Chapter 3

Effects of Fullerene Nanoparticles on Semen Quality

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Abstract

Fullerene or Buckminsterfullerene (also known as "Buckyballs"), which is composed entirely of 60 carbon (C) atoms, is a kind of molecule that is considered to be the most prominent member of the nano-materials family. Fullerene has been an attractive research topic in the field of nano-materials since 1985, the date when it is first discovered, due to the unique physicochemical properties and biological activities. Carbon 60 (C_{60}) Fullerene (FUL) nanoparticles, prepared through various dissolution and modification methods, exhibit different and distinct biological effects. Carbon 60 (C_{60}) Fullerene (FUL) and some of its derivatives are known to provide effective protection in vivo and in vitro against oxidative stress, without causing acute or subacute toxicity. Carbon 60 (C_{60}) Fullerene (FUL), which has been the subject of numerous studies particularly in recent years, has been proven to have beneficial biological effects as neuro-protectant, anti-cancer, anti-inflammatory, anti-atherogenic and radioprotective agents on the grounds of its unique bio-antioxidant properties that can manifest unexpectedly even at small concentrations and doses.

1. Introduction

Galaxies and stars formed approximately 300.000 years after the Big Bang, which occurred 13,7 billion years ago. There are a high percentage of hydrogen (H), some helium (He), and lesser amounts of other heavy elements in the first ring of stellar development. The phenomenon that keeps the stars in equilibrium against the gravitational pull of the stellar core is the release of heat as the H present in the structure fuses into He. The decrease in the amount of H over time results in the weakening of this heat source. In a supernova explosion, stars consequently scatter elements such as

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C, oxygen (O_2) and iron (Fe) into space. Hence, C became one of the basic elements of the life on Earth as a consequence of such a supernova explosion (Hanaoka et al., 2002).

C, which is one of the most important elements, ranks the fourth after H, He and O_2 in terms of the amount existing in the universe. It exists both in pure form and as a compound. C, as one of the basic building blocks of all living creatures, constitutes 18.5% of the human body. C atom, with 6 electrons, bears nonmetallic properties and is the first element in Group IV of the Periodic Table. Furthermore, C has the highest hybridization tendency among all Group IV-A elements (Saito, 1998).

C initially played a minor role for chemists working on creating and shaping a new substance. However, this fact changed significantly when the classical graphite and diamond structures were replaced by the C-allotrope family enriched by Fullerene (FUL). Unlike graphite and diamond, FULs have spherical molecules consisting of a combination of pentagons and hexagons and they can be dissolved in some organic solvents. The most known FULs containing the least C is Buckminsterfullerene C60, which is shaped like a soccer ball (Figure 1). The principle that creates FULs is a consequence of Euler's Theorem, which states that 12 pentagons are needed to fulfill each spherical mesh of n hexagons (Demirbakan, 2015). FULs with high numbers of C atoms are accompanied by multiple isomers and point group symmetry (Godly and Taylor, 1997).

The structure of these three-dimensional systems has attracted the attention of many scientists, as they have a more aesthetic appearance compared to smaller two-dimensional molecules. For this reason, Buckminsterfullerene C60 has become one of the molecules that has been widely researched in a very short time (Demirbakan, 2015).

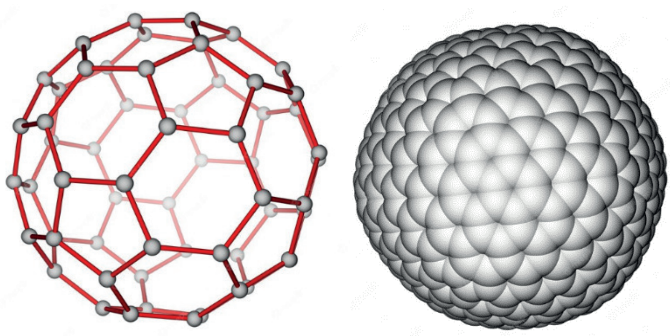

Figure 1. Schematic presentation of the Buckminsterfullerene C60 (left) Balls and Sticks model, (right) Space Filling model.

2. History of Carbon 60 (C_{60}) Fullerene

For the first time in 1966, Deadalus also known as D. E. H Jones suggested that it would be possible to generate C-cages (so called as FULs); however, this idea was not supported by the scientific community. In 1970, exactly 4 years after this idea was put forward, the synthesis of the bowl-shaped molecule called 'Corannulene' was found to be similar to the idea put forward before. Eiji Osawa was the first who hypothesized the spherical icosahedral (I_h) symmetric football structure for the C_{60} molecule (Barth and Lawton, 1966). The first article on FULs was also published in 1970 by the Japanese chemist Osawa who suggested that FULs could theoretically be stable (Yoshida and Osawa, 1971). However, these publications were not well known around the world as they were published in Japanese.

It was observed in 1984 that large, carbon-only clusters (C_n, n=30–190) can be produced upon laser vaporization of graphite. FULs were experimentally investigated in 1985, when Kroto visited Rice University in Houston (Kroto et al., 1985). Furthermore, Smalley et al. from the same University developed a laser ablation technique on a solid, such as graphite, to study refractory clusters with mass spectrometry (Dietz et al., 1981). These studies helped to observe C_{60} FUL with an intense mass spectrum peak. In the light of the results derived by this experimental study; Kroto and Smalley discovered the stable, 32-face truncated icosahedral (I_h) shaped C_{60} (with 12 regular pentagonal faces and 20 regular hexagonal faces), generated on similar principles and named also as Buckminsterfullerene after the architect Buckminster Fuller known for its geodesic dome and announced it to the world of science with their article published in Journal of Nature dated November 14, 1985 (Figure 2) (Kroto et al., 1985).

Figure 2. The geodesic dome built in 1967 by R. B. Fuller at the Montreal Fair.

3. The Structure of Carbon 60 (C_{60}) Fullerene

Truncated icosahedral (I_h) shaped C_{60} [60-I_h] FUL, which looks like a football and approximately 1 nm in diameter, is the smallest and most stable FUL. The pentagonal structures contain single bonds (–) and the hexagonal structures contain double bonds (=). The structure of [60-I_h] FUL has been revealed by theoretical and experimental studies. It has a number of features like all 12 pentagons being isolated by hexagons and the bonds (bonds [5,6]) between a single hexagon and a single pentagon being longer than the bonds (bonds [6,6]) connecting two hexagons (Demirbakan, 2015; Schulman et al., 1987).

While the hexagonal patterns in the FUL structure is only planar, the bonding structure consisting of pentagons provide multi-dimension (Schmalz et al., 1986; Bendikov et al., 2004).

Due to the structural properties, FULs are compounds suitable for chemical modifications. Therefore, it is possible to transform FULs into structures with various physical and chemical properties by using different modifications. For instance, Hydroxyl (-OH), Carboxyl (-COOH) and Amine (-NH2) groups can be introduced onto the surfaces of FUL nanoparticles in order to impart hydrophilic properties or it is possible to obtain endohedral metallofullerenes, which are used as radiotracers in X-ray imaging, by placing metal atoms in the FUL cage (Bosi et al., 2003).

Contrary to the methods for the chemical modification of FUL, a method has been developed to produce water-soluble and chemically unmodified C_{60} FUL without using any solvents or stabilizers and obtained preparation was named as "Hydrated C_{60} Fullerene" (C60HyFn). Stable Hydrated C60HyFn solutions in water contains single hydrated C60 FUL molecules as well as their variable clusters with a size of 3-36 nm (Andrievsky et al., 1995; Andrievsky et al., 1999; Andrievsky et al., 2002; Avdeev et al., 2004). C60HyFn has been the subject of numerous studies over the last 20 years and has been found to have beneficial effects as a neuro-protectant, anticancer, anti-inflammatory, anti-atherogenic and radioprotective agent. Unexpected manifestation of the beneficial effects of C60HyFn, even at very small concentrations and doses, is attributed to its unique bio-antioxidative properties (Andrievsky et al., 2009; Andrievsky et al., 2005; Podolski et al., 2007; Tykhomyrov et al., 2008; Andrievsky et al., 2010).

Consequently, FULs have a significant potential power in many areas at the molecular level due to their unique electron structure and chemical properties (Diederich, 1997). Various synthesized FUL derivatives have been observed to serve promising developments particularly in medical applications or nano-technology.

4. On the Health Effects of Carbon 60 (C_{60}) Fullerene

C60 FUL, which is the third allotrope of C and is a kind of molecule composed entirely of 60 C-atoms, is considered to be the most prominent member of the nano-materials family. Due to its unique physico-chemical properties and significant biological activities, C60HyFn derivative in water-soluble form has been widely researched in many areas by emphasizing the strong antioxidant activity caused by FUL particularly at very low doses. Recent studies revealed that FUL and some of its derivatives have beneficial effects and exhibit effective protection in the treatment of diseases related to oxidative stress (Andrievsky et al., 2009; Markovic and Trajkovic, 2008; Yin, 2009).

FUL is assumed to have the ability to initiate and catalyze reactions with reactive oxygen species (ROS) besides reacting directly with free radicals. This assumption explains how FUL can be effective even at very low doses (Andrievsky et al., 2009).

Studies have revealed that pure C_{60} FUL does not cause acute or subacute toxicity on humans, mice, rats and guinea pigs. Furthermore, it is known that chemically modified FULs are connected to nano-drug carrier systems when used alone or in the form of cylindrical C Nanotubes (CNTs) (Kolosnjaj et al., 2012; Aydın, 2016).

In a study, it was determined that the administration of doxorubicin caused a significant increase in lipid peroxidation (LPO) levels and changed antioxidant enzyme activities in male rats. It was further reported that FUL treatment is quite effective in preventing oxidative stress (Srdjenovic et al., 2010).

The administration of FUL together with cyclophosphamide on rats was found to result in improvement in oxidative stress and antioxidant system parameters (Elshater et al., 2018).

In another study conducted on rats with diabetes, C60HyFn administration was reported to provide a protective effect against the damage in the seminiferous tubules of the testicles due to oxidative stress and prevents the adverse effects on epididymal sperm concentration and motility in addition to reproductive organ weights at varying levels (Bal et al., 2011).

Some in-vitro studies conducted on rams have revealed that FUL added to the semen extender has a positive effect on spermatozoon motility and membrane integrity for the purpose of both short-term and long-term semen storage (Özer Kaya et al., 2021; Güngör et al., 2022).

Similar studies performed on pigs have revealed that FUL added to the semen extender protects spermatozoa against oxidative stress in short-term storage at 4°C (Xinhong et al., 2019).

The number of studies on C60 FUL have recently been increasing and kept up to date. However, the number of studies on male reproductive characteristics and male fertility are still very few.

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