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Mini-Review

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A Dyanamic Organic Ball: Pharmaceutical Application

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ABSTRACT

The discovery of fullerene in 1985 opened the door to a wide area of study. Fullerenes have been used in a variety of fields because of their cage-like structure, high reactivity, and ease of substitution and complexation with different metals. The formation of adducts with different types of metal and compound bulky ball of carbons has a wide range of therapeutic applications. Their application explore from diagnosis to treatment. After modification, these bulky balls can be used as an anti-oxidant, anti-microbial, anti-HIV, anti-tumor, neuroprotective and antiviral agent.

Key words: Fullerene; Bulkyball; Exohedral fullerenes; Metallofullerene

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INTRODUCTION

Fullerenes were first discovered in 1985 by Robert Curl, Harold Kroto, and Richard Smalley [1]. Fullerene is a chemical compound constructed completely of carbon atoms and hollow, spherical or ellipsoid molecules held together by a cage-like structure with pentagonal and hexagonal faces. Because of its resemblance to Richard Buckminster Fuller, a well-known architect who popularised the geodesic dome, the molecule was named after him. Buckminster fullerene and Buckyballs are two terms used to describe fullerenes (Figure 1)**.**

Figure 1: Similarity between geodesic dome and bucky ball fullerene

In 1996, Professor Sir Harold Kroto and two Rice University chemists, Dr. Richard E. Smalley and Dr. Robert F. Curl Jr., were awarded the Nobel Prize in Chemistry for their discovery of fullerene.

LITERATURE REVIEW

Properties of Fullerenes

Fullerenes, along with the two forms of diamond, the two forms of graphite, chaoit, and carbon (IV), are the seventh allotropic type of carbon to be discovered. Fullerenes can be dissolved in CS2, toluene, xylene, and dichlorobenzene, but they are insoluble in water. Fullerenes are stable at room temperature (Figure 2) [1-3].

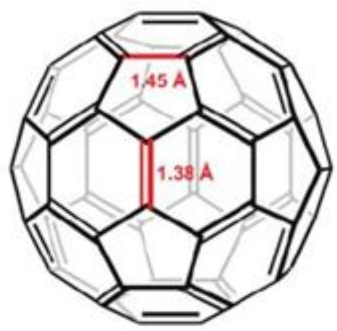

Figure 2: Bonds in fullerene

Because of π-π^*-electron transitions, Thin layers of fullerenes and solutions are coloured:

- C60 purple/violetred
- C70 brick-red
- C76 light yellow-green C 84 brown and
- C86 olive-green.

In sp hybridization, the most common type of fullerene C60 has 60 carbon atoms. It is arranged on a sphere with a diameter of 7.1 A^0. There are 20 hexagons and 12 pentagons in total. There are two types of C-C bonds: d5-6=1.46 A0 and d6-6=1.38 A^0 at the pentagon-hexagon and hexagon-hexagon boundaries, respectively. Single and double bonds are commonly used terms to describe the two forms of bonds.

In the chemical literature a perfect matching is often called a Kekul´e structure and in the model of carbon molecules the edges of a perfect matching correspond to double bonds [2].Fullerenes are a well-known electron acceptor with excellent thermal stability; as a result of these properties, they've found use in organic solar cells, superconductors, and ferromagnetic materials.

C60 and C70 have the ability to be reduced reversibly by up to six electrons. The presence of triply-degenerate low-lying LUMOs results in a high electron affinity (lowest unoccupied molecular orbital). The molecule has also been observed to oxidise; however, oxidation is irreversible. The molecule C60 has a localised pi-electron mechanism, which prevents it from exhibiting super aromaticity properties [4] (Table 1).

Table 1: Fullerenes and colour of their solutions

Fullerenes	Molar mass (g/mol)	Colour of the solution
C60	720.6	Purple/violet
C70	840.7	Brick red
C76	912.76	Light yellow green
C84	1008.84	Brown
C86	1032.86	Olive-green

Species of Fullerenes

The following are some of the most common fullerene species.

Alkali-doped fullerenes: Fullerenes react with alkali metal to form an interesting class of compounds known as alkali-doped fullerides due to their high electronegativity [5]. Alkali metal atoms occupy the vacuum between Buckyballs in alkali-doped fullerides and donate a valence electron to the nearby C60 molecule. Compounds containing alkali atoms such as potassium or rubidium act as superconductors, conducting electric current without resistance at temperatures below 20-40 K. e.g., K_3C_{60}, Rb_3C_{60}.

Endohedral fullerenes: Endohedral fullerenes allow another atom to be encased within hollow fullerenes. Endohedral fullerenes are a subset of fullerene derivatives [6]. They're called metallofullerenes because the atom trapped inside is a metal. C82, C84, and even higher fullerenes make up the majority of endohedral materials. Some noble gases, such as lanthanum, yttrium, and scandium, contain stable endohedral compounds. While the cage is being designed, endohedral material must be synthesised. Eg: La@C82 and Sc2@C84.

Exohedral fullerenes: Exohedral fullerenes are the most important and flexible fullerene species. A chemical reaction between fullerenes and other chemical groups produces it. Functionalized fullerenes are another name for fullerene derivatives. Since fullerenes have a conjugated-system of electrons, they can undergo two forms of primary chemical transformations: addition reactions and redox reactions, which generate covalent exohedral adducts and salts, respectively. Since fullerenes are water insoluble, a variety of fullerene derivatives with improved solubility profiles have been developed [7].

Heterofullerenes: Heterofullerenes are another significant subset of modified fullerenes. They are heteroanalogues of C_{60} and higher fullerenes, in which one or more carbon atoms in the cage are replaced by hetero-atoms such as trivalent nitrogen or boron [8]. The aza (60) fullerene $C_{59}N$ and its dimer $(C_{59}N)_2$ are the most basic nitrogen fullerene derivatives (Figure 3)**.**

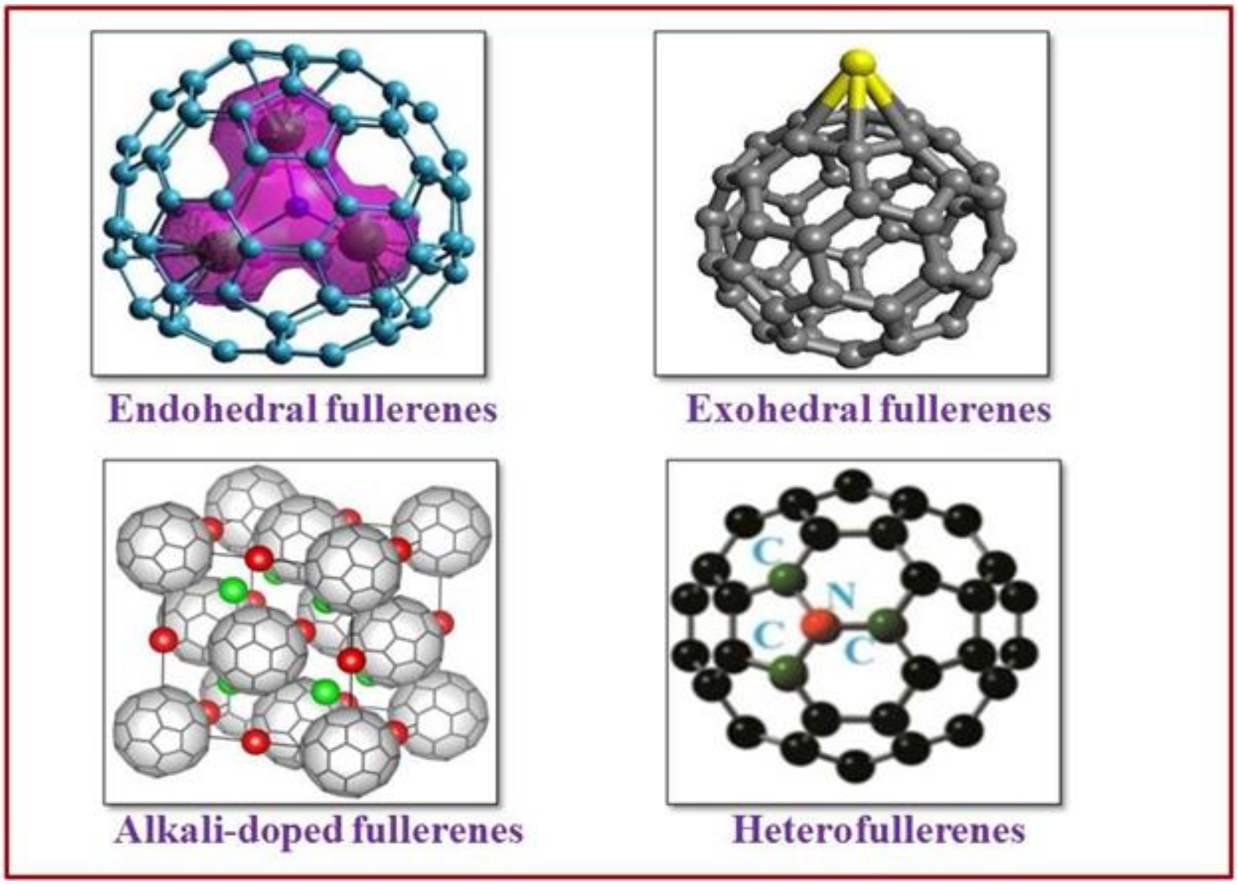

Figure 3: Species of fullerenes

Application of Fullerenes

Fullerenes are biologically interesting because they are inert, empty, and indefinitely modifiable. They are not absorbed when given orally in the water-soluble form; but, when given intravenously, they are quickly spread to different body tissues. They are excreted in their natural state by the kidneys. Water-soluble fullerenes have been shown to have a low acute toxicity. All of these exciting properties suggest uses for fullerenes in biology and medicinal chemistry, as well as a promising future for fullerenes as therapeutic agents [9].

Fullerenes for Diagnosis

Metallofullerene is a novel class of contrast-enhancing agent for magnetic resonance imaging (MRI) that may have clinical applications. The $Gd3^{+}$ ion was encapsulated in a fullerene cage, which is a structure that maintains the metal ion's properties, prevents leakage, and thus prevents dissociation and toxicity *in vivo*. Because of the presence of three $Gd3^{+}$ ions per molecule, the Gd3N@C80 fullerene with the highest relaxivity has seen increased use. Additionally, such trimetaphase MRI contrasts may aid in the detection of atherosclerotic plague built up in blood vessel walls in patients with CAD (coronary artery disease). This wound aids in early diagnosis by supplying physicians and patients with forewarning details prior to a myocardial infarction stroke.
Because of their resistance to metabolism and high kinetic stability, metallicofullerenes are a novel alternative to chelating compounds. As a result, metallofullerenes may be useful as a modern, more stable radiometal transporter *in vivo*. An [Gd3+-fullerol] and [166HO3+-fullerols] could be ideal bone-seeking agents for bone-marrow ablation in the treatment of myeloma and could be incorporated into a blood-pool MRI technology [10].

Photoacoustic Imaging

For certain functionalized fullerenes, polyhydroxy fullerenes (PHF; $C_{60}(OH)_xO_yN_{az}$) and carboxy fullerenes (CF; $C_{60}(C(COOH)_2)_3$, a new therapeutic term called "acoustic-explosion" has recently been proposed. Sustained glowing of functionalized fullerenes was observed when they were exposed to low-intensity continuous-wave laser irradiation in the presence or absence of oxygen. Photoacoustic imaging has been used for polyhydroxylated and carboxyl fullerenes [11,12].

Their antitumor effects may be linked to oxidative stress reduction, anti-angiogenesis, and immunostimulatory activity.

DISCUSSION

Fullerenes for Therapeutics

Anti-HIV activity: The HIV-I-specific enzyme aspartate protease is a viable target for antiviral therapy in AIDS. Except for Asp-25 and Asp-125, the active site of this enzyme resembles an open ended cylinder lined almost entirely by hydrophobic amino acids. Fullerenes containing amino derivatives that are complementary to the aspartate residue on HIV protease bind directly within the cavity of the enzyme and fully inactivate it, inhibiting the virus's proliferation and replication mechanisms and reducing its virulence. This research has the potential to revolutionise HIV care mechanisms in the near future [13,14].

Anti-ageing: Dugan et al. investigated the anti-ageing effects of a carboxyfullerene SOD (a small-molecule synthetic enzyme superoxide dismutase (SOD) mimetic). Chronic treatment decreased age-related oxidative stress and mitochondrial radical production while also extending the lifespan of the treated animals. In animals, an antioxidant with mitochondrial activity and nervous system penetration not only extends their lives but also helps them recover from age-related cognitive decline [15].

Anti cancer: Fullerenes are used in gene therapy and as newer drug delivery mechanisms for cancer, diabetes, fungal infections, and viral infections. The system's key benefits are drug targeting to the site of action and an improved safety profile [16] (Table 2).

Table 2: Carbon nanoparticles used for medical application

Product	Description	Use
AuroLase™	Gold nano shell	Head and neck cancer
INGN 401	Nanoparticle formulation of tumor	Lung cancer
	suppression gene FUS1	
Abraxane®	Albumin bound taxane	Non-small cell lung

	Particles	cancer
Doxil®	Liposomal doxorubicin	Ovarian tumor
MRX 952	Nanoparticle preparation – to	Tumors
	encapsulate camptothecin analogues	
Targeted Nano Therapeutics (TNT)™	TNT with polymer coated iron oxide magnetic particle	Solid tumors
system		
Cyclosert-Camptothecin – IT 101	β-Cylcodextrin polymer drug delivery system	Solid tumors

Novel Drug Delivery System

The ability to deliver highly effective therapeutic compounds to diseased sites is critical for treating all human illnesses effectively. Controlled synthesis of fullerenes and nanotubes makes this possible (Figure 4) [17].

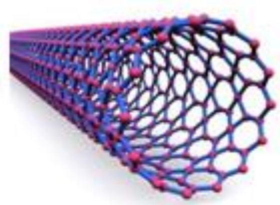

Figure 4: Nanotube

As a drug delivery system, it has a few applications:

- Hollow success-buckyballs for cancer treatment.
- Antibody combination delivers antitumor drugs
- Buckyballs to fight allergy
- Buckyballs as powerful anti-oxidant
- Buckyballs as inhibitor of HIV

CONCLUSION

According to the findings, fullerenes are critical in the development of novel pharmaceutical drug delivery systems that target drugs to specific sites. As a result of its similarity to Richard Buckminster Fuller, a notable designer who popularised the geodesic dome, the molecule was named after him. Buckminster fullerene and Buckyballs are two terms used to portray fullerenes.

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