THE ROLE OF CARBON-BASED NANOMATERIALS IN DRUG DELIVERY SYSTEMS: A REVIEW OF SYNTHESIS METHODS, AND APPLICATIONS

[1] **Yogesh. R**, [2]**Bavya Muthuchamy**,[3] **Dharshini Saravanan**

[1]Student, [2]Student, [3]Student

[1] Department of Pharmaceutics,[2,3]Department of pharmaceutical chemistry

[1] Swamy Vivekanandha college of pharmacy Namakkal, India

[1] yogesh.r.yogesh003@gmail.com, [2]bavyapharm@gmail.com, [3]dharshinipharma18@gmail.com

***Abstract*— Carbon is among the most abundant and adaptable elements in the universe. It can generate compounds with unique properties based on atom arrangement. Carbon-based nanomaterials, composed of carbon atoms organized at the nanoscale and that have potential applications in medicine, energy, electronics, and environmental technology. These carbon-based nanomaterials, such as carbon nanotubes (CNTs), graphene, and fullerenes, are being investigated for drug delivery. These materials can be functionalized to target specific tissues or cells, increase drug stability, solubility, bioavailability, and reduce toxicity, ultimately improving treatment outcomes. In this review, We are going to discuss about the various types of carbon-based nanomaterials, including, carbon nanotubes (CNTs), graphene, fullerenes, as well as how they synthesized and used in drug delivery systems.**

***Keywords*— Carbon, Carbon-based nanomaterials, potential applications, carbon nanotubes (CNTs), graphene, fullerenes, drug delivery, synthesized**.

I.INTRODUCTION

Carbon is among the most abundant and adaptable elements in the universe. Carbon's allotropic qualities allow it to generate compounds with unique properties based on the arrangement of nearby atoms. Diamond and Graphite are two such examples. Diamond is the hardest material, while graphite is weak and brittle[1]. Carbon-based nanomaterials are advanced materials made primarily of carbon atoms and organized at the nanoscale (usually less than 100 nm). Their distinct physical, chemical, electrical, and mechanical qualities make them very adaptable to a variety of applications, including medicine, energy, electronics, and environmental technology[2]. Carbon-based nanomaterials have the potential to revolutionize the field of drug delivery, Their unique properties and advantages make them an attractive option for researchers and clinicians. Carbon-based nanostructures have emerged as promising transporters of drugs. Their distinguishing characteristics, including as high surface area and conductivity, make them perfect for this application. Carbon nanotubes, graphene, and fullerenes are being investigated for their possible use in drug delivery. It is possible to functionalize these materials to target particular tissues or cells and also, Nanomaterials based on carbon can increase the stability, solubility, and bioavailability of drugs. They can also reduce drug toxicity and side effects and by using Targeted drug delivery carbon-based nanomaterials can improve treatment outcomes. In this review, We are going to discuss about the various types of carbon-based nanomaterials, including, carbon nanotubes (CNTs), graphene, fullerenes, as well as how they synthesis and used in drug delivery systems[3].

❖ TYPES OF CARBON-BASED NANOMATERIALS:

1.Carbon Nanotubes (CNTs)

2.Fullerenes

3.Graphene

1.Carbon Nanotubes (CNTs):

Carbon nanotubes (CNTs) are cylindrical structures made of carbon atoms arranged in a hexagonal pattern, similar to graphene sheets rolled into tubes. They exhibit remarkable properties such as high tensile strength, excellent electrical conductivity, and thermal stability. The special qualities of carbon nanotubes (CNTs), such as their large surface area, biocompatibility, and capacity to pass through cell membranes, make them extremely promising for use in drug delivery systems. They can provide as effective delivery systems for medications, genes, or biomolecules to certain bodily targets. By enabling controlled and prolonged medication release, functionalized CNTs improve therapeutic efficacy and minimize negative effects[4].

❖ **TYPES OF CARBON NANOTUBES:**

1. Single-Walled Carbon Nanotubes (SWCNTs): These CNTs have a single layer of carbon atoms, with a diameter of around 1-2 nm.
2. Multi-Walled Carbon Nanotubes (MWCNTs): These CNTs have multiple layers of carbon atoms, with a diameter of around 10-100 nm[5].

TABLE:1 PROPERTIES OF (SWCNTS), (MWCNTS)[5]

PROPERTIES	(SWCNTs)	(MWCNTs)
Physical Properties: Diameter	1-2 nm	10-100nm
Length	Shorter length	Larger length 100-1000 nm.
Surface Area	higher surface area	Less surface area
Chemical Properties: Functionalization	more difficult to functionalize	Easy to functionalize
Solubility	Solubility	Soluble
Biological Properties Toxicity	more toxic	Less toxic
Biocompatibility	Less biocompatible	more biocompatible

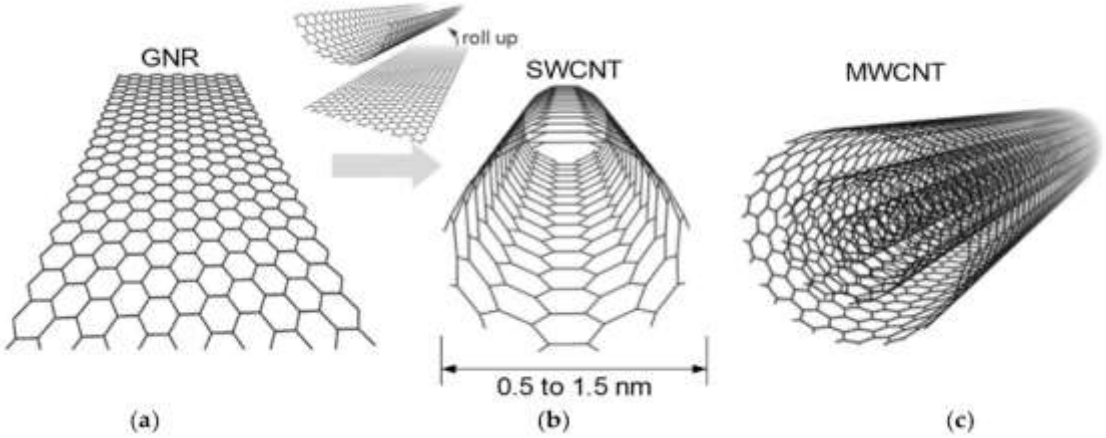

FIG-1 (SWCNTS), (MWCNTS) CARBAN NANOTUBES.

❖ **SYNTHESIS TECHNIQUES FOR CARBON NANOTUBES:**

1.Electric-Arc Discharge:

Graphite electrodes are often struck in an inert environment (argon or helium) to create carbon nanotubes (CNTs), a procedure that also produces fullerene molecules using carbon soot. A practical and conventional method for producing the high temperatures required to evaporate automobiles is the carbon arc, atoms into a plasma at 3000 degrees Celsius[6]. The yield of CNTs depends on the stability of the plasma formed between the electrodes, the current density, inert gas pressure, and cooling of electrodes and chamber. Helium (He) produces the greatest results among the many inert gases, most likely as a result of its high ionization potential[7].

The arc chamber and well-cooled electrodes aid in optimizing the production of nanotubes during the arc growth process. Regarding the In order to produce MWNTs, the arc evaporation process is tuned to limit soot creation and deposit 75% of the evaporated carbon from a pure graphite anode onto the facing graphite cathode surface. The arc deposit is composed of a soft black powder with roughly two thirds carbon nanotubes and one third graphitic nanoparticles inside, and a hard gray outer shell composed of pyrolitic graphite. The ideal synthesizing conditions were between 20 and 25 V and 50 and 100 Amp dc, and the helium pressure maintained at 500 torr. Arc discharge is a straightforward procedure that produces high-quality, architecturally superior CNTs. Nevertheless, traditional arc discharge is unstable and irregular. Process, and it is unable to generate a significant amount of CNTs. Since the electrode spacing varies and the CNTs are generated on the cathode surface, the electric fields are not homogeneous and the current flow is irregular. As a result, carbon nanoparticles and impurities always coexist with nanotubes, and the density of carbon vapor and the distribution of temperature are not uniform. Numerous attempts have been undertaken to produce a steady and highly efficient discharge in order to address this issue, and numerous studies have been carried out to comprehend the nanotube development mechanism[8]. Generated CNTs in huge quantities using the plasma rotating arc discharge technique. During this procedure, the graphite anode rotates quickly. for the CNT synthesis. The anode's spin creates stable plasma and evenly distributes the micro discharges. Turbulence is created by the centrifugal force of spinning, which also accelerates carbon vapor perpendicular to the anode. It is gathered on the graphite collector that was positioned at the plasma's edge rather than condensing at the cathode surface[9,10].

They have reported the simplified arc method for the continuous synthesis of CNTs. This method requires only a dc. power supply, graphite electrodes, and a container of liquid nitrogen; there is no need for pumps seals, water-cooled vacuum chambers, or purge-gas handling systems, which are necessary for the production of CNTs via conventional arc discharge. They stated that the reaction may be scaled up for commercial uses with a CNT yield and can proceed continuously. similar to that of a typical arc reaction that has been tuned. With four to eight layers, long, parallel walls, and just sporadic surface pollution, the nanotubes were generally of excellent quality. Actually, compared to tubes formed using other techniques, those developed utilizing the liquid-nitrogen process seem to have consistently cleaner surfaces. There is no indication that nitrogen has been incorporated into the tubes, which are entirely made of carbon. Almost all of the sophisticated and costly equipment needed for conventional nanotube growth procedures is eliminated by this carbon arc nanotube synthesis approach. The arc discharge method synthesis of MWCNTs require no catalyst, catalyst species are however, necessary for the growth of SWCNTs. The first report on the production of SWCNTs was by Ijima and Ichihashi. By arcing a Fe–graphite electrode in an argon environment of methane, these authors created SWCNTs. Here, a hole is created. in the cathode, which is made entirely of graphite, and the graphite anode, which is filled with a composite mixture of metal and graphite granules. Transition metals like Fe, Co, and Ni as well as rare earth metals like Y and Gd are among the catalysts utilized to create isolated SWCNTs[11,12].

Where as composite catalyst such as Fe/Ni and Co/Ni have been used to synthesize ropes (bundles) of SWCNTs. The tubes used in these tests have an average diameter of 1.2nm.They examined SWCNTs made with various catalysts and discovered that tubes creating a highway-junction pat are created by a Co or a Fe/Ni bimetallic catalyst. tern. Ni catalyst causes the metal particles to expand radially into long, thin tubes. high yield of SWCNTs produced by dc. arc discharge with a modest quantity of a mixture of graphite, Ni, and Fe powders at low helium gas pressure (100 torr)[13].

In addition, they introduced sulfur promoter to improve the yield, which gave rise again to the highest yield at low gas pressure. reported the large-scale production of SWCNTs under the arc conditions of 40 ∼50 A dc. and helium pressure of 500 or 700 torr using a graphite rod with a hole filled with the powder of a mixture of Y–Ni alloy and graphite or CaC2–Ni and Ni as anode[14].

High-purity graphite electrodes, metal powders (just for creating SWCNTs), and high-purity He and Ar gases are typically used in the arc process; hence, the associated costs correlated with the increased production of MWCNTs and SWCNTs. Despite the material's high degree of crystallinity, the tubes' diameter and length are completely uncontrollable. Regretfully, byproducts such amorphous carbon, encapsulated metal particles, and polyhedral graphite particles are also produced in the case of MWCNTs and SWCNTs, respectively[15,16].

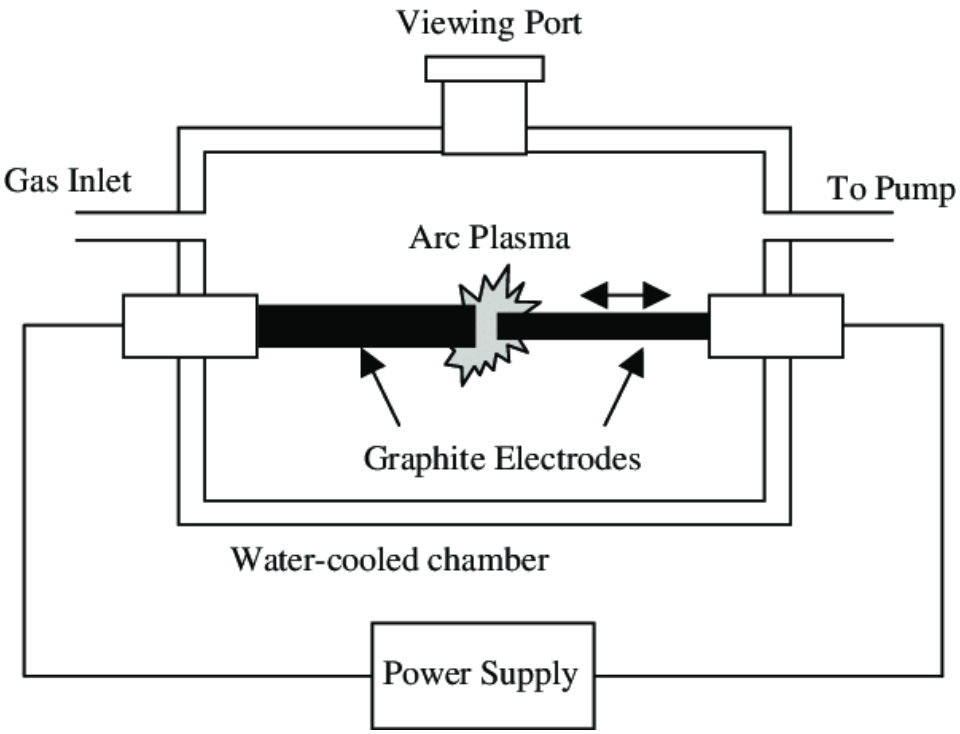

FIG-2 ELECTRIC-ARC DISCHARGE

2.Laser ablation methods:

SWCNTs of excellent quality and purity can be synthesized using this technique. Using bimetal NiCo and NiFe catalysts, they created SWCNTs by laser ablation at 1200 C for one hour[17]. According to their research, the width of the generated SWCNTs increased as the loading of Fe increased. Using a continuous-wave CO2 laser ablation approach, they produced SWCNTs by increasing the laser intensity from 500 W to 850 W. Raman spectroscopy revealed that the SWCNT yield stayed nearly constant for a Fe content of up to 0.5%. With SWCNT bundles ranging in diameter from 6 to 20 nm, the yield of SWCNTs was calculated to be roughly 70%. On applying the technique of continuous-wave mode CO2 laser ablation at room temperature to produce crystalline MWCNTs with a better yield[18].

Additionally, by altering the laser intensity during the laser ablation of a carbon target in liquid, a graphene sheet and various carbon nanomaterial pore sizes ranging from 7 to 16 nm can be created. SWCNTs, which resemble entangled threads with lengths of several hundred micrometers, are produced with the highest purity and yield by the pulsed laser ablation approach[19]. The maximum SWNT yield is correlated with increasing furnace temperatures and laser intensities. MWCNTs are ablated at room temperature using a continuous-wave mode CO2 laser[20].

By modulating the laser intensity during the laser ablation of a carbon target in liquid, a graphene sheet and various carbon nanomaterial pore sizes ranging from 7 to 16 nm are produced. SWCNTs, which resemble entangled threads with lengths of several hundred micrometers, are produced with the highest purity and yield by the pulsed laser ablation approach. The maximum SWNT yield is correlated with increasing furnace temperatures and laser intensities. Graphite in liquid nitrogen was used to create carbon nanostructures and graphene nanosheets using a laser ablation process. In the case of the products at lower laser fluence, a considerable amount of graphene nanosheets were produced[21]. An SnO2/MWCNTs nanocomposite structure was reported to be effective as an adsorbent for the removal of Cu(II) from wastewater. Fluorine and carbon nanoparticles were produced with a laser fluence more than 1.1 J/cm2a. At a pH of 5.7, the SnO2/MWCNT nanocomposite, which was created by pulsed laser ablation, had a good adsorbing efficiency. It was demonstrated that the adsorption capacity's effectiveness rises as copper concentration rises until the surface is saturated with copper ions. The laser's employed parameters are 10Hz repetition rate, 7ns pulse width, and 1064 nm wavelength[22].

The MWCNTs and SnO2-prepared suspension nanocomposite was placed in a plastic filter holder and heated to 300 C for two hours in a nitrogen environment. Nano-onions, nanorods, and MWNTs are synthesized by adding to over 100 carbon layers using the sonochemical/hydrothermal process. CNTs made via the hydrothermal process have interior cavities with widths ranging from 10 to 80 nm, are roughly 60 nm in diameter, and are 2–5μm long. Using argon as an inert gas, electrolysis produces nanotubes in fused NaCl at 810 C by electrowinning alkaline-earth metals on a graphite cathode. By cathodically reducing CO2 to elemental carbon on metallic electrodes, MWCNTs developed in this method have diameters of 10–20 nm and lengths of 500 nm. A 50 kW solar reactor and a Ni-Co catalyst are employed in the solar approach to produce SWNT in gram amounts. The vaporization temperature, which stayed between 2627 and 2727 C, had an impact on the quality of the material that was formed[23].

❖ APPLICATION OF CNTS IN DRUG DELIVERY:

1.Carbon Nanotubes for Gene Therapy by DNA Delivery[24]:

By introducing a DNA molecule into the cell nucleus, gene therapy aims to fix a faulty gene that causes some chronic or inherited disorders. A few deliveries Liposomes, cationic lipids, and recently identified nanoparticles like carbon nanotubes are examples of DNA transfer mechanisms.

DNA probes are shielded from enzymatic breakage and interference from nucleic acid binding proteins when attached to SWCNTs; DNA-SWCNT When compared to DNA utilized alone, the combination shows better biostability and boosts DNA's capacity for self-delivery.

In fact, stable complexes between cationic CNTs and plasmid DNA have shown improved gene therapy potential in comparison to using unprotected DNA. It was discovered that CNTs conjugated with DNA released DNA prior to its destruction by the cell's defense mechanism, greatly enhancing transfection. The use of CNTs as gene therapy vectors has shown that these engineered structures can effectively transport the genes inside mammalian cells and keep them intact because the CNT-gene complex has conserved the ability to express proteins. They have developed novel functionalized SWCNT-DNA complexes and reported high DNA expression compared with naked DNA.

2. Anti-cancer drug delivery:

TABLE 2: ANTI-CANCER DRUG DELIVERY[5]

CNT	TYPE OF CANCER	INVIVO/INVITRO	DRUG	METHOD OF LOADING
SWCNTs	Ovarian cancer	NA	Gemcitabine	Use external source of particles in selected direction
SWCNTs	leukemia	invitro	daunorubicin	Incubated in phosphate buffer solution 37 degree C for 16hrs with SWCNTs
(MWCNTs)	Human gastric carcinoma	Invitro and in mice	HCPT	Used as hydrophilic spacer

II.FULLERENES[25]:

Fullerenes, often referred to as "buckyballs," are spherical molecules composed entirely of carbon atoms arranged in a closed-cage structure. In drug delivery systems, they are valued for their high stability, versatile functionalization, and capacity to encapsulate therapeutic agents within their structure. Functionalized fullerenes can enhance drug solubility, improve bioavailability, and provide targeted delivery to specific cells or tissues. Their antioxidant properties also make them potential candidates for mitigating oxidative stress in various diseases. Fullerenes represent a promising avenue in the development of advanced drug delivery technologies.

❖ **CLASSIFICATION BASED ON STRUCTURE[25]:**

1.Spherical fullerenes: These fullerenes, which have the formula C60 and a spherical shape, are the most prevalent kind.

2.Ellipsoidal fullerenes: These fullerenes have an ellipsoidal shape and a formula of C70.

❖ **CLASSIFICATION BASED ON SIZE[25]:**

1.Small fullerenes: These fullerenes have fewer than 60 carbon atoms, such as C20, C24, and C28.

2.Large fullerenes: These fullerenes have more than 100 carbon atoms, such as a C180.

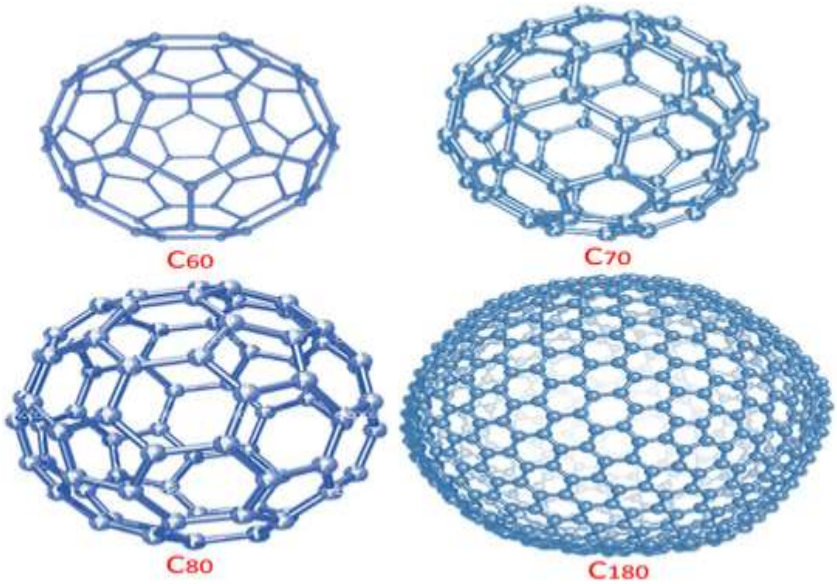

FIG-3 TYPES OF FULLERENES

❖ **SYNTHESIS TECHNIQUES FOR FULLERENES:**

1.Combustion method: Incomplete combustion of hydrocarbons in sooting flames is the basis of another method for creating fullerenes[26]. Fullerene ions in flames were discovered in 1987, and in 1991, the premixed chamber design and laminar sooting flame of a premixed mixture of benzene and oxygen at low pressure were successfully used to extract sizable yields of fullerenes. This method's fullerene amount and composition are influenced by flame parameters such as pressure, C/O ratio, residence time, and gas velocity during benzene burning[27].

Among these, pressure plays a significant role, and fullerene can form at low pressures, such as the astrophysical environment, at temperatures below 1700 K. Additionally, fullerene has been produced by combustion techniques such as laser pyrolysis of vapor hydrocarbons and laser irradiation of polycyclic aromatic hydrocarbons (PAHs)[28].

2.Microwave method:

Apart from the well-known techniques already discussed, there are technologies that use microwaves to create fullerene. Using naphthalene and microwave-induced N2 plasma at atmospheric pressure in a cylindrical coaxial cavity, fullerene was produced[29]. They reported that this process was an efficient way to synthesize fullerene. Molecular species such as benzene or naphthalene can be excited and ionized by microwave-induced nitrogen plasma, and the plasma's state can be readily regulated by varying the microwave power[29].

Graphite powder has recently been converted to fullerenes by another microwave-based fullerene manufacturing method. Because it heats the precursors uniformly, the microwave method has advantages over traditional heating techniques. The amount of graphite powder and microwave intensity increased the yield of synthesized fullerene in this study, but time and temperature had little effect on fullerene production[30].

❖ APPLICATION OF FULLERENES IN DRUG DELIVERY SYSTEM:

Fullerenes have several promising applications in drug delivery systems due to their unique structural and chemical properties:

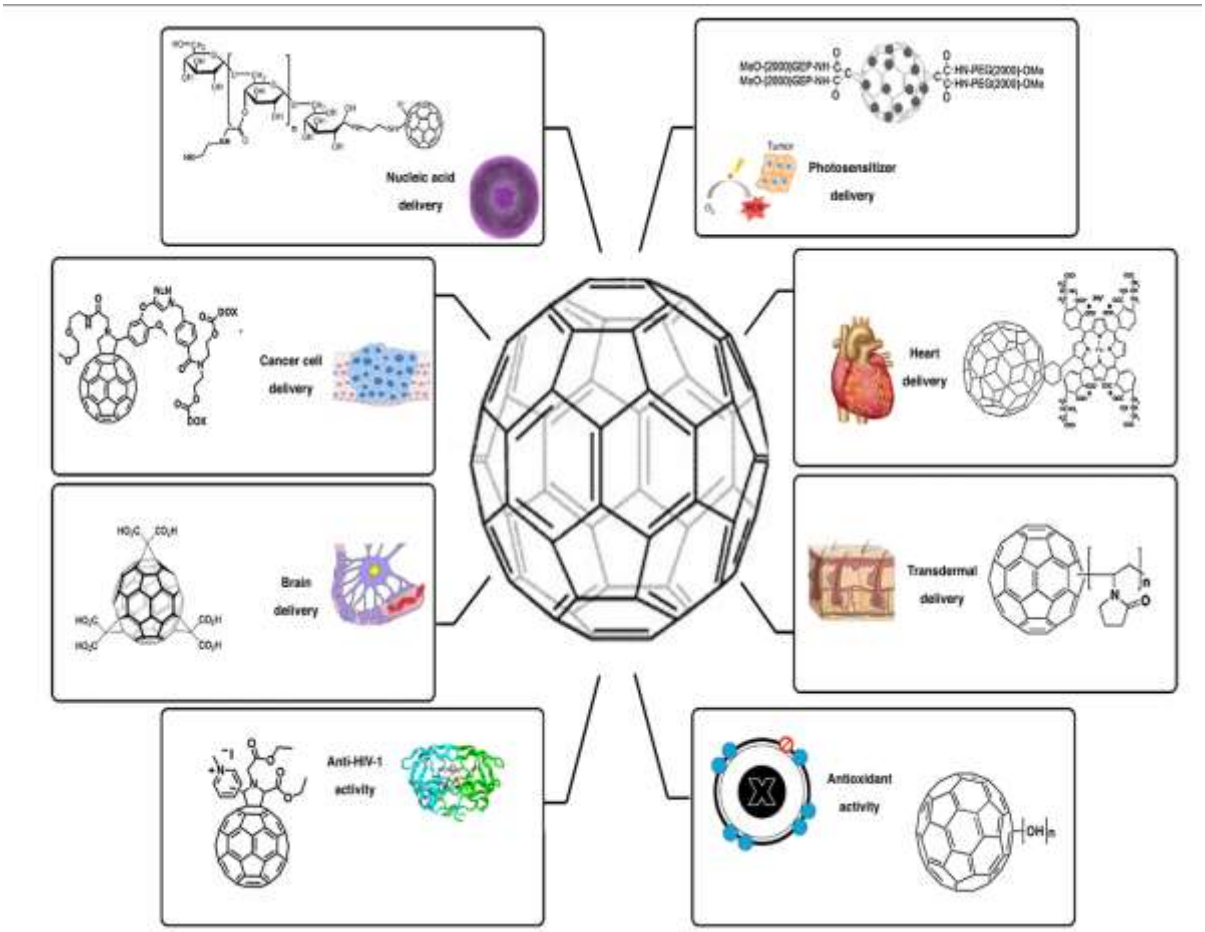

FIG-4 FULLERENES IN DRUG DELIVERY SYSTEM

1.NUCLEIC ACID DELIVERY[31]:

Because of their distinct structural and chemical characteristics, fullerenes have demonstrated significant promise in nucleic acid delivery systems. Nucleic acids, like DNA or RNA, can be effectively bound by functionalized fullerenes and shielded against enzymatic destruction. By making it possible for the nucleic acids to reach particular cells or tissues, they improve therapeutic precision and enable targeted delivery. Furthermore, by getting past obstacles like cell membranes, fullerenes can enhance the cellular uptake of nucleic acids.

2.PHOTOSENSITIZERS DELIVERY SYSTEM[32]:

In photodynamic treatment (PDT), fullerenes are showing promise as efficient photosensitizer carriers. Because of their special structure, they can conjugate or encapsulate photosensitizing compounds, increasing their solubility and stability. Fullerenes have the ability to produce reactive oxygen species (ROS) when exposed to light, which are essential for eliminating infections and cancer cells. By increasing the accuracy of photosensitizer administration, functionalized fullerenes guarantee that the therapeutic effects are concentrated in the targeted region. They are therefore a potentially useful instrument in developing PDT for the treatment of cancer and other medical uses.

3.CANCER CELL DELIVERY[33]:

Because of their special characteristics, fullerenes are becoming more and more recognized as novel cancer cell transport vehicles. By specifically targeting cancer cells, functionalized fullerenes can reduce harm to healthy organs. Anti-cancer medications can be encapsulated by them, improving their stability and guaranteeing regulated release at the tumor site. Additionally, fullerenes are useful in photodynamic therapy (PDT) for the treatment of cancer because of their capacity to produce reactive oxygen species (ROS) when exposed to light. Fullerenes are positioned as prospective instruments in the advancement of cancer treatments due to these diverse applications.

4.HEART DELIVERY[34]:

Because of their special qualities, fullerenes may find use in medicine delivery systems connected to the heart. By delivering cardiovascular medications straight to the heart, functionalized fullerenes can increase therapy accuracy and effectiveness. Their capacity to encapsulate medicinal substances guarantees regulated release, mitigating adverse effects and augmenting medication stability. Furthermore, the antioxidant qualities of fullerenes may aid in reducing oxidative stress, which is frequently linked to cardiac conditions. These developments make fullerenes a possible tool for creating novel cardiovascular treatments.

5.BRAIN DELIVERY[35]:

Fullerenes have promising applications in brain drug delivery systems due to their unique properties. Functionalized fullerenes can cross the blood-brain barrier, enabling targeted delivery of therapeutic agents to the brain. They can encapsulate drugs, protecting them from degradation and ensuring controlled release at specific sites. Additionally, fullerenes' antioxidant properties may help mitigate oxidative stress, which is often associated with neurodegenerative disorders. These advancements position fullerenes as valuable tools in developing treatments for brain-related conditions.

III.GRAPHENE[36]:

Because of its remarkable qualities, graphene a single sheet of carbon atoms organized in a hexagonal lattice has completely changed drug delivery methods. Its biocompatibility guarantees safe interaction with biological systems, and its large surface area enables effective drug loading. Therapeutic medicines can be delivered precisely thanks to functionalized graphene's ability to target particular cells or tissues. Additionally, controlled medication release is made easier by graphene's sensitivity to external stimuli like heat or light. Graphene is a suitable material for developing medication delivery methods because of these characteristics.

❖ **TYPES OF GRAPHENE[36]:**

1.Graphene Oxide (GO): Because of its strong water dispersibility, GO is frequently used to load and distribute hydrophobic medications. Its functional groups make targeted delivery and alteration simple.

2. Reduced Graphene Oxide (rGO): rGO is derived from GO and has restored electrical and thermal properties. It is used in stimuli-responsive drug delivery systems.

3.Graphene Quantum Dots (GQDs): These tiny graphene bits are perfect for delivering medications and imaging agents because of their high biocompatibility and low toxicity.

4. Functionalized Graphene: Graphene modified with polymers or biomolecules enhances drug loading capacity and enables targeted delivery.

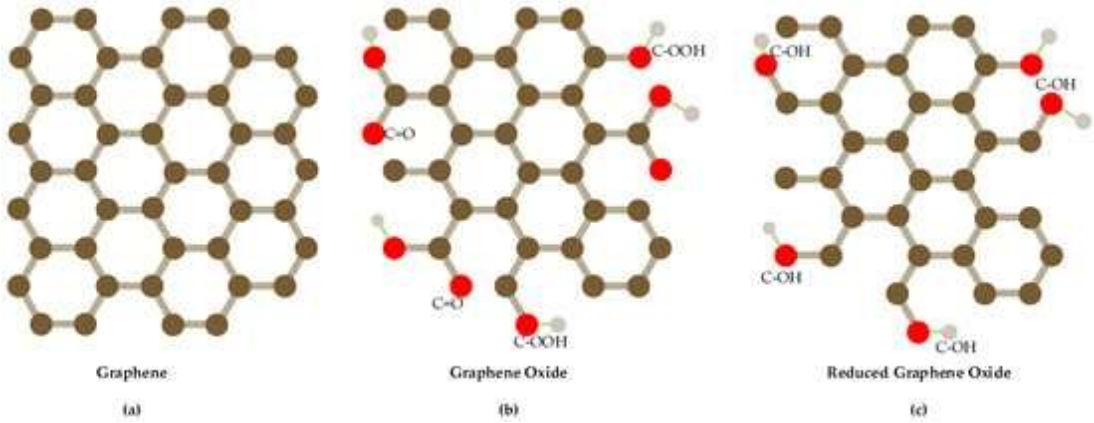

FIG-5 TYPES OF GRAPHENES

1.Chemical oxidation method:

The chemical oxidation method, sometimes referred to as the oxidation cutting method, is a very popular technique in which H2SO4, HNO3, or other oxidants typically break the carbon bonds of graphene, graphene oxide, or carbon nanotubes[37]. An experimental setup that produced high purity GQDs using intense nitric acid reflux and Vulcan XC-72 carbon black as a carbon source. GQD yield and purity were 75 weight percent and 99.96 weight percent, respectively. The generated GQDs displayed multicolour photoluminescence (PL) ranging from green to red at various excitation wavelengths[38].

They synthesized GQDs using a pot of hydrothermal technique without any further post-treatment processes, using hydrogen peroxide (H2O2) as the oxidant and black carbon as the precursor, avoiding the use of concentrated acids and the introduction of metal contaminants[39]. Synthetic GQDs ranged in diameter from 3.0 to 4.5 nm. strong light stability, salt tolerance, low toxicity, and strong biocompatibility are all features of this 90-minute synthesis procedure. It is a quicker and more environmentally friendly way to synthesize GQDs than many other methods that have been published. Then, using GO as the precursor, Halder et al. [46] oxidized and cracked it in two hours with the aid of H2O2 to produce GQDs products, which likewise didn't require additional purification procedures.

Due to the use of strong oxidants such as H2SO4 and HNO3, the chemical oxidation method is not very safe, and the generated chemical waste is liable to pollute the environment[40].

2.Hydrothermal methods:

The hydrothermal approach is a quick and easy way to make GQDs. Ultimately, GQDs can be produced by applying high pressure and temperature to a range of macromolecular or tiny molecular starting materials[41]. The idea is to create GQDs by

breaking the bonds between carbon compounds at high pressures and temperatures. They have employed a one-step solvothermal approach to create GQDs in an N, N-dimethylformamide (DMF) environment using H2O2[42].

GQDs are created via a one-step solvothermal process in an N, N-dimethylformamide (DMF) environment using H2O2. Throughout the whole preparation process, no contaminants were added, and concentrated sulfuric and nitric acids were never used to treat raw materials. Without dialysis, high purity GQDs might be produced by evaporation/re-dissolution and flotation. The findings demonstrated that the GQDs' thickness and width were primarily dispersed between 1 and 1.5 nm and 20 to 40 nm, respectively. The quantum yield (QY) under neutral circumstances was 15%. The PL signal showed good stability over a range of pH values, suggesting that it has a wide range of potential applications in various settings[43].

Numerous benefits of this approach include its low cost, high quantum yield, simplicity in experimental setup, lack of purification and dialysis requirements, etc. The produced GQDs showed good water solubility and were ecologically benign, indicating their potential uses in biomedical and bioelectronic systems.In just five hours, reduced graphene oxide quantum dots (rGOQDs) were effectively created[44]. GO and DMF were used as the raw materials for additional hydrothermal treatment in a poly(tetrafuoroethylene) (Tefon)-lined autoclave at 200 °C after they prepared GO using graphite as the starting material using an improved Hummers' method. Nitrogen (N) derived from DMF was used as the surface doping agent, and the synthesized rGOQDs had a QY of 24.62%[45].

❖ APPLICATION OF GRAPHENE QUANTUM DOTS (GQDs) IN DRUG DELIVERY SYSTEM:

Graphene Quantum Dots (GQDs) are emerging as a promising tool in drug delivery systems due to their unique properties.

❖ EPR-pH delivery-release[46]:

1.Enhanced Permeability and Retention (EPR) Effect: This effect is frequently seen in tumor tissues, where the leaky vasculature makes it possible for nanoparticles, such as GQDs, to collect there more efficiently than in healthy tissues. Because of this, GQDs are a great option for focused medication distribution.

2. pH-Responsive Drug Release: In contrast to normal tissues, tumor surroundings frequently have a lower pH (acidic). To ensure that the medicine is delivered precisely at the tumor site, GQDs can be designed to release their pharmacological payload in reaction to this acidic environment. This improves treatment efficacy and reduces adverse effects on healthy tissues.

❖ ligand-pH delivery-release mode[47]:

1.Ligand Targeting: GQDs have particular ligands—molecules that attach to receptors—affixed to their surface. These ligands are developed to identify and attach to receptors that are overexpressed on cancerous and other sick cells. This increases the accuracy of drug administration by guaranteeing that the GQDs largely accumulate at the target site.

2. pH-Responsive Release: The acidic environment, which is typical in tumor tissues or inflammatory areas, causes the release of the medication payload once the GQDs arrive at their target site. By limiting adverse effects on healthy tissues, this pH-sensitive system guarantees that the medication is released just where it is intended.

❖ Core/Shell-photothermal/magnetic thermal delivery-release mode[48]:

1.Core/Shell Structure: The GQDs are enclosed in a core/shell configuration, with the stability and functional characteristics provided by the shell and the drug payload contained in the core.

2. Photothermal Effect: Certain light wavelengths cause the GQDs to absorb energy and transform it into heat. Targeting sick tissues like tumors, this localized heating may cause the medicine to be released from the core.

3. Magnetic Thermal Effect: Heat is produced by magnetic nanoparticles included into the core/shell structure reacting to external magnetic fields. Enhancing targeting and managing drug release are further uses for this magnetic thermal effect.

CONCLUSION:

In conclusion, carbon-based nanomaterials have emerged as extremely attractive opportunities in drug delivery systems because of their distinct physicochemical features, which include high surface area, great biocompatibility, and functionalization potential. Several synthesis methods, including arc discharge, hydrothermal synthesis, and chemical oxidation, and other methods, are used to produce carbon nanotubes, fullerenes, and graphene quantum dots. These nanomaterials enable regulated and targeted medication release, which improves treatment efficacy while reducing adverse effects. Their applications include cancer therapy, gene delivery, antibiotic therapies, heart delivery, brain delivery, making them an essential component in modern delivery system. Future research should concentrate on, large-scale synthesis, and regulatory issues for clinical use.

REFERENCES:

1. Carbon-Based Nanomaterials **J.R. Siqueira, Jr.*, Osvaldo N. Oliveira,**
2. **K. Koziol, B.o. Boskovic, N. Yahya,** synthesis of carbon nanostructures by CVD method, in: N. Yahya (ed.), Carbon and oxide Nanostructures, advanced structured Materials, 5, springer-Verlag, Berlin, Heidelberg, 2010.
3. **A.J. Page, F. Ding, s. Irle, K. Morokuma,** Insights into carbon nanotube and graphene formation mech anisms from molecular simulations: a review, rep. Prog. Phys. 78 (2015) 38.
4. **Y. Li, J. Wu, N. Chopra**, Nano-carbon-based hybrids and heterostructures: progress in growth and ap plication for lithium-ion batteries, J. Mater. sci. 50 (2015) 7843–7865.
5. Carbon nanotubes -A novel drug delivery system | PPT
6. **T.W.Ebbesen and P.M.Ajayan,** Nature 358, 220 (1992).
7. **S.Seraphin, D.Zhou, J.Jiao, J.C.Withers, and R.Loufty**, Carbon 31, 685 (1993).
8. **E.G.Gamaly and T.W.Ebbesen,** Phys. Rev. B 52, 2083 (1995)
9. **N.Hatta and K.Murata, Chem**. Phys. Lett. 217, 398 (1994).
10. D.T.Colbert, J.Zhang, S.M.McClure, P.Nikolaev, Z.Chen, J. H. Hafner, D.W.Owens, P.G.Kotula, C.B.Carter, J.H.Weaver, and R.E.Smalley, Science 266, 1284 (1994).
11. **S. Iijima and T. Ichihashi**, Nature 363, 603 (1993).
12. **D.S.Bethune, C.H.Kiang**, M.S.de Vries, G.Gorman, R.Savoy, J.Vazquez, and R.Beyers, Nature 363, 605 (1993).
13. Y.S.Park, K.S.Kim, H. J. Jeong, W.S.Kim, J.M.Moon, K.H. An, D. J.Bae, Y.S.Lee, G.S.Park, and Y.H.Lee, Synt. Metals 126, 245 (2002).
14. **C.Liu, H.M.Cheng, H.T.Cong**, F.Li, G. Su, and B.L.Zhou et al., Adv. Mater 12, 1190 (2000).
15. **Y.Ando, X.L.Zhao, K.Hirahara, K.Suenaga, S.J.Bandow, and S.Iijima,** Chem. Phys. Lett. 323, 580 (2000).
16. **M.Takizawa, S.J.Bandow, T.Torii, and S.Iijima, Chem. Phys. Lett. 302, 146 (1999).**
17. **Zhang,M.;Yudasaka, M.; Iijima, S.** Production of Large-Diameter Single-Wall Carbon Nanotubes by Adding Fe to a NiCo Catalyst in Laser Ablation. J. Phys. Chem. B 2004, 108, 12757–12762**.**
18. **Zhang, H.; Ding, Y.; Wu, C.; Chen, Y.; Zhu, Y.; He, Y.; Zhong,** S. The Effect of Laser Power on the Formation of Carbon Nanotubes Prepared in CO2 Continuous Wave Laser Ablation at Room Temperature. Phys. B Condens. Matter 2003, 325, 224–229.
19. **Bota,P.M.; Dorobantu, D.; Boerasu, I.; Bojin, D.;** Enachescu, M. NewLaserAblationChamberforProducingCarbonNanomaterials Using Excimer Laser. Mater. Res. Innov. 2015, 19, 33–39.
20. **Yuge, R.; Toyama, K.; Ichihashi, T.; Ohkawa, T.; Aoki, Y.; Manako, T.** Characterization and Field Emission Properties of Multi Walled Carbon Nanotubes with Fine Crystallinity Prepared by CO2 Laser Ablation. Appl. Surf. Sci. 2012, 258, 6958–6962.
21. **Tabatabaie, N.; Dorranian, D.** Effect of Fluence on Carbon Nanostructures Produced by Laser Ablation in Liquid Nitrogen. Appl. Phys. A 2016, 122, 558.
22. **Mwafy,E.A.; Mostafa, A.M.** Efficient Removal of Cu (II) by SnO2/MWCNTs Nanocomposite by Pulsed Laser Ablation Method. Nano-Struct. Nano-Objects 2020, 24, 100591.
23. **Szabó, A.; Perri, C.; Csató, A.; Giordano, G.; Vuono, D.; Nagy, J.B.** Synthesis Methods of Carbon Nanotubes and Related Materials. Materials 2010, 3, 3092–3140.
24. Carbon Nanotubes: Applications in Pharmacy and Medicine **HuaHe,1,2 Lien Ai Pham-Huy,3 Pierre Dramou,1 Deli Xiao,1 Pengli Zuo,1 and ChuongPham-H**
25. **Fullerenes | PPT**
26. **I. Voicu, et al.** Chem. Phys. Lett. 256 (3) (1996) 261–268.
27. **J.B. Howard,** Symposium (International) on Combustion, Elsevier, 1992.
28. **M.M. Boorum, et al.** Science 294 (5543) (2001) 828–831.
29. **T. Ikeda, T. Kamo, M. Danno,** Appl. Phys. Lett. 67 (7) (1995) 900–902.
30. **R. Hetzel, et al.** Fuller. Nanotub. Carbon Nanostruct. 20 (2) (2012) 99–108.
31. **12 Youn, Y.S. et al. (2017**) Multifunctional nano-sized fullerenes for advanced tumor therapy. J. Pharm. Investig. 47, 1–10
32. **Meisel, P. et al. (2005)** Photodynamic therapy for periodontal diseases: state of the art. **J. Photochem. Photobiol. B 79, 159–170**
33. **Carbon nanotubes -A novel drug delivery system | PPT**
34. **Tran, N. (2011)** Blood–brain barrier. In Encyclopedia of Clinical Neuropsychology **(Kreutzer, J., DeLuca, J., Caplan, B., eds), Springer pp. 426–426**
35. **5 Piotrovskiy, L. et al. (2016)** Enhanced brain penetration of hexamethonium in complexes with derivatives of fullerene C60. pp. 173–175, Springer
36. **Graphene | PPT**
37. **Iannazzo D, Pistone A, Ferro S, De Luca L, Monforte AM, Romeo R, Buemi MR, Pannecouque C.** Graphene quantum dots based systems as HIV inhibitors. Bioconjug Chem. 2018;29:3084–93.
38. **Liu F, Sun Y, Zheng Y, Tang N, Li M, Zhong W, Du Y.** Gram-scale synthesis of high-purity graphene quantum dots with multicolor photolumines cence. RSC Adv. 2015;5:103428–32.
39. **Lu Q, Wu C, Liu D, Wang H, Su W, Li H, Zhang Y, Yao S.** A facile and simple method for synthesis of graphene oxide quantum dots from black carbon. Green Chem. 2017;19:900–4.

40. **Halder A, Godoy-Gallardo M, Ashley J,** Feng X, Zhou T, Hosta-Rigau L, Sun Y. One-pot green synthesis of biocompatible graphene quantum dots and their cell uptake studies. ACS Appl Bio Mater. 2018;1:452–61.
41. **Teymourinia H, Salavati-Niasari M, Amiri O, Farangi M.** Facile synthesis of graphene quantum dots from corn powder and their application as down conversion effect in quantum dot-dye-sensitized solar cell. J Mol Liq. 2018;251:267–72.
42. **Tian R, Zhong S, Wu J, Jiang W, Shen Y, Jiang W, Wang T.** Solvothermal method to prepare graphene quantum dots by hydrogen peroxide. Opt Mater. 2016;60:204–8.
43. **Wang L, Wu B, Li W, Wang S, Li Z, Li M, Pan D, Wu M.** Amphiphilic graphene quantum dots as self-targeted fluorescence probes for cell nucleus imaging. Adv Biosyst. 2018;2:1700191.
44. **Tian R, Zhong S, Wu J, Jiang W, Shen Y, Jiang W, Wang T.** Solvothermal method to prepare graphene quantum dots by hydrogen peroxide. Opt Mater. 2016;60:204–8.
45. **Zhang JH, Sun T, Niu A, Tang YM, Deng S, Luo W, Xu Q, Wei D, Pei DS.** Perturbation effect of reduced graphene oxide quantum dots (rGOQDs) on aryl hydrocarbon receptor (AhR) pathway in zebrafish. Biomaterials. 2017;133:49–59.
46. **Khodadadei F, Safarian S, Ghanbari N.** Methotrexate-loaded nitrogen doped graphene quantum dots nanocarriers as an efficient anticancer drug delivery system. Mater Sci Eng, C. 2017;79:280–5.
47. **Jia Q, Li Z, Guo C, Huang X, Song Y, Zhou N, Wang M, Zhang Z, He L, Du M.** A γ-cyclodextrin-based metal–organic framework embedded with graphene quantum dots and modified with PEGMA via SI-ATRP for anticancer drug delivery and therapy. Nanoscale. 2019;11:20956–67.
48. **Choi SY, Baek SH, Chang SJ, Song Y, Rafique R, Lee KT, Park TJ.** Synthesis of upconversion nanoparticles conjugated with graphene oxide quan tum dots and their use against cancer cell imaging and photodynamic therapy. Biosens Bioelectron. 2017;93:267–73