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Review Article

Fullerene nanoparticle in dermatological and cosmetic applications

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Abstract

Nanoparticles are equipped with exceptional properties which make them well suitable for diverse and novel applications. Fullerene is one of the nanomaterials that has valuable applications in the field of biomedicine. It possesses exceptional antioxidant capacity which has made it a promising core ingredient in many dermatological and skin care products. However, fullerene has the potentials to display a range of activities resulting in cell death or dysfunction. This review outlines the achievements made so far by reporting studies that have focused on incorporating fullerene in skin care products and cosmetics and assessed their beneficial effects. We have also documented reports that have assessed toxicity of this novel carbon allotrope toward skin cells and discussed its possible dermal reactions. Aside from pointing out the recent developments, areas that can benefit from further researches are identified.

Key words: Fullerene; Ultraviolet rays; Toxicity; Oxidative stress; Melanogenesis; Acne

From the introduction of the first FDA-approved nano-drug in 1995, nanomedicine has constantly revolutionized medical therapeutics and diagnostics. Manipulating molecules and atoms in the nanoscale has empowered researchers to come up with novel particles and formulations that possess more beneficiary characteristics and less unwanted features. Dermatological research and cosmetic industry has also benefited from this new path and have employed innovative nanomaterials including nanosomes, liposomes, fullerenes, and solid lipid nanoparticles, among many other nanomolecules, to improve quality of their products. With increasing amount of nanoparticles that are being used in commercial applications, concerns about their effects on human health and environmental safety are becoming more prominent and calls for close and rapid attention.

Fullerene is one of the nanomaterials that has valuable applications in the field of biomedicine. It possesses exceptional antioxidant capacity which has made it a great ingredient to be used in sunscreen, skin whitening and antiaging products. However, it seems that fullerene and its derivatives can display a range of activities that can cause cell death or dysfunction. This review takes a closer look at different aspects of fullerene and its usage in skin preparations and cosmetics. It also documents reports about the dermal toxicity of this novel carbon allotrope as well as dermal reactions. In addition to the recent developments, future directions and possible challenges in this field are outlined. It should also be noted that previous studies have assessed different types of fullerenes (which can affect their physicochemical properties and function) and different experimental methods. The authors have tried to include appropriate information when available, but in some cases, characterization of the materials, procedure or some other information was unclear or incomplete. Thus, care should be taken with drawing firm conclusions about fullerene, especially in categories with missing information.

Fullerene's history

Fullerenes are hollow clusters of carbon atoms with sp^2-hybridization. The first fullerene was discovered in 1985, while Kroto et al[1] were vaporizing graphite using Nd:YAG laser. A

Abbreviations: γ-CD/F, γ-cyclodextrin-fullerene; CF, carboxyfullerene; LpsmF, liposome fullerene; PEG-F, polyethylene glycol fullerene; PVP/F, polyvinylpyrrolidone fullerene; UV, ultraviolet; TEWL, transepidermal water loss.

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polygon structure with 60 vertices and 32 faces resembling a soccer ball was the structure they suggested that could best describe the stable configuration of this 60-carbon atom (Figure 1). Since then, numerous higher order fullerenes such as C70, 76, 84, 90, 94[2,3] or lower order fullerenes such as C28 and C36[4,5] have been discovered, all belonging to the same family of hollow cage carbon structure. Among them, fullerene C60 (pristine fullerene) has remained the most common and stable type.

Soon after C60 discovery, researchers began to assess its physical and chemical properties as well as its beneficial applications, but C60 production was limited and expensive. It was not until 1990 when a new method, known as the Krätschmer-Huffman, was introduced and allowed fullerene mass production.[6] Subsequently, fullerene found its way in the chemical and material science applications, such as electromechanical amplifier, semiconductors, polymers, etc.[7–10] However, understanding fullerene's biological characteristics and suggesting novelty biomedical applications for it needed more effort, because pristine fullerene was not readily water soluble and further chemical modifications were required to increase its availability for living systems. Today, many ways of adjusting fullerene structure are known which can be classified within two major categories: a) those in which the structure of the fullerene remains the same; these include: encapsulation, and formation of suspension (either by long term stirring, solvent exchange, or a biologic solubilizer); and b) those which chemically modify the fullerene structure by adding covalent attachment of solubilizing appendages to form functionalized fullerene, such as adding amino acids, steroids, hydroxyl groups, carboxyl groups, etc.[11–21] These modifications helped researchers explore biological applications of fullerene which is an interesting chapter in fullerene's history.

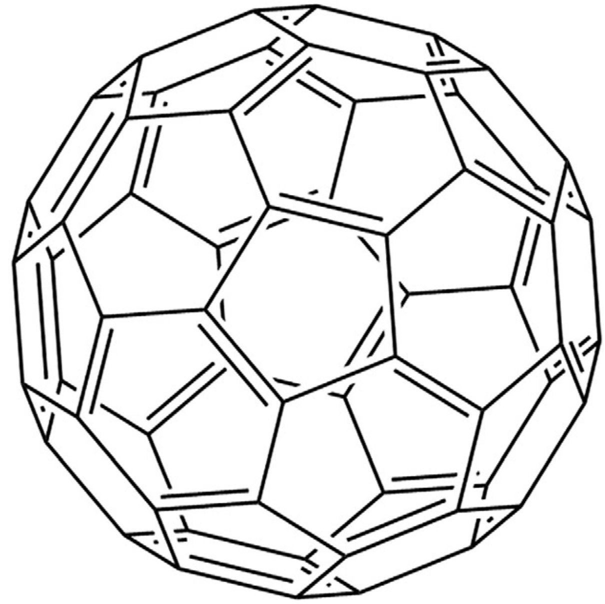

Figure 1. Soccer ball shape of fullerene.

Fullerene's biomedical applications

Fullerene is a nanomaterial with promising applications in the field of biomedicine. The first biological applications of fullerene were reported in 1993, when researchers found its photo-induced cytotoxicity as well as photo-induced DNA cleavage activity,[22] along with antiviral properties against HIV-1 in acutely and chronically infected cells[23]; this effect was inserted through inhibition of the HIV protease,[19,23,24] and reverse transcriptase.[19,23] Subsequent studies followed this curiosity-driven path and revealed its notable biological activities. Important properties that have brought appraisal for fullerene are its small size, electron transfer and antioxidant abilities, photoactivity, hydrophobicity and high reactivity which allows structural modifications.[25,26] These characteristics made fullerene a good candidate for therapeutic and diagnostic applications.[27]

An important fullerene characteristic is efficient free radical scavenging activities due to its redox properties, for which it was called "radical sponge" by Krusic et al[14] In 1997, Dugan et al used antioxidant properties of fullerene derivatives in biological systems and proposed carboxyfullerene as a neuroprotective agent.[28] Since oxidative stress plays an important role in many pathological conditions such as cancers, neurodegenerative disorders (like Parkinson's, Alzheimer's, and multiple sclerosis), diabetes mellitus, rheumatoid arthritis, atherosclerosis and hypertension, as well as physiological processes such as aging,[29–31] employing fullerene as a novel treatment has become a topic of considerable interest among researchers.[21,26,32,33]

Fullerene has also been studied as targeted therapeutic agent in osteoporosis[34] and cancer.[35] Other researchers have assessed fullerene as an anti-inflammatory, antiviral, or antibacterial agent, proposed it as a carrier for drug and gene delivery, and assessed its role in the field of diagnostic and medical imaging.[27,36–38] Fullerene has also been suggested as an important ingredient in dermatologic and cosmetic products,[39,40] which is further discussed in this paper.

Fullerene, skin care and cosmetics

Throughout history, topical drugs and formulations have been among the most common routes of medicine delivery. Early records of Egyptians and Babylonians provide recipes of ointments and creams used for beautification and treatment of ailments.[41] Since then, many other nations have also used topical preparations; but it was only during the past century when new scientific basis was formed for it. From the first understanding of the role of formulation base in efficacy of a preparation in 1940-50s, to introduction of transdermal drug delivery in 1970s and new age of nanodermatology, the science behind topical preparation has constantly been revolutionized.[42] Today, we are aware of the challenges in developing topical formulations, such as interaction of the drugs and vehicles with the skin, rate of compound release, and skin absorption and toxicity of both drug and excipient. Therefore, many researchers focus on improving current formulations and try to come up with novel ideas to overcome these challenges.[43]