

Bioactivities and Animal Clinical Studies of Fat-Soluble Carbon-60: A Minireview

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ABSTRACT

Carbon-60 (fullerene) is a football-shaped carbon compound composed of 60 carbons with a molecular weight of 720. The discovery of carbon-60 earned three scientists the 1996 Nobel Prize in Chemistry. Carbon-60 is an inorganic form of carbon. While most inorganic carbons are typically biologically inert, Carbon-60 stands out due to its existence as distinct molecules rather than extended arrays of atoms. Owing to its antioxidant properties, carbon-60 has found application in cosmetology and dermatology. However, its low solubility in water (10^{-11} g·l⁻¹) has limited its study and medical application. Therefore, concerns have arisen regarding the dispersion of fat-soluble carbon-60 in aqueous solutions or human body fluids. Our research demonstrated that carbon-60 oil exhibits a more potent antioxidant effect compared to water-soluble vitamin C in aqueous solutions, whereas fat-soluble vitamin E shows no antioxidant effects in such solutions. In vitro studies involving cellular and animal models have suggested that carbon-60 oil effectively inhibits the pro-inflammatory actions of human neutrophils in cell culture media and reduces level of inflammatory marker of C-reactive protein in the blood of beagle dogs. C-reactive protein in the blood mainly serves as a marker for cardiovascular and cerebrovascular inflammation, possibly promoting such inflammation. Some research indicates that oral administration of carbon-60 oil to mice extends their lifespan and effectively treats colitis. In summary, this review discusses, in the context of carbon-60, recent advancements in antioxidant activity, skin inflammation, colitis treatment and potential use for treatment of C-reactive protein related diseases. This review is essential for understanding the future potential of carbon-60 as an oral drug for treating colitis and cardiovascular and cerebrovascular inflammatory diseases.

Keywords: Carbon-60 Oil; Fullerene; Fat Solubility; Lifespan; Drug Delivery; Antioxidant; Anti-Inflammation; Colitis; C-Reactive Protein; Cardiovascular and Cerebrovascular Diseases

Mini Review

Carbon, with the chemical symbol C and atomic number 6, is classified within group 14 of the periodic table [1]. Carbon atoms exhibit diverse bonding capabilities, resulting in the formation of various carbon allotropes. Well-known allotropes include graphite, diamond, amorphous carbon, and fullerenes. Carbon-60 (C-60), also called fullerene, comprises 60 carbon atoms arranged in a football-shaped structure, with a molecular weight of 720 (<https://en.wikipedia.org/wiki/Buckminsterfullerene>). In 1996, three scientists were awarded

the Nobel Prize in Chemistry for their pioneering discovery of C-60 [2-4] (<https://www.sesres.com/unlocking-the-mysteries-of-carbon-60-discovery-and-implications/>). C-60 is an inorganic form of carbon. However, inorganic forms of carbon exhibit limited biological activity and minimal clinical applications in humans. Research has shown the therapeutic potential of liposoluble C-60 in addressing inflammatory skin diseases, cancers, and intestinal diseases owing to its robust antioxidant properties [5]. C-60 holds promise for applications in the fields of cosmetics, medical devices, and medicine [6,7]. In 1992, the Journal of the American Chemical Society highlighted the

potent free radical scavenging abilities of C-60 fullerene and first introduced the concept of the “free radical sponge.” Studies and recent patents have demonstrated the robust scavenging ability of fullerene against reactive oxygen species and its remarkable potential as a biological antioxidant, advocating its utilization as an active ingredient in the preparation of cosmetic formulations [8].

Therefore, given its vital effects on skin health, hair follicle growth, and anti-aging, markets in Japan, United States, and China have incorporated C-60 into cosmetic formulations to treat, prevent, and protect against skin damage [9-14]. Our previous patent application showed the efficacy of fat-soluble C-60 oil in alleviating itching caused by mosquito bites [15,16], suggesting its ability to effectively penetrate human skin. Previous study also suggest C-60 as a viable alternative for the treatment of allergic and inflammatory conditions [17]. Our previous study demonstrated the efficacy of orally administered fat-soluble C-60 oil in treating colitis in mice [18]. Relevant patents and additional studies have further supported the role of fat-soluble C-60 oil in colitis treatment in mice [19-22]. Fat-soluble C-60 is insoluble in water but soluble in edible oil at concentrations ranging from 1–4 g/L. Various studies have underscored the antioxidant and anti-inflammatory properties of fat-soluble C-60 [23-28]. Investigating the transmission pathways of fat-soluble C-60 in aqueous solutions or human bodily fluids constitutes an intriguing research avenue [29-36]. Our previous study elucidated that fat-soluble C-60 oil disperses in aqueous solutions, producing a potent antioxidant effect [5]. Fat-soluble C-60 oil exerts a more robust antioxidant effect compared to vitamin C in aqueous environments [5]. Similarly, even a small volume of fat-soluble C-60 oil effectively inhibits the proinflammatory effects of human neutrophils in cell culture media [5]. Conversely, fat-soluble vitamin E fails to produce antioxidant effects in aqueous solutions. These studies were the first to propose the hypothesis that fat-soluble C-60 could disperse in aqueous solutions or human bodily fluids [5].

Researchers at the Chinese Academy of Sciences discovered the efficacy of fat-soluble C-60 in treating central nervous system diseases [37], suggesting its direct entry into the central nervous system [5] and subsequent anti-inflammatory effects [37]. French scientists conducted related research, wherein they orally administered C-60 oil to mice once a week, thereby almost doubling their lifespan [38]. Our previous research yielded notable findings: oral administration of fat-soluble C-60 oil significantly reduces the levels of the inflammatory marker C-reactive protein in the blood of beagle dogs [5], suggesting its entry into tissues and organs, thereby producing anti-inflammatory effects. C-reactive protein in the blood serves as a marker for cardiovascular and cerebrovascular inflammation and may promote such conditions [39]. These findings collectively suggest that oral administration of fat-soluble C-60 oil may offer therapeutic or preventive benefits for cardiovascular and cerebrovascular inflammatory diseases [5,39-41]. In summary, orally administered fat-soluble

C-60 enters tissues and cells in the body, thereby lowering the inflammatory marker C-reactive protein levels and treating inflammatory diseases in humans. It is expected to serve as a therapeutic agent for skin inflammation, colitis, cardiovascular and cerebrovascular inflammation, as well as central nervous system inflammation. C-60 demonstrates potential as a versatile anti-inflammatory drug for managing systemic inflammatory diseases.

References

- Demming A (2010) King of the elements? *Nanotechnology* 21(30): 300201.
- Kroto HW, Heath JR, O'Brien SC, Curl RE, Smalley (1985) C60: buckminsterfullerene. *Nature* 318: 162-163.
- F Diederich, R Ettl, Y Rubin, R L Whetten, R Beck, et al. (1991) The higher fullerenes: isolation and characterization of C76, C84, C90, C94, and C700, an oxide of D5h-C70. *Science* 252: 548-551.
- Palit DK, Sapre AV, Mittal JP, CNR Rao (1992) Photophysical properties of the fullerenes, C60 and C70. *Chem Phys Lett* 19195(1): 1-6.
- Hui M, Jia X, Li X, Lazcano Silveira R, Shi M (2023) Anti-Inflammatory and Antioxidant Effects of Liposoluble C60 at the Cellular, Molecular, and Whole-Animal Levels. *J Inflamm Res* 16: 83-93.
- Galvan YP, Alperovich I, Zolotukhin P, Evgenia Prazdnova, Maria Mazanko, et al. (2017) Fullerenes as anti-aging antioxidants. *Current Aging Sci* 10(1): 56-67.
- Mousavi SZ, Nafisi S, Maibach HI (2017) Fullerene nanoparticle in dermatological and cosmetic applications. *Nanomedicine*. 13(3): 1071-1087.
- Lens M (2009) Use of fullerenes in cosmetics. *Recent Pat Biotechnol* 3(2): 118-123.
- Mousavi SZ, Nafisi S, Maibach HI (2017) Fullerene nanoparticles in dermatological and cosmetic applications. *Nanomedicine* 13(3): 1071-1087.
- Shigeki Inui, Hisae Aoshima, Aki Nishiyama, Satoshi Itami (2017) Improvement of acne vulgaris by topical fullerene application: unique impact on skin care. *Nanomedicine* 7(2): 238-241.
- Inui S, Mori A, Ito M, Sayuri Hyodo, Satoshi Itami, et al. (2014) Reduction of conspicuous facial pores by topical fullerene: possible role in the suppression of PGE2 production in the skin. *J Nanobiotechnology* 12: 6.
- Shinya Kato, Risa Kikuchi, Hisae Aoshima, Yasukazu Saitoh, Nobuhiko Miwa (2010) Defensive effects of fullerene-C60/liposome complex against UVA-induced intracellular reactive oxygen species generation and cell death in human skin keratinocytes HaCaT, associated with intracellular uptake and extracellular excretion of fullerene-C60. *J Photochem Photobiol B* 98(2): 144-151.
- Kato S, Aoshima H, Saitoh Y, Nobuhiko Miwa (2010) Fullerene-C60/liposome complex: defensive effects against UVA-induced damages in skin structure, nucleus and collagen type I/IV fibrils, and the permeability into human skin tissue. *J Photochem Photobiol B* 98: 99-105.
- Gudkov SV, Guryev EL, Gapeyev AB, Mars G Sharapov, Nikolai F Bunkin, et al. (2019) Unmodified hydrated capital ES, Cyrillic 60 fullerene molecules exhibit antioxidant properties, prevent damage to DNA and proteins induced by reactive oxygen species and protect mice against injuries caused by radiation-induced oxidative stress. *Nanomedicine* 15(1): 37-46.
- Xinrong Li (2020) Noval application of C-60 and activity detection method thereof.

16. (2021) New application of C-60 and method for measuring activity of products thereof.
17. Shershakova N, Baraboshkina E, Andreev S, Daria Purgina, Irina Struchkova, et al. (2016) Anti-inflammatory effect of fullerene C60 in a mice model of atopic dermatitis. *J Nanobiotechnology* 14: 8.
18. Lazcano-Silveira R, Jia X, Liu K, Liu H, Li X, et al. (2022) Carbon 60 Dissolved in Grapeseed Oil Inhibits Dextran Sulfate-Induced Experimental Colitis. *J Inflamm Res* 15: 4185-4198.
19. Liao X, Zhao Z, Li H, Wu B, Huo J, et al. (2021) Fullerene nanoparticles for the treatment of ulcerative colitis. *Sci China Life Sci* 1: 54.
20. Application of rhamnolipid/fullerene compound in medicine for treating colitis and improving intestinal microbiota.
21. Preventive or therapeutic agent for inflammatory bowel disease.
22. Agent for preventing or treating ulcerative colitis and novel fullerene derivative.
23. Galvan YP, Alperovich I, Zolotukhin P, Evgenia Prazdnova, Maria Mazanko, et al. (2017) Fullerenes as anti-aging antioxidants. *Current Aging Sci* 10(1): 56-67.
24. Dellinger A, Zhou Z, Lenk R, Darren MacFarland, Christopher L Kepley, et al. (2009) Fullerene nanomaterials inhibit phorbol myristate acetate-induced inflammation. *Exp Dermatol* 18: 1079-1081.
25. Ryan JJ, Bateman HR, Stover A, Greg Gomez, Sarah K Norton, et al. (2007) Fullerene nanomaterials inhibit the allergic response. *J Immunol* 179(1): 665-672.
26. Saito E, Kuo R, Pearson RM, Nishant Gohel, Brandon Cheung, et al. (2019) Designing drug-free biodegradable nanoparticles to modulate inflammatory monocytes and neutrophils for ameliorating inflammation. *J Control Release* 300: 185-196.
27. Liu QH, Jin L, Mahon BH, Mahendra D Chordia, Francis H Shen, et al. (2013) Novel treatment of neuroinflammation against low back pain by soluble fullerol nanoparticles. *Spine* 38(17): 1443-1451.
28. Dellinger AL, Zhou ZG, Kepley CL (2014) A steroid-mimicking nanomaterial that mediates inhibition of human lung mast cell responses. *Nanomedicine* 10(6): 1185-1193.
29. Song MY, Liu SF, Yin JF (2011) Interaction of human serum album and C60 aggregates in solution. *Int J Mol Sci* 12(8): 4964-4974.
30. Fu XF, Fang YL, Zhao HL, S Liu (2018) Size-dependent binding of pristine fullerene (nC60) nanoparticles to bovine/human serum albumin. *J Mol Struct* 1166: 442-447.
31. Fromen CA, Kelley WJ, Fish MB, Rehemani Adili, Jeffery Noble, et al. (2017) Neutrophil-particle interactions in blood circulation drive particle clearance and alter neutrophil responses in acute inflammation. *ACS Nano* 11(11): 10797-10807.
32. Sastre J, Mannelli I, Reigada R (2017) Effects of fullerene on lipid bilayers displaying different liquid ordering: a coarse-grained molecular dynamics study. *Biochim Biophys Acta Gen Subj* 1861(11 Pt A): 2872-2882.
33. Ha Y, Katz LE, Liljestrand HM (2015) Distribution of fullerene nanoparticles between water and solid supported lipid membranes: thermodynamics and effects of membrane composition on distribution. *Environ Sci Technol* 49(24): 14546-14553.
34. Ikeda A, Kiguchi K, Shigematsu T, Nobusawa K, Kikuchi JI, et al. (2011) M. Location of [60] fullerene incorporation in lipid membranes. *Chem Commun* 47(44): 12095-12097.
35. Dellinger A, Zhou ZG, Norton SK, Lenk R, Conrad D, et al. (2016) Uptake and distribution of fullerenes in human mast cells. *Nanomedicine* 6(4): 575-582.
36. Russ KA, Elvati P, Parsonage TL, A Dews, JA Jarvis, et al. (2016) C60 fullerene localization and membrane interactions in RAW 264.7 immortalized mouse macrophages. *Nanoscale* 8(7): 4134-4144.
37. Li X, Deng R, Li J, Li H, Xu Z, et al. (2023) Oral [60] fullerene reduces neuroinflammation to alleviate Parkinson's disease via regulating gut microbiome. *Theranostics* 13(14): 4936-4951.
38. Baati T, Bourasset F, Gharbi N, Leila Njim, Manef Abderrabba, et al. (2012) The prolongation of the lifespan of rats by repeated oral administration of [60] fullerene. *Biomaterials* 33(19): 4936-4946.
39. Sproston NR, Ashworth JJ (2018) Role of C-Reactive Protein at Sites of Inflammation and Infection. *Front Immunol* 9: 754.
40. Rizo-Téllez SA, Sekheri M, Filep JG (2013) C-reactive protein: a target for therapy to reduce inflammation. *Front Immunol* 14: 1237729.
41. Luan YY, Yao YM (2018) The Clinical Significance and Potential Role of C-Reactive Protein in Chronic Inflammatory and Neurodegenerative Diseases. *Front Immunol* 9: 1302.

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