

## The Application of Fullerene Materials in Neurological Diseases and Disorders

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### Abstract

Fullerene materials are composed of carbon atoms and compatible with biological systems in humans and animals. They have been investigated for applications in humans for nearly fifty years. Fullerene materials reduce free radicals in cells, provide anti-inflammatory effects, and inhibit tumor growth. However, the primary antioxidant benefit of fullerene materials might be the activation of nuclear factor (erythroid-derived 2) factor 2 (Nrf2). Fullerenol nanoparticles reduce the sequelae of brain injuries caused by ischemia. Fullerene materials delay the functional deterioration of neurons and reduce the symptoms and prevalence of diabetic neuropathy. Due to their mechanical and electrical properties, nanocarbon materials stimulate cells and neurons and have been used as frameworks in neuron stem growth and neuronal development. Fullerene materials can be used for the prevention or treatment of specific neurological disorders due to their complementary effects, biocompatibility, and low toxicity in humans. Nevertheless, fullerene materials' safety, manufacture, and dosage should be further evaluated and established for their therapeutic use in humans.

**Keywords:** Allotrope; Diabetic Neuropathy; Free Radical; Fullerene; Stroke

### Abbreviations

AMPA: Alpha-Amino-3-Hydroxy-5-Methyl-4-Isioxazole Propionic Acid; AQP-1: Aquaporin-1; MCAO: Middle Cerebral Artery Occlusion; mDA: Midbrain Dopaminergic; NMDA: N-Methyl-D-Aspartate; Nrf2: Nuclear Factor (Erythroid-Derived 2) Factor 2

### Introduction

Nanocarbon fullerene materials have various physical structures and features; however, their chemical properties are similar. These qualities have led to diverse applications in many fields, such as medicine, veterinary medicine, and application [1–3]. Carbon allotropes and nanotechnology materials, such as nanoparticles, nanotubes, graphene, and fullerene, have been widely applied in research [4–7] and specific neurological diseases and disorders. Due to their biocompatibility and minimum interference with metabolic processes in humans, fullerene materials can be used to diagnose and treat specific neurological disorders, including diabetic neuropathy, cerebral infarction, stroke, post-traumatic conditions, and ischemia [8,9].

### Discussion

Most neurological diseases and disorders have adverse effects on metabolic and biological processes in the human body. The application of fullerene materials promotes enhanced health outcomes: carbon nanotubes and nanocarbon fullerenes have diverse applications in the prevention and treatment of neurological diseases and disorders. Nanocarbon fullerenes have been adopted for laboratory and academic research to assess their beneficial effects in humans, animals, and plants [10].

Fullerenol nanoparticles significantly reduce the sequelae of brain injuries induced by ischemia. These fullerene materials inhibit the post-traumatic processes involved [11]. Through inhibition of aquaporin-1 (AQP-1) and oxidative damage, these fullerene materials reduce the edema caused by brain injuries. Steady administration of fullerenol slows the infarction process in the striatum and cortex by more than 70% before middle cerebral artery occlusion (MCAO) occurs [12]. Fullerenol inhibits infarction without altering normal and healthy cellular metabolic processes. Experimentally, fullerenols minimize the actions of nitrates and midbrain dopaminergic (mDA) neurons in rats with ischemia, which leads to a reduction of brain edema in the rodents.

Carboxylated fullerenes are compatible with the body's cells, tissues, and organs, act as neuroprotective agents, and demonstrate free radical scavenging properties [13–15]. However, the primary antioxidant benefit of fullerene materials might be the activation of nuclear factor (erythroid-derived 2) factor 2 (Nrf2) [16,17]. Various fullerene materials readjust reactions at the cellular level that otherwise might lead to the deterioration of nerve endings. Carboxylic acid fullerene prevents the death of cortical neurons when exposed to alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) or N-methyl-D-aspartate (NMDA) molecules [8]. The carboxylated fullerenes, which are polar in their chemical structure, inhibit processes that limit the survival of neurons. Fullerene materials delay the functional deterioration of neurons and toxicity, especially in the presence of specific molecules, such as the abeta1-42 protein [9].

Specific variegated fullerene materials have been shown to reduce the prevalence of diabetic neuropathy or stroke, using rat models. The free radical scavenging action of fullerene materials contributes to the protection of neuron receptors and associated disorders. However, to date, fullerene materials' effect on neuron endings (nerve terminals) has not been adequately explained in research studies.

Fullerene materials are used as frameworks in neuron stem growth processes and neuronal development. Due to their mechanical and electrical properties, these nanocarbon materials stimulate cells and neurons [18]. Fullerene materials help transmit electrical signals around cells and dynamize electrical conductivity. Neuronal electrical conductivity must be assessed to curtail neurological disorders in humans [19]. Nanocarbon tubes can redress electrical interference and neuronal reactions, reducing the prevalence of infections [20]. When applied in neurological diseases or disorders, specific fullerene materials appear biocompatible with no apparent toxicity; healthy cellular activities are maintained in their presence [21,22].

In some case, the symptoms of diabetic neuropathy are reduced by magnesium-25, carrying porphyrin-fullerene nanoparticles. Although this neurological condition currently does not have a viable and universal treatment, nanoparticles protect neurons over time. Diabetic neuropathy can lead to mitochondrial dysfunction and oxidative stress, which pose a danger to the survival of neurons in the human body [23,24]. Specific nanoparticles can be introduced into the body to control neuropathy as these materials demonstrate high biocompatibility and low toxicity. In particular, Mg-PMC16 magnesium nanoparticles have demonstrated antioxidant effects in body cells and neurons, promoting neurological health. The nanoparticles present in the magnesium isotope trigger oxidative and substrate phosphorylation pathways that help maintain neurological mechanisms and improve the functionality of neurons [25].

Also, nanoparticles stimulate the production of energy in cells that lack oxygen. They exhibit antioxidant properties and low toxicity [10,13–15,21,22]. Over time, as the fullerene of the magnesium allotrope accumulates on neuronal mitochondria, oxidative stress is reduced [26,27]. Although such materials are relatively expensive, the presence of fullerene molecules in the body reduces the symptoms of diabetic neuropathy due to their antioxidant and antiapoptotic properties [26].

## Conclusion

Fullerene materials can be beneficially applied in specific neurological diseases and disorders. They demonstrate high biocompatibility and low toxicity in the presence of human cells and tissues. They exhibit free radical scavenging actions, regulate oxidative stress, and activate Nrf2. Fullerene materials are applied in the diagnosis and treatment of various neurological conditions. They protect the nerves,

which reduces the prevalence of neurological diseases and disorders in humans. Fullerenol nanoparticles limit the sequelae of brain injuries and edema; carboxy fullerenes protect the nerve cells. Also, neural stem growth is promoted by the use of fullerene materials in the body. Finally, diabetic neuropathy is significantly reduced by magnesium-25 carrying porphyrin-fullerene nanoparticles, which control oxidation in the mitochondria.

The future seems promising for the application of fullerene materials in specific neurological diseases and disorders. However, the outcomes in the manufacturing process of experimental-grade and pharmaceutical-grade 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. Also, their dosage, timing, and duration should be further evaluated and established for therapeutic use in specific conditions by evidence-based research [1].

### 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, as a mini-review, is designed as a brief introduction to fullerene materials, regarding their application in neurological diseases and disorders. Other articles by the same authors have been published on the application of NOLFs and fullerene materials in the human respiratory system cardiovascular system, gastrointestinal system, veterinary medicine, agriculture, pharmacology and toxicology, and further topics. These distinct mini-review articles could have been merged 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 NOLFs to the broadest audience of students, researchers, and medical practitioners as possible. The authors hope that the introduction to NOLFs' application in various and diverse disciplines spawns curiosity and further research regarding NOLFs and fullerene materials. Fullerene materials seem poised to become a vital part of the future of medicine, veterinary medicine, and agriculture. However, more research is needed to determine any adverse effects of their long-term use. Also, the NOLF 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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