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Review Article

The Application of Fullerene Derivatives in Human Nutrition: Brain Health, Immunity, Longevity, Quality of Life, Skin Tone, Sports Performance, Vitality, and Weight Loss

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Abstract

Fullerene derivatives—most most notably Carbon 60 (C_{60})—have been investigated for their beneficial applications in humans. Fullerene, as a super antioxidant, protects cells from the harmful effects of free radicals. They may assist in weight loss, strengthen the immune system, improve the signs of aging, increase longevity, augment sports performance, enhance vitality, and improve quality of life—when used with a balanced diet and exercise.

Many C_{60} products can be purchased from e-commerce sites for oral consumption. However, the appropriate dose is not provided, or the given doses are not matching among the products. Despite the positive claims regarding their use and anecdotal evidence, none of the C_{60} preparations have been approved by the USFDA, MHRA UK, or EMA for human use.

Although specific fullerene materials display biocompatibility, there are no short-term or long-term toxicity studies to date. Thus, "buyer beware". Those who choose to ingest such fullerene materials should consider themselves as self-experimenters and the fullerenes not as a bonafide treatment or preventive agent, pending the outcome of future research.

Keywords: *Antioxidant; Carbon 60; Fuller; Fullerene; Longevity; Sports Performance, Vitality*

Abbreviations

C_{60}: Carbon 60; EMA: European Medicines Agency; EML: Estimated Lifespan; QoL: Quality of Life; MHRA UK: United Kingdom Medicines and Healthcare Products Regulatory Agency; USFDA: U.S. Food and Drug Administration

Introduction

Fullerene, the third carbon allotrope, was discovered by Harold Kroto, Robert Curl, and Richard Smalley in 1985, for which they received the Nobel Prize. Fullerene occurs in natural sources. The molecule can be synthesized in the laboratory, vaporizing graphite in an inert gaseous atmosphere [1-4]. Of the various fullerene shapes, C_{60} is spherical with 60 carbon atoms, measuring less than a nanometer. C_{60} is known as "buckminsterfullerene" for its resemblance to geodesic domes, popularized by Buckminster Fuller.

Since its discovery, fullerene has been actively investigated in the physical, chemical, and biomedical sciences [1-6]. The research has provided valuable insights into the molecule and its potential applications in various fields, especially biomedical sciences. Although several studies have supported its potential role in various applications, fullerene's toxicity profile remains undetermined. Thus, it is essential to explore the molecule's toxicity profile via short-term and long-term toxicity studies in experimental models [2,5-7].

Scientific evidence for the beneficial role of fullerene in humans is inconclusive. However, several online sites recommend it as a "high antioxidant food". Fullerene is a super antioxidant that protects cells and metabolic processes from the harmful effects of free radicals. It may help healthily lose weight, strengthen the immune system, improve aging signs, increase longevity, enhance vitality, and improve quality of life (QoL) when used with a balanced diet and moderate exercise. It may also provide benefits of increased energy level, sound sleep, better skin tone, improved brain health, and enhanced sports performance.

This review offers scientific evidence for the applications of fullerene in humans and currently marketed fullerene-based nutritional products.

Discussion

Role in prolongation of lifespan

Baati., *et al*. (2012) studied the role of C_{60} in improving the lifespan of rats. Oral administration of C_{60} dissolved in olive oil (at a concentration of 0.8 mg/mL and a dose of 1.7 mg/kg of body weight) did not demonstrate chronic toxicity [2,6]. The lifespan study published by Baati., *et al*. (2012) is one of the most cited literature in many e-commerce websites mentioning fullerene's nutritional applications [2,7].

In the lifespan study, after 14 days of acclimatization, the C_{60}-olive oil group (n = 6) was administered an oral gavage of C_{60} dissolved in olive oil once a day at week-1, once a week until the end of month-2, and once every 2 weeks until the end of month-7. The rats were weighed before and after each oral administration. The inside and outside of their cages were observed once a day for any deviation from everyday activities, signs and symptoms of illness(morbidity), and mortality. All rats, except for one from the water-only control group, survived until the end of the study. At the end of month-25, the solution was discontinued. The control group rats showed signs of aging and ulcerative dermatitis, but the C_{60}-olive oil group showed no visible signs or symptoms of illness. There was no significant increase in daily calorie intake or bodyweight in all rats (especially the C_{60}-olive oil group).

At month-38, all control group animals were dead, per their natural lifespan of 30–36 months. However, 67% of the olive oil-only control group rats and 100% of the C_{60}-olive oil group rats were alive. Statistical analysis (non-parametric Kaplan–Meier and log-rank tests) revealed that the animals' estimated lifespan (EML) was 42 months in the C_{60}-olive oil group, 22 months in the water-only control group, and 26 months in the olive oil-only control group. Thus, compared to the water-only control group, the EML increased by 18% and 90% in the olive oil-only control group and C_{60}-olive oil group, respectively.

The researchers concluded that C_{60} (dissolved in olive oil) did not elicit any signs of acute or chronic toxicity and that the ELS in this group almost doubled compared to the water-only and olive oil-only control groups.

In this toxicity study, the protective effect of C_{60}-olive oil on CCl_4-induced toxicity was examined. The rats (n = 6) were administered a single dose of water-only (control group), olive oil-only (control group), or C_{60}-olive oil (treatment group) through oral and intraperitoneal (i.p.) routes. At 24 hours after administering a single dose of CCl_4 (1 mL/kg) through the i.p. route, the rats were euthanized. CCl_4 administration caused symptoms of lethargy, inactivity, and piloerection in rats. These symptoms disappeared within 5 hours in the olive oil-only and C_{60}-olive oil groups, whereas they persisted in the water-only control group until death. Postmortem examination (microscopic and biochemical analyses) revealed that C_{60} dissolved in olive oil protected the rat livers from CCl_4-mediated cytotoxic injury, possibly through its free radical-scavenging activity (already explored in other *in vivo* studies) [2,7].

The Baati., *et al*. (2012) study is one of the first studies to explore the role of C_{60} in improving lifespan. The substance prolonged the lifespan of rats up to 46 months (natural lifespan, 30–36 months). The compound's administration was stopped at month-17 when one control group rat died. It might be presumed that prolonged administration could have further extended the animals' lifespan. However, further studies are needed to establish the role of C_{60} in extending lifespan.

Role as an antioxidant

A considerable number of published studies have explored the protective role of the molecule against oxidative stress. One of the initial studies on fullerene's antioxidant properties was conducted by Chiang., *et al*. (1995). Fullerene acted as an effective scavenger of superoxide anions synthesized by the xanthine oxidase system [8]. Nielsen., *et al*. (2008) and Markovic and Trajkovic (2008) also explored the antioxidant properties of fullerene [9,10]. Mirkov., *et al*. (2004) proposed that fullerene's antioxidant effect may be mediated through its direct interaction with nitric oxide [11]. Lin., *et al*. (1999) demonstrated that fullerene's water-soluble derivative effectively protected the brain from iron-induced oxidative stress in experimental rats [12]. However, the primary antioxidant benefit of fullerene materials might be through the activation of Nrf2 [13]. Taguchi., *et al*. (2011) highlighted the critical role of Nrf2 in reducing free radical proliferation via increasing endogenous antioxidant enzymes [14].

Role in diet-induced obesity

Halenova., *et al*. (2018) reported on the potential of water-soluble pristine C_{60} in reducing obesity. The molecule restored glucose homeostasis and prooxidant-antioxidant homeostasis and reduced chronic inflammation associated with diet-induced obesity in rats [15].

Role in memory protection (brain health)

Fullerene's activity against amyloid accumulation and its potential role in managing Alzheimer's disease has been explored. Gordon., *et al*. (2017) examined the effect of hydrated fullerene on intrahippocampal pathways responsible for learning and memory after amyloid-β25-35 peptide infusion in male Wistar rats [16]. Pretreatment with hydrated fullerene protected the rats from amyloid-β25-35-induced damage to the intrahippocampal pathway. Vorobyov., *et al*. (2015) studied hydrated fullerene's protective role in a rat model of Alzheimer's disease due to amyloid infusion. Fullerene mediated neuroprotective effects via presynaptic dopamine receptors [17].

Role as an anti-inflammatory and immunomodulatory agent

Several studies have investigated the role of fullerene as an anti-inflammatory agent. Shershakova., *et al*. (2016) considered the role of fullerene in atopic dermatitis [18]. BALB/c female mice sensitized via the epicutaneous route with ovalbumin were administered fullerene (C_{60} solution) via epicutaneous and subcutaneous routes. Fullerene restored the normal skin function, as evidenced by a decrease in eosinophil and leukocyte infiltration in the skin and shifting the immune response from Th2 to Th1 [18]. Two other studies supported these findings. The results of studies by Pescatori., *et al*. (2013) and Henderson., *et al*. (2014) underscored the anti-inflammatory and immunomodulatory potential of fullerene in various skin and autoimmune conditions [19,20].

Commercially-available fullerene C_{60} supplements

Without implying researcher endorsement, some Commercially-available C_{60} preparations are as follows:

- Carbon 60 Australia (Performadog)
- Vitality C_{60} (Allure imports)
- C_{60}-oo (Super-Nutrition)

- Ultra-Pure C_{60} in Olive Oil (pure C_{60} olive oil)
- C_{60} Extra Virgin Olive Oil 500 mL, Lipo Fullerenes 99.95%, Bucky Balls, and Family Bottle (Telomas BioLabs Ireland Ltd)
- C_{60} Fullerene (Infinite Age)
- C_{60} Fullerene in Olive Oil (C_{60} supply)
- Carbon 60 Olive Oil (Good and Cheap).

Most of these products can be purchased from e-commerce sites. The respective company websites specify potential health benefits of fullerene C_{60} and its suggested use in animals or humans via an oral route. However, an appropriate dose is not provided, or the given doses are not matching among the products. Some of these products are also specified to be used for research/experimental purposes. Despite the optimistic claims, none of the C_{60} preparations have been approved by the U.S. Food and Drug Administration (USFDA), United Kingdom Medicines and Healthcare Products Regulatory Agency (MHRA UK), or European Medicines Agency (EMA) for human use.

Biocompatibility and toxicity of fullerene C_{60}

According to Kerna and Flores (2020), "Fullerene materials are composed of carbon atoms, which make them compatible with the human body. . . . the pristine fullerene atoms remain stable in the body and do not interfere with biological processes" [21]. D'Amora., *et al*. (2017) noted, "Fullerene materials introduced into cells and protein structures enhance various metabolic reactions due to their biocompatibility with tissues and organs. . . . NOLF materials advantageously impact cell-signaling pathways and catalytic activities with seemingly no toxic reactions" [22].

However, Kerna and Flores (2020) noted, "The outcomes in the manufacturing process of experimental-grade nanocarbon onion-like fullerene materials can be inconsistent (even within the same batch), making it challenging to perform reliable assessments and reproducible studies of their biological benefits, biocompatibility, and potential toxicity." The researchers continued, "Further research on the potential beneficial effects and possible adverse effects of fullerene materials in human cells or tissues should be conducted to confirm or deny any medical advantages associated with their chemical structures and properties" [23].

Fard., *et al*. (2015) posited, "In recent decades, the use of nanomaterials has received much attention in industrial and medical fields. However, some reports have mentioned the adverse effects of these materials on biological systems and cellular components" [24].

Conclusion

Can or should specific fullerene derivatives be used as nutritional supplements? The potential anti-inflammatory, immunomodulatory, and antioxidant properties of fullerene are prominent and promising. Moreover, fullerene's protective effects against CCL_4-induced liver damage, cyclophosphamide-induced genotoxicity, and its role in increasing rats' lifespan should not be undervalued. The conspicuous and significant limitation is that these studies have been conducted *in vitro* or *in vivo* in rats, not humans. Moreover, there are no short-term or long-term toxicity studies of fullerene to date. Although fullerene's nutritional benefits are aggressively proclaimed in e-commerce websites, these assertions lack scientific authentication and evidence-based confirmation, relying on assumptions and anecdotal evidence. However, based on the preliminary research, C_{60} could become a promising adjunct in the future of medicine and as a nutritional or dietary supplement. Further research on the potential beneficial effects and possible adverse effects of fullerene materials in human cells and tissues should be conducted to confirm or deny any medical advantages associated with their chemical structures and properties [21].

Conflict of Interest Statement

The authors declare that this paper was written in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

Supplementary Note

This paper is designed as a brief introduction to fullerenes regarding their application in human nutrition as a review. Other articles have been (or will be) published on the application of specific fullerene materials in the cardiovascular system, respiratory system, gastrointestinal system, neurological system, endocrine system, veterinary medicine, agriculture, pharmacology and toxicology, and other topics. These distinct mini-review articles could have been combined into a much lengthier review or research article. However, to have done so, the subject matter would have resulted in only one publication in one journal to exclude other medical specialties. The purpose of these papers is to disseminate the purported biocompatibility and beneficial effects of fullerenes to the broadest audience of students, researchers, and medical practitioners as possible. The authors hope that the introduction to the application of fullerene derivatives in various and diverse disciplines spawns curiosity and further research regarding fullerene materials. Fullerene materials seem poised to become a vital part of the future of human medicine, veterinary medicine, and agriculture. However, more research is needed to determine any adverse effects of their long-term use. Also, the specific fullerene materials' manufacturing process requires standardization to provide consistent quality and batch samples. Dosage and duration of treatment with fullerene materials for specific conditions need to be established by evidence-based research.

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