REVIEW PAPER

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The effects of fullerene (C60)-enriched olive oil on human health

Yasin Ozdemir[1], Zekiye Goksel[1], Tarik Yorukoglu[2]

[1]Food Technologies Department, Ataturk Central Horticultural Research Institute, Yalova, Turkey

[2]Food Engineering Department, Kahramanmaraş Sütçü İmam University, Kahramanmaras, Turkey

Corresponding author:
Assoc. Prof. Yasin Ozdemir
Food Technologies Department, Ataturk Horticultural Central Research Institute, Yalova, Turkey
E-mail address: yasin.ozdemir@tarimorman.gov.tr

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Abstract

Fullerene (C60), a spherical molecule composed of 60 carbon atoms, has garnered significant attention due to its unique chemical properties and potential health benefits. When dissolved in olive oil, C60 exhibits powerful antioxidant and anti-inflammatory properties, which have been explored in various biomedical and cosmetic applications. Although olive oils enriched with C60 are available as food supplements in different countries, clinical studies in humans are reported to be very limited. C60-enriched olive oil products are often marketed with strong claims. However, it is important that these claims are supported by scientific evidence. The available data are generally based on animal studies and laboratory experiments. Research on the safety of long-term use in humans has not been found. Dosage and route of administration are critical in this regard. In this review, current approaches to C60-enriched olive oil, mechanisms of action, especially antioxidant activity and anti-inflammatory properties, potential positive effects on health, and toxicity risks are discussed and the compiled information is presented collectively.

Keywords: *C60; food supplement; antioxidant; anti-inflammatory.*

INTRODUCTION

Fullerene (C60) is a class of carbon-based nanomaterials and C60 is one of its most well-known members. C60, also known as Buckminsterfullerene, was discovered in 1985 by Harold Kroto and his colleagues [1]. The molecule's sphere-like structure provides high antioxidant capacity and radical-scavenging abilities [2]. The advent of nanotechnology has enabled the development of novel materials like fullerene C60, a spherical molecule composed of 60 carbon atoms with unique chemical properties [3,4]. The lipophilic nature of C60 allows its dissolution in vegetable oils, such as olive oil, which serves as a biocompatible carrier for its therapeutic applications [4]. In C60, there are twelve pentagonal rings in between the twenty hexagonal benzene rings. The structural properties of C60 are given in **Figure 1**.

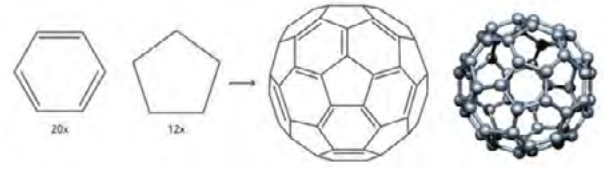

Figure 1. Structural properties of C60 [5,6].

The Nobel Prize in Chemistry was awarded in 1996 for the discovery of C60, underscoring its importance. C60's solubility in olive oil enhances its potential use in healthcare, as demonstrated by various in vivo and in vitro studies. C60-enriched olive oil was reported as a lifespan-prolonged agent in a rodent feeding experiment [7]. Fullerene C60 and olive oil have been shown to reduce DNA damage and decrease chromosomal aberrations. Studies indicate that C60 and olive oil exhibit protective effects against cyclophosphamide-induced mutagenicity and genotoxicity. Additionally, research suggests that C60 and olive oil represent a

promising field of study as potential antigenotoxic agents against the harmful side effects of chemotherapeutics [8]. Antioxidative capabilities of C60 make it a promising candidate for medical and biological applications, including drug delivery systems and therapeutic interventions for oxidative stress-related conditions [7]. Despite its potential, fullerene C60 raises concerns regarding toxicity and its influence on metabolic homeostasis [9]. Recent research has focused on elucidating the effects of fullerene C60 on glucose and lipid metabolism and its interaction with gut microbiota, a critical regulator of metabolic health [10]. Olive oil enriched with C60 is available for sale in the United States and many European Union countries. In some countries, such as Turkey, the production and sale of these products is not yet authorized. This review presents findings on the biological effects and therapeutic applications of C60-enriched olive oil.

MECHANISMS OF ACTION

Antioxidant Properties

C60's antioxidant properties stem from its ability to absorb free radicals and reduce oxidative stress. The molecule's structure enables it to interact with reactive oxygen species and reduce cellular damage. Research has shown that C60-enriched olive oil enhances the activity of key antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase [3]. Additionally, studies have found that C60's radical-scavenging abilities are significantly stronger than conventional antioxidants, making it an exceptional tool for combating oxidative damage in biological systems [11]. Therefore, C60 is informally sold as a "health food" ingredient in the United States and the European Union [12]. C60 dissolved in olive oil functions as a very strong antioxidant and has a therapeutic effect on inflammatory skin diseases, cancers, and intestinal disorders [13,14].

Notably, fullerene C60 supplementation has been shown to increase ascorbate oxidation in serum, indicating enhanced oxidative stress in this compartment [10]. This effect may be attributed to fullerene C60 aggregation in biological fluids, leading to reactive oxygen species generation [3]. Further studies are needed to elucidate the conditions under which fullerene C60 acts as a prooxidant versus an antioxidant [7]. It has been reported that C60 may reduce neuronal inflammation and apoptosis by helping to maintain cellular homeostasis and prevent oxidative stress thanks to its potent antioxidant properties [15]. The potential of C60 to reduce amyloid-beta plaques related to Alzheimer's disease is emphasized. This is reported to be a promising therapeutic property of C60 for the reduction of cognitive decline [3].

Anti-inflammatory Effects

C60 also exhibits anti-inflammatory properties by modulating pro-inflammatory cytokines and transcription factors. Studies have reported reduced levels of inflammatory mediators, such as tumor necrosis factor-alpha and interleukin-6, in animal models treated with C60-enriched olive oil [16]. These effects make it a promising candidate for managing inflammatory diseases and chronic conditions. Furthermore, C60's interaction with nuclear factor kappa B signaling pathways suggests its potential role in autoimmune disease treatment [3].

Histological analyses of the liver, kidney, spleen, heart, and small intestine revealed no significant pathological alterations due to C60 supplementation. However, mild inflammatory responses were observed in some tissues, which were attributed more to the oil mixture than to C60 itself [10]. Oral treatment with C60-enriched oil significantly prevented the change in body weight, reduced most of the clinical signs of the disease, colon weight, and microscopic damage score. It also significantly improved the profile of analyzed cytokines. It also protected the cells from the effect of dextran sulfate sodium as it reduced the levels of reactive oxygen species [16].

HEALTH BENEFITS OF C60-ENRICHED OLIVE OIL

Olive oil enriched with C60 has been reported to significantly extend the lifespan of rats. Rats fed 4 mg/kg body weight of C60 every two weeks showed no abnormalities. Rats in the control group lived up to 38 months, while rats consuming C60-enriched olive oil lived up to 66 months. The results are thought to indicate the potential of C60 to promote longevity by reducing oxidative damage [7].

The anti-aging property of C60 has been associated with the possibility that it acts as a mitochondrial protonophore. Furthermore, C60's scavenging capacity for reactive oxygen species and its ability to act as a mild mitochondrial respiratory uncoupler may also enable it to exert anti-aging effects [17]. As a result of a study examining the effect of long-term consumption of C60 on the lifespan and health status of mice, the lifespan of mice consuming C60 was prolonged. It has been claimed that C60 fullerenes are a potential geroprotector drug due to their ability to effectively capture free radicals, and it has been reported that there is a deep interest in C60 for life extension [18].

C60 has the ability to cross the blood-brain barrier allowing it to exert neuroprotective effects. Studies have shown that it reduces oxidative stress in neuronal cells and protects them against neurodegenerative diseases such as Parkinson's and Alzheimer's. It has been interpreted that the antioxidant properties of C60 may reduce neuronal inflammation by protecting

cells [11]. As a result of a study on animal brain tissues, it was reported that C60 may be used in the treatment of neurodegenerative diseases [19].

C60 has been reported to be useful for the cosmetics industry due to its anti-aging and skin-healing properties. Formulations enriched with C60 have been shown to reduce inflammatory skin conditions and promote collagen synthesis in the skin, resulting in reduced wrinkles and increased elasticity [4]. The most prominent beneficial effects of C60 have been reported to be radiation injury protection, neuro-protection, drug and gene transfer, anticancer therapy, adjuvant in different therapies, bone repair, and biosensing, but it is crucial to elucidate how C60 immunomodulates the human immune system [20].

C60 consumption to reduce liver inflammation and alleviate oxidative damage in hepatocytes has been reported to have potential in the treatment of liver diseases, including non-alcoholic fatty liver disease and toxin-induced liver injuries [21]. The hepatoprotective effects of two doses of C60 added to extra virgin olive oil were investigated against Thioacetamide-induced hepatotoxicity in rats. As an effective free radical scavenger, C60 is considered a potential liver protective agent. It was found that low-dose C60 was more effective in protecting against liver oxidative stress [22].

Turmeric, C60, and C60-turmeric mixtures were found to reduce oxidative stress in the lung tissue of diabetic rats, increase the antioxidant defense capacity of the tissue and exhibit tissue-protective properties against cell death (apoptosis). C60 was found to have protective effects against hyperglycemia-induced oxidative damage in lung tissue [23]. This study demonstrated the ameliorative effects of cinnamon apple plant extract and C60 on hematological and biochemical disorders induced by the intraperitoneal injection of carboplatin in male rats. According to the results of the study, C60 protected blood values. Cinnamon apple leaf extract and C60 were reported to protect cells against free radicals [24].

C60 and turmeric have various biological activities that can be shown to be antioxidant, anti-inflammatory, anticancer, neuroprotective, and hepatoprotective. C60 and turmeric have been reported to protect cells against oxidative damage caused by reactive oxygen species. C60 and C60-turmeric may be promising agents to prevent damage caused by hyperglycemic conditions in kidney tissue [25]. In another study, C60 and olive oil significantly reduced cadmium chloride-induced genotoxic effects in the liver and kidney. Several chromosomal abnormalities induced by CdCl2 were corrected by C60 and olive oil. Due to these effects, C60 and olive oil were found to exhibit anti-genotoxic effects against cadmium chloride-induced genotoxicity in rats [26].

SAFETY AND TOXICITY

In a study on rats, C60 supplementation via a mixture of olive and coconut oil showed tissue-specific bioaccumulation, with liver, heart, and adrenal glands showing the highest levels, while the spleen and brain showed minimal accumulation. Despite these accumulations, C60 supplementation did not show toxic effects on liver histology [10]. C60 is generally considered non-toxic when dissolved in olive oil. The lipophilic carrier has been reported to be able to ensure bioavailability while reducing the risk of toxicity [3]. Animal studies have reported no acute or subacute toxic effects even at high doses of olive oil enriched with C60 [11].

Limited clinical trials on the long-term safety of C60-enriched olive oil in humans have been conducted but it is commented that information on chronic exposure and potential side effects is still insufficient. Therefore, despite the promising results reported, the long-term safety of C60-enriched olive oil in humans requires further investigation [7].

CONCLUSION

Olive oil enriched with C60 has the potential for functional food production. Thanks to its antioxidant, anti-inflammatory, and neuroprotective properties, it offers a wide range of health benefits, from chronic disease prevention to anti-aging. However, further research is needed to determine its clinical suitability and address safety concerns. With continued advances in nanotechnology and in vivo testing, new products, such as C60-enriched olive oil, are likely to become more diversified and their potential beneficial effects and toxic properties more clearly determined.

Although olive oil enriched with C60 is available for sale in some countries, some studies indicate that large-scale clinical trials are needed to confirm the efficacy and safety of this product in humans. Furthermore, standardization of C60 formulations and dosages is critical to achieve reproducible results. Future research should explore the synergistic effects of C60 with other bioactive compounds and its potential role in combating chronic diseases such as diabetes, cancer, and cardiovascular disorders.

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Efekti fuleren (C60)-obogaćenog maslinovog ulja na zdravlje ljudi

Yasin Ozdemir[1], Zekiye Goksel[1], Tarik Yorukoglu[2]

[1]Odeljenje za tehnologiju hrane, Ataturk Centralni institut za hortikulturna istraživanja, Jalova, Turska

[2]Odeljenje za inženjerstvo hrane, Univerzitet Kahramanmaraş Sütçü İmam, Kahramanmaraš, Turska

Kratak sadržaj

Fuleren (C60), sferični molekul koji se sastoji od 60 atoma ugljenika, prikupio je značajnu pažnju usled jedinstvenih hemijskih karakteristika i potencijalnih benefita na zdravlje. Kada se rastvori u maslinovom ulju, C60 prikazuje snažna antioksidativna i antiinflamatorna svojstva, koja su ispitivana u vezi sa brojnim biomedicinskim i kozmetičkim primenama. Iako je maslinovo ulje obogaćeno sa C60 dostupno kao suplement ishrani u nekim državama, kliničke studije su veoma limitirane. Proizvodi sa C60-obogaćenim maslinovom uljem su često dostupni na tržištu uz snažne tvrdnje. Ipak, važno je da ove tvrdnje budu poduprte naučnim dokazima. Dostupni podaci su generalno zasnovani na studijama na životinjama i laboratorijskim eksperimentima. Istraživanje bezbednosti dugotrajne upotrebe kod ljudi još uvek nije ispitano. U ovom pogledu, doziranje i način administracije su neophodni. U ovom revijalnom radu, trenutni pristupi C60-obogaćenom maslinovom ulju, mehanizmi delovanja, a posebno njegova antioksidativna i antiinflamatorna svojstva, potencijalni pozitivni efekti na zdravlje i rizici usled toksičnosti su razmatrani, a prikupljene informacije su zajednički prikazane.

Ključne reči: *C60; suplementi u ishrani; antioksidanti; antiinflamatori.*