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Fullerenes a carbon molecule with vivid biomedical applications

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Abstract: *Nanotechnology is becoming a more popular field of study due to its numerous uses in health sector and pharmaceutical industries. Several novel formulations with improved physicochemical and pharmacokinetic properties available at present that pose potential like better penetration of drug, enhancement of bioavailability, improved therapeutic efficacy, and stability. Fullerenes are the nano-materials that have emerged as a newer technique for incorporating active molecules that could be used for diagnosis and drug delivery. The fullerene molecule is made completely of carbon (C_{60}). Their strong antioxidant activity and free radical quenching ability render it suitable for cosmeceutical applications. This review emphasises the pros and cons of fullerenes along with the exploration of numerous biomedicinal applications in pharmaceutical and health sciences.*

Key Words: *Fullerenes, Antioxidant, Bioavailability, Drug delivery, Diagnostic, Cosmeceutical.*

1. INTRODUCTION:

A fullerenes are pure form of carbon containing at least 60 atoms. Fullerenes found in shape like Hollow sphere ,ellipsoid , or tube form . fullerenes have spherical form are known as Bucky-balls , and cylindrical form are as carbon nanotube or Bucky tube. It have similar structure of graphite, they are linked by hexagonal and some time pentagonal ring. (1)

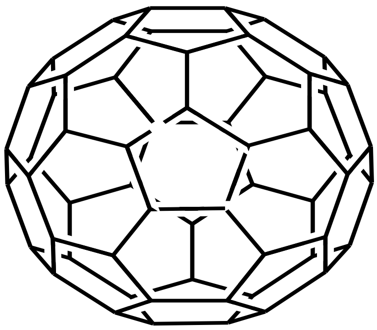

Figure 1. Structure of fullerenes

2. CLASSIFICATION OF NANOMATERIALS BASED ON DIMENSION:

One-dimensional (1D) nanomaterials, two-dimensional (2D) nanomaterials, and three-dimensional (3D) nanomaterials are the different types of nanomaterials that exist.

2.1 One-dimension nanomaterials- These appeared in the word Nano. (2) which depicts the billionth of any unit that results in the production of one-dimensional nanomaterials like a thin film These nanoparticles are used in chemistry, pharmaceutics, electronics, and engineering, among other fields. (3) The thin films or monolayers range in size from 1 to 100 nanometers. These nanomaterials are extremely useful in research and are employed in the fabrication of electronics, storage systems, and nano-scaled LEDs. (4) Biosensors, optoelectronic sensors. (5,6) magneto optics (7,8) optical devices, and fibre optic systems composed of nanotubes, nanobelts, and nanowires are all examples of one-dimensional nanomaterials. (9-10)

2.2 Two-dimension nanomaterial- 2D nanostructures have two dimensions that are larger than the nanometric range and have a unique shape. 2D nanomaterials are employed as building blocks for critical components of nanoparticles. (11) Nanocontainers, carbon nanotubes, sensors, photocatalysts, nanoreactors, and templates for 2D structures are all examples of two-dimensional nanomaterials.

2.3 Three-dimension nanomaterial- The functionality of nanoparticles is determined by their shape size dimension and morphology, which are the fundamental parameters for nanostructure application and efficiency. (12) Three-dimensional nanomaterials have sparked interest in medical science and research throughout the last decade. These nanoparticles have a wide range of uses in catalysis, batteries, and the transfer of reactants and product through magnetic materials. Fullerenes, Dendrimers, and Quantum dots are three-dimensional nanoparticles. (13)

3. SYNTHESIS OF FULLERENES:

Fullerenes are synthesized by different method most common used are laser ablation. (14) and chemical vapour deposition (CVD) methods. historically fullerenes are produced by CVD process, Graphite is vaporised by arc discharge and flaming processes. However, these techniques are not particularly effective, hence further development and advancement in this area are required. . Therefore, it is still a challenge for researchers to create new, effective methods for the synthesis of fullerene with high yields and purity. However, the CVD approach has an advantage over arc discharge and laser vaporisation in that it requires a lower temperature for the creation of fullerenes. Two techniques—microwave-enhanced CVD and hot-filament CVD—were presented for the synthesis of fullerene by Kleckley et al. (15)

Hot-filament CVD

Figure displays a flowchart of the hot-filament CVD. (15) The chamber is made of stainless steel, and the filament is tungsten wire. . The filament hangs vertically, and bottom terminal of the filament is connected to a braided copper wire, while the top terminal is fixed. For thin-film deposition, a stainless steel substrate holder is utilised. The filament currents ranges between 50 A and 60 A, and the filament temperatures are normally between 2000 C and 2200 C. In order to generate CVD diamond-thin films, the substrate temperature should typically be between 950°C and 1000°C. The feed gases are 99.999 percent pure hydrogen and 99.8 percent pure methane. The chamber's pressure level is maintained between 30 and 100 Torr.

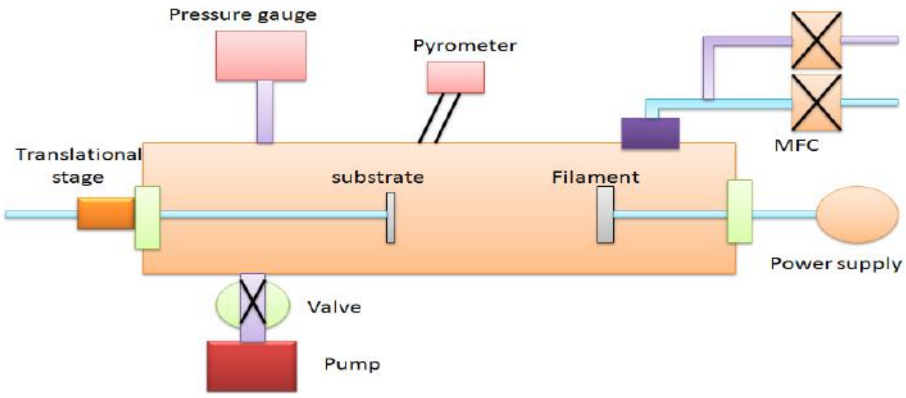

Figure 2. schematic diagram of hot filament chemical vapor depostion (CVD) chamber.

Microwave-Enhanced CVD

Microwave CVD apparatus is shown in Figure. (15) The reaction chamber is made up quartz tube. a 100 W 2.45 GHz generator that served as the excitation source and coupled to an Evenson-type cavity the input gases are Ar, H2, and C2H2. Normal pressures ranged from 1 Torr to 10 Torr. It was discovered that the deposition process could only last a few minutes at p > 25 Torr because a conducting coating was forming inside the quartz tube. The plasma zone appeared to be much more stretched and glow-like at lower pressure. A yellowish coating was developed on the interior wall of the quartz tube at p 10 Torr. After 30 minutes of exposure to the plasma, the film's tint shifted to a dark brown color.

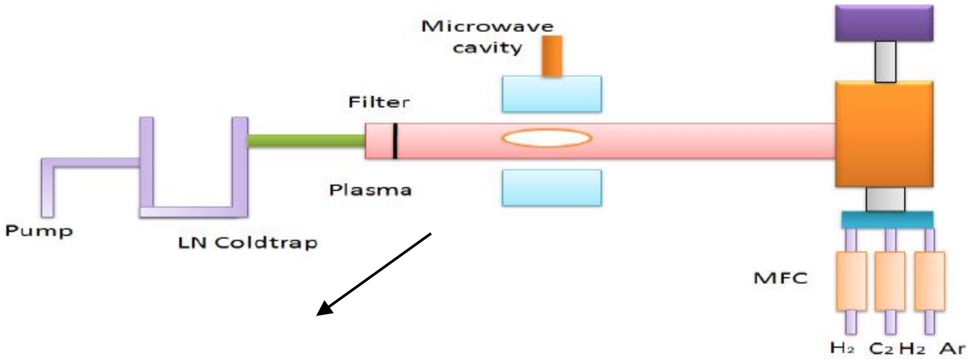

Figure 3. Schematic diagram of microwave-enhanced CVD chamber.

4. FULLERENES HISTORY:

After graphite and diamond, fullerenes are the third carbon allotrope (a molecule made completely of pure carbon). They have a variety of morphology like spherical, ellipsoid, or triangular. A cylinder made up of hundreds of carbon atoms Fullerenes are named after Richard Buckminster Fuller, a pioneer in the field of architecture. Geodesic domes, which follow the same principles, were created by him. The archetypical and the archetypal Fullerene C_{60} is the tiniest fullerene (buckminsterfullerene). The 60 carbon atoms of this spheroidal molecule are organised in a configuration that resembles a soccer ball. Researchers have discovered the fullerene C_{60} molecule in 1985 and were awarded the Nobel Prize in Chemistry in 1996 for their discovery of a novel form of pure carbon. (16) Thereafter, fullerene was introduced in Shungite, as a dark carbon-rich Precambrian rock from Karelia in northeastern Russia [2]. Fullerene C_{60} was first synthesised in tiny quantities, but with the invention of the Krätschmer-Huffman in 1990, a sizable synthesis of C_{60} began. (17) Other fullerenes (C_{70}, C_{76}, C_{84}, and so on) have since been synthesised in huge quantities. Although fullerenes have been explored to have a wide range of biological functions, their hydrophobic character and poor solubility in polar solvents have been key obstacles to their utilisation in biological research and medicinal chemistry.(18) Organofullerenes have received a lot of attention in medicinal chemistry recently because of their enhanced aqueous solubility compared to fullerene C_{60}, membranotropic characteristics, and interactions with many biomolecules. (19) Table 1 provides the solubility data of fullerenes in various solvents at room temperature.

Table1. Solubility of Fullerene (C60) at Room Temperature [4]

Solvent	Solubility mg/ml
Water	1.3×10^{-11}
Ethanol	0.001
Methanol	0.00004
Toluene	2.8
Benzene	1.5
1,2-dichlorobenzene	24
N-methyl-2-pyrrolidone	0.89
Octane	0.025
Hexane	0.043
Cyclohexane	1.2
Chloroform	0.25
Decalin	4.6
Pyridine	0.89
Trichloroethylene	1.4
1-Chloronaphthalene	51
1-Methylnaphthalene	33

The nanoparticle fullerenes show different properties which are displayed in figure 1. (20,21)

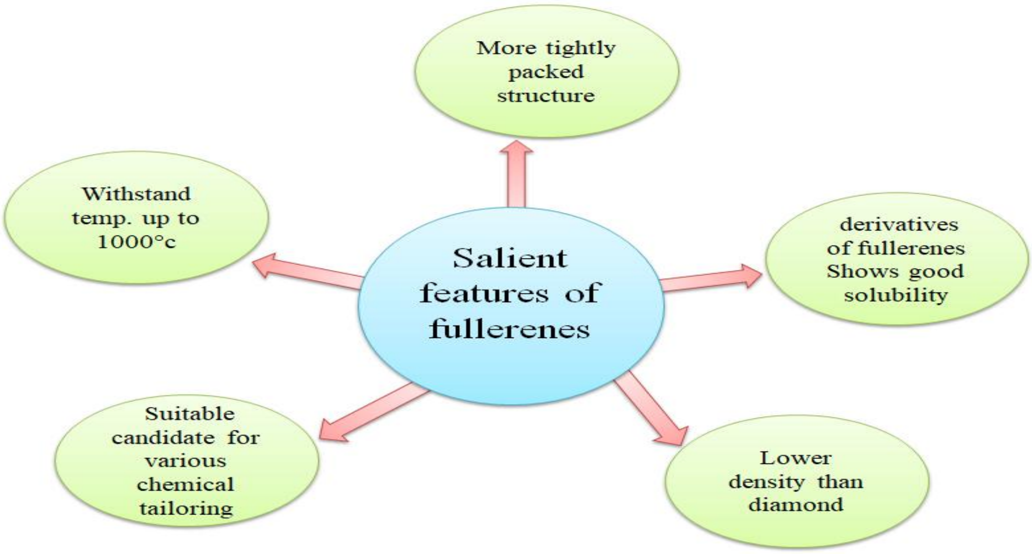

Figure 4. Salient features of fullerenes

4.1 ADVANTAGES OF FULLERENES:

- Fullerenes possess good tensile strength.
- They are nano matric in size so can be used for specific drug targeting
- Have good thermal stability
- Fullerenes offer antioxidant property
- Suitable candidate for various chemical targeting, so different derivatives can be produced with immense benefit in drug delivery. (22)

4.2 LIMITATIONS OF FULLERENES:

- They demonstrate oxidative degradation and photolytic decomposition. (23)
- Due to the conversion of singlet excited state to triplet state with lower energy deactivation processes ground state quenching, quenching by molecular oxygen, and electron transfer to molecules occurs

5. TYPES OF FULLERENES:

Fullerenes are C_{60} or C_{70} fullerenes, Fullerenes are made up of hollow nanomaterials cage. Electrons conduct electricity because of their high electrical conductivity. Exclusive features such as affinity, structure, strength, and adaptability make commercial interest of fullerenes in different sectors. (24) Fullerenes are made up of carbon units that are pentagonal or hexagonal. Fullerenes have sp2 hybridised carbon atoms that connect them. Fullerenes constructed of C_{60} or C_{70} have diameters of 7.114 and 7.648 nm, respectively. Both single layer and multiple layered can be used. Fig. 3 represents different types of fullerenes

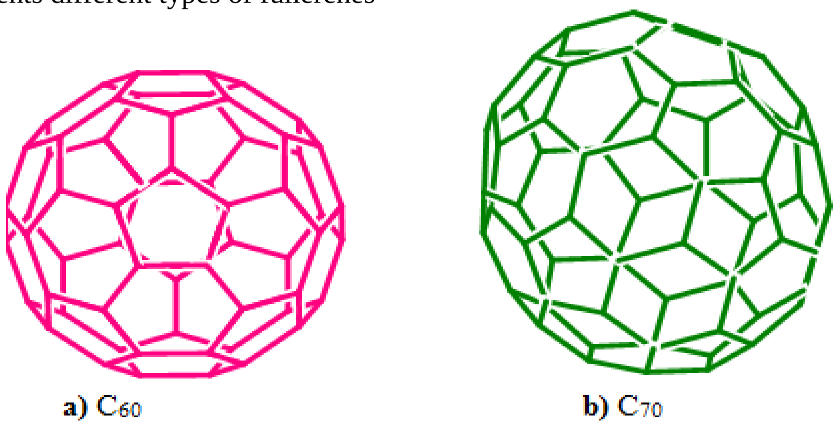

Figure 5. Typical structures of C_{60} and C_{70} types of Fullerenes

BIOMEDICAL APPLICATION OF FULLERENES

Antiviral activity: Fullerene derivatives acts as anti-HIV agents they fit smartly in the active site of the viral protease. fullerene derivatives of cationic and anionic type inhibit the replication of HIV-RT and hepatitis C virus. Anionic type of fullerenes have antioxidant activity and cationic type shows antiproliferative and antibacterial properties. (25)
Antioxidant and Neuroprotective Activity: Fullerenes have neuroprotective properties because they can react with oxygen species and Hydroxyl radicals, which can destroy lipids, proteins, DNA, and other macromolecules without consuming them. Fullerenes are known as radical sponges because they are the most effective radical scavenging agent on the planet. (26,27) Fullerenes are also used in medicine as an antioxidant. Apoptosis can be caused by cellular (reactive oxygen species) ROS generation in pathological conditions. As a result, fullerene derivatives can protect cells from apoptosis by neutralising reactive oxygen species (ROS). (28)
Fullerenes in Drug and Gene Therapy: Fullerenes are inorganic nanoparticles with a tiny size (less than 1 nm). Due to the hydrophobic nature of the fullerene core, fullerenes can become water-soluble and be used in a variety of applications. capable of delivering medicines and genes to cells by incorporating hydrophobic moieties Derivates of Fullerenes can cross the cell membrane and bind to mitochondria. (29)
X-ray contrast agent: X-ray contrast agents can be made from fullerene derivatives.C_{60}fullerenes have been suggested as MRI contrast agents. In vitro and in vivo NMR are particularly promising. Gadolinium complexes (containing gadolinium) are used in imaging. Gd3 + ions within the fullerene cage) is also known as gadofullerene. Heavy radio metal is hazardous, and it can't get out. (30)

Antimicrobial Activity: The fullerenes possess antimicrobial activity because of it intercalation into biological membrane different type of strains of fungi and bacteria such as bacillus subtilis, Escherichia coli Candida albicans, and Mycobacterium avium showed positive results. (31)

THERAPEUTIC APPLICATION:

Carrier for Drug Delivery: Amphotericin B is targeted to cells using carbon nanotubes cylindrical fullerenes with varied functions. When doxorubicin was given with nanotubes, the intracellular penetration was increased. Carbon nanotubes are used as lubricants or glidants in tablet manufacture because of their nanosize. (32)

Genetic Engineering: In the development of bioimaging genomes, proteomics, and tissue engineering, carbon nanotubes fullerenes and carbon nanohorns (CNHs) are utilised to control genes and atoms. Nanotubes and nanohorns can bind to antigens on their surfaces, making them potential antigen sources in vaccinations. (33)

FULLERENES IN COSMETIC TECHNOLOGY:

Since oxidative stress and apoptosis are linked to skin ageing, fullerenes have been shown to have powerful antioxidant properties as well as a lack of cytotoxicity in human cells. Many scientists were prompted to evaluate keratinocytes to promote rejuvenation products. (34) Cosmetic applications have been made with various types of fullerene C_{60} and its derivatives. The cosmetic industry was particularly interested in the molecular complexation of fullerenes with cyclodextrins, PVP, and liposomes. Because of its radical scavenging characteristics, fullerene C60 was encapsulated by establishing a stable combination between water-soluble cyclodextrins (cyclic oligosaccharides) and fullerene. (35) The first research on the utilisation of liposomes to encapsulate fullerene was the inclusion of fullerene C_{60} and C_{60} adducts into phosphatidyl-ethanolamine liposomes. (36) The PVP-fullerene complex "Radical Sponge, fullerene mixture in an ethanol solution of PVP - was the first water-soluble fullerene derivate used in cosmetic applications. (37) Another significant advancement was the encapsulation of fullerene C_{60} into liposomes for cosmetic purposes. (38

Fullerene C_{60} and its derivatives significant antioxidant capabilities were the primary basis for their promise in cosmetic applications. (39-42) Several investigations have shown that the PVP/fullerene combination is an effective ROS scavenger. Fullerene-antioxidant PVP's activity is thought to be involved in the early stages of lipid peroxidation and the generation of hydrogen peroxides to prevent apoptosis-like cell death. (43) Using electron spin resonance (ESR) spectroscopy, it was discovered that fullerene-PVP (400-2700 M) effectively quenched hydroxyl radicals. (43) Using human skin keratinocytes HaCaT, researchers investigated the intracellular inhibitory potential of UV irradiation-induced and *tert*-Butyl hydroperoxide (t-BuOOH)-induced oxidation of a variety of fullerene-PVP. Both UVB-induced and t-BuOOH-induced apoptosis-like cell death were significantly reduced by fullerene-PVP. (43)
This fullerene-PVP complex was found to have a strong inhibitory effect on ß-carotene discolouration, indicating that it could be used as a powerful radical scavenger. Because liposomes are now widely used in cosmetics, including fullerene C_{60} into them was critical. Liposomes are spherical bi-layer phospholipid aggregates that form in aqueous solutions as a result of mechanical rearrangement of the bimolecular layers in which phospholipids spontaneously assemble when dispersed in an aqueous solution. By dissolving 0.2 % (w/w) pure fullerene in toluene (10 %t w/w) and, if necessary, also agitating it, a solution of 0.2 % (w/w) pure fullerene in toluene (10 % w/w) is created. (44) Lens et al. investigated the antioxidant capabilities of C_{60} and two fulleropyrrolidine derivates encapsulated in phospholipid multilamellar liposomes (N-methyl (2-quinolyl) fulleropyrrolidine 60, Q-C_{60} and N-methyl (2-indolyl) fulleropyrrolidine 60, I-C60). (45) Another potentially essential element of fullerenes' biological properties relevant for cosmetic application is their effect on UV-induced melanogenesis (melanin production). (46)

Xiao et al. studied the effect of fullerene-PVP "Radical Sponge, on melanogenesis in normal human epidermal melanocytes (NHEM) and human melanoma HMV-II cells and discovered that this fullerene complex significantly inhibited melanogenesis in these human skin cells within a non-cytotoxic dose range. (47)

In two types of human melanocytes, the same group discovered that "Radical Sponge, suppresses UVA-induced rise of intracellular ROS levels. (48) These findings may entice researchers to look into the role of fullerene derivates in the creation of new topical therapies for the prevention and treatment of skin cancer. Sunscreens could benefit from fullerenes. The skin should be protected against both UVA and UVB rays, as well as from immunosuppression and DNA damage when using an effective sunscreen composition. A patent for a sunscreen including carbon nanotubes (fullerene-related structures made up of molecular-scale tubes of graphitic carbon) was recently published. (49)

6. CURRENT & FUTURE ASPECTS:

Fullerene C_{60} and its derivatives have been investigated and employed as active components in the production of a variety of cosmetic products in recent years. The cosmetics industry is a rapidly expanding industry that examines the application of cutting-edge science in cosmetics. In the last few years, fullerenes have been the focus of cosmetic research due to their ability to absorb free radicals as effectively as they can. Even though the results were highly promising, cited in a slew of research assessing biological activity the use of fullerenes in cosmetics is gaining popularity. The options are still restricted. Moreover, many members of the scientific community are worried of the acceptability and safety of Fullerenes. The determination of percutaneous penetration is an important feature in the creation and evaluation of cosmetic products since the efficacy of a product containing an active ingredient is dependent on the active ingredient's transport to the skin. Rouse et al. discovered that fullerenepeptides travel through the epidermis within the intercellular gaps of the stratum granulosum rather than via cells using transmission electron microscopy (TEM). (50)

However, more research is needed to fully understand the process of fullerene penetration through the skin, their activity on the skin surface, and their interactions with ROS at the membrane and cellular level. In Asian countries, the use of fullerene-containing cosmetics is highly common. Fullerene has earned a reputation as a powerful skin whitening agent in recent years, and it has been employed to make whitening/lightening cosmetic products. (47)
several researcher has shown that fullerene-PVP Radical Sponge, can reduce the activity of tyrosinase (a crucial enzyme in melanogenesis), its anti-melanogenic potential will be examined further by examining its effect on melanocytes. melanogenic substances produced by keratinocytes (such as alphaMSH, endothelin-1, and basic fibroblast growth factor). (48) We may expect a lot of fullerenes to be used in make-up because the industry is continually expanding. Many firms are researching new fullerene derivates as prospective candidates for active ingredients in their cosmetic products in response to the growing need for cosmetic rejuvenating skin treatments. (51,52)

7. CONCLUSION:

Many discoveries and significant aspects of these carbon molecules have been amassed over the last few years, resulting in the development of a new and intriguing scientific field. The classification, production, characterisation, and uses of numerous nanoparticles were extensively discussed. In recent years, C_{60} and its derivatives have been studied and used as active ingredients in a variety of cosmetic products.

AUTHOR CONTRIBUTION: NKP and AK drafted the manuscript, APK was involved in evaluation of content and SKM was engaged in critical review of manuscript.

DISCLOSURE STATEMENT:
The authors state to have no potential conflicts of interest.

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