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REVIEW ARTICLE

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Deeper insight into ferroptosis: association with Alzheimer's, Parkinson's disease, and brain tumors and their possible treatment by nanomaterials induced ferroptosis

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ABSTRACT

Ferroptosis is an emerging and novel type of iron-dependent programmed cell death which is mainly caused by the excessive deposition of free intracellular iron in the brain cells. This deposited free iron exerts a ferroptosis pathway, resulting in lipid peroxidation (LiPr). There are mainly three ferroptosis pathways viz. iron metabolism-mediated cysteine/glutamate, and LiPr-mediated. Iron is required by the brain as a redox metal for several physiological activities. Due to the iron homeostasis balance disruption, the brain gets adversely affected which further causes neurodegenerative diseases (NDDs) like Parkinson's and Alzheimer's disease, strokes, and brain tumors like glioblastoma (GBS), and glioma. Nanotechnology has played an important role in the prevention and treatment of these NDDs. A synergistic effect of nanomaterials and ferroptosis could prove to be an effective and efficient approach in the field of nanomedicine. In the current review, the authors have highlighted all the latest research in the field of ferroptosis, specifically emphasizing on the role of major molecular key players and various mechanisms involved in the ferroptosis pathway. Moreover, here the authors have also addressed the correlation of ferroptosis with the pathophysiology of NDDs and theragnostic effect of ferroptosis and nanomaterials for the prevention and treatment of NDDs.

KEYWORDS

Ferroptosis; neurodegenerative; Parkinson's disorder; glioblastoma; glutathione

1. Introduction

Annually, on a global level, an escalating trend of people affected by Neuro Degenerative Disorders (NDDs) [1]. NDDs are diseases related to neurons and neural circuits. NDDs include Alzheimer's disease (AD) and Parkinson's disorder (PD), glioblastoma (GBS), ischemia stroke (IS), and multiple sclerosis (MS) [2,3]. NDDs are always involved with the wasting of the cortex and hippocampus which causes abnormality in feeling and movement [4]. Currently, there is a huge gap in understanding and implementing a comprehensive treatment of such NDDs due to the blood–brain barrier (BBB) and less anatomical brain study [5]. To date, several investigations have shown the significant positive effect of conventional drugs on such NDDs [6] for instance Esposito and their group suspended the bromocriptine crystals with a combination of lipid tristearin/tricaprin and coated them with poloxamer-188 [7]. Further, the investigator obtained improved results with the nanosized bromocriptine for the treatment of PDs. In another study, in order to treat amyotrophic lateral sclerosis hydralazine was loaded on the mesoporous silica (SiO_2) nanoparticles (NPs), and polyethylene glycol (PEG) was used to coat them. The combination of both the above-mentioned materials ameliorated the damage caused to both cell membranes and mitochondria. This process was induced by exposure to a normally lethal amount of acrolein in vitro [8]. For the treatment of MS, a group of investigators led by Basso formulated a nanosized fullerene derivative (water-soluble) (ABS 75) whose functionalization was carried out with an N-Methyl-D-aspartate receptor (NMDAR) antagonist [9]. From all the above investigations, it was found that there were two major drawbacks of conventional therapeutic

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This article has been corrected with minor changes. These changes do not impact the academic content of the article.