alanine Adduct As Radical Scavenging Agent:**

Water-soluble C60 α alanine adduct has been synthesized and scavenging ability for super oxide anion O⁻² (-) and hydroxyl radical has been demonstrated. It shows excellent efficiency in eliminating these anions and radicals and will be useful in radical related biomedical field.^[22]

C. Diagnostic Applications:

Fullerenes may be especially useful for shuttling metal contrast agents through the body for magnetic resonance imaging (MRI) scans. Researchers have designed carbon-60 and other fullerene molecules with an atom of gadolinium inside and with chemical appendages that make them water-soluble. In typical MRI contrast agents, the metal gadolinium is linked to a non-fullerene molecule. For most diagnostic tests, this molecule is excreted from the body quickly. However, fullerene-encapsulated gadolinium might one day be a safer option for certain diagnostic tests in which doctors leave the contrast agent in longer time. Trimetaspheres are a larger version of the fullerene, with 80 carbons caging up to three metal or rare earth atoms, such as scandium, lanthanum or yttrium, which are covalently bonded to nitrogen. In trimetaspheres the nitrogen complex spins freely within the larger cage of carbons. They have potential uses as contrast agents for medical magnetic resonance imaging, as light emitting diodes, and potentially for molecular electronics and computing.^[16]

TOXICITIES:

Although C60 has been thought in theory to be relatively inert, the studies suggest the molecule may prove injurious to organisms.

I. Environmental Toxicity:

An experiment by Eva Oberdörster at Southern Methodist University, which introduced fullerenes into water at concentrations of 0.5 parts per million, found that large mouth bass fish suffered a 17-fold increase in cellular damage in the brain tissue after 48 hours. The damage was of the type lipid

peroxidation, which is known to impair the functioning of cell membranes. There were also inflammatory changes in the liver and activation of genes related to the making of repair enzymes. The overwhelming evidence of the essential non-toxicity of C60 (not C > 60) in previously peer-reviewed articles of C60 and many of its derivatives indicates that these compounds are likely to have little (if any) toxicity, especially at the very low concentration at which it is used (~1-10 μM). Desorption behavior of carbon nanotubes shows that high adsorption capacity and reversible adsorption of poly aromatic hydrocarbons (PAH) on nanotubes imply the potential release of PAHs. If PAH-adsorbed CNTs are inhaled by animal and human beings it may lead to a high environmental and public health risk.^[23]

II. Biological Toxicity:

A study published in December 2005 in Biophysical Journal raises a red flag regarding the safety of C60 when dissolved in water. It reports the results of a detailed computer simulation that finds C60 binds to the spirals in DNA molecules in an aqueous environment, causing the DNA to deform, potentially interfering with its biological functions and possibly causing long-term negative side effects in people and other living organisms. Despite of the hydrophobic behavior fullerenes strongly bound to the nucleotides. C60 bind single stranded DNA and deform the nucleotides significantly. Unexpectedly, when double stranded DNA is in α form, fullerene penetrate into the double helix from the end, form stable hybrids, and frustrate the hydrogen bond between end group base pair in the nucleotide. The simulation results suggest the C60 molecules have potentially negative impact on the structure, stability and biological functions of DNA molecule.^[23,24]

SUMMARY AND CONCLUSION

Fullerene is referred as The Most Beautiful Molecule by some scientist because of its unique and symmetric structure. Their physical and chemical properties have explored new opportunities in the field of research and development. Their small, hollow interiors, spherical shape, high physical and chemical affinity for active sites in some important enzymes provide therapeutic opportunities. More over 60 carbons skeleton provides 60 places for a chemical groups to get attached in almost any configuration. Such unique properties has led to the development of drug candidates for treating diseases including HIV, cancer and neurological conditions. It can also be used as a new diagnostic tool. Clinical trials are required to define the risk and benefit ratio of fullerenes. Thus it can be concluded that the fullerene are likely to become the future of mature nanomedicine and nanosurgery.

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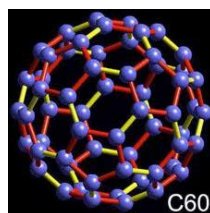


Figure 1: C60 or Buckminsterfullerene

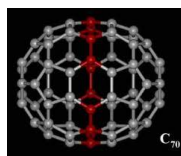


Figure 2: Fullerene C70



Figure 3: Fullerene C78



Figure 4: Fullerene C84

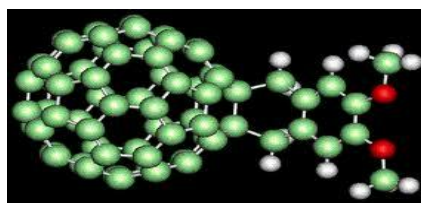


Figure 5: Derived fullerenes

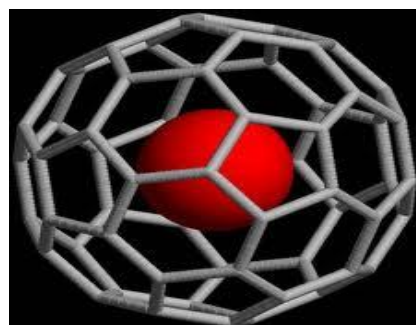


Figure 6: Metal Endohedrals

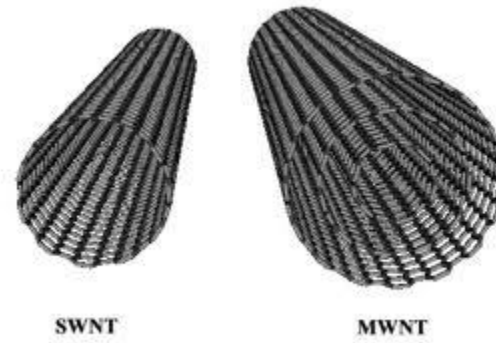


Figure 7: Carbon Nanotubes

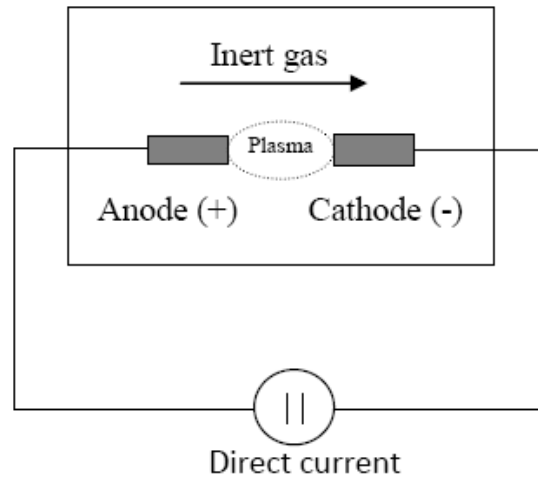


Figure 8: Arc discharge method

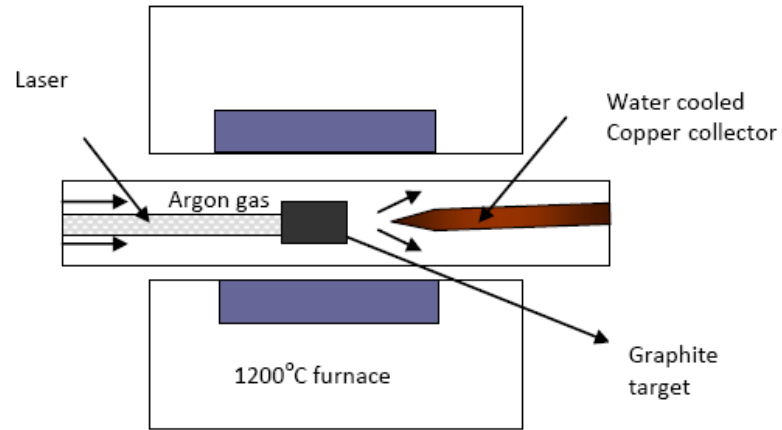


Figure 9: Laser ablation methods

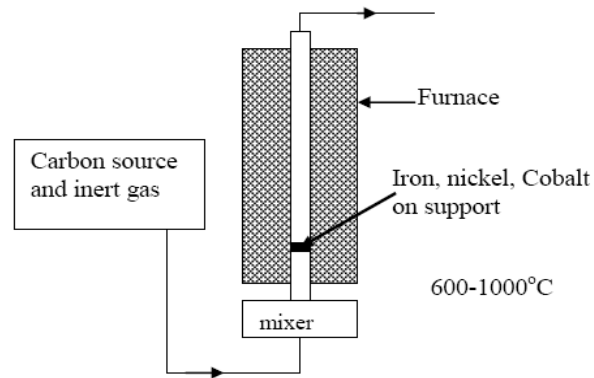


Figure 10: Chemical Vapor Deposition

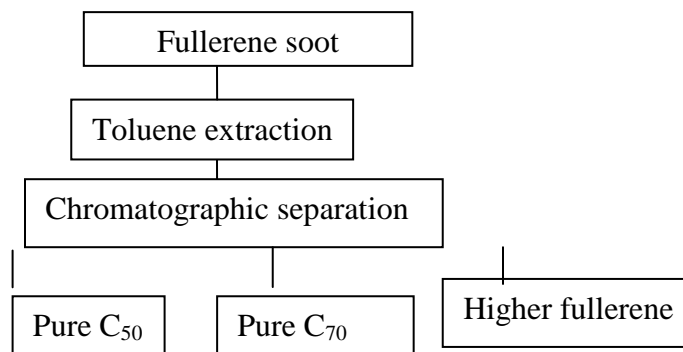


Figure 11: Separation of pure fullerene

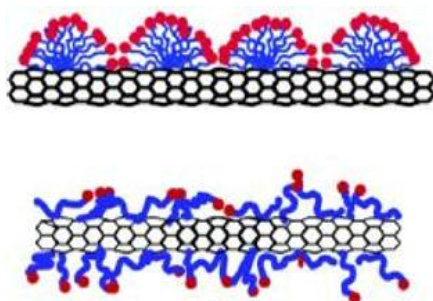


Figure 12: How surfactants adsorb on the tube surface

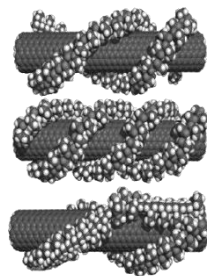


Figure 13: Some possible wrapping arrangements

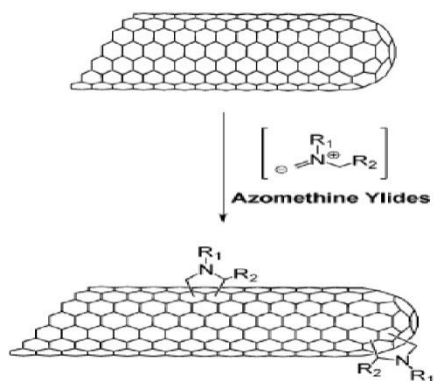


Figure 14: Covalent Functionalization on the External Sidewalls