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A Survey of Innovations in the Diagnosis and Treatment of Multiple Sclerosis Nanoscale

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Abstract

Multiple Sclerosis (MS) is a multifactorial disease with several physiologic and pathogenic mechanisms and pathways. In MS the immune system attacks the myelin sheath that provides insulation to the nerve cells in their brain, spinal cord and optic nerve. With the damaged and compromised nerve membrane, the nerve cells are not able to conduct electrical signals properly, resulting in limb numbness, paralysis, blindness and other neurological disorders [1-15]. The main purpose of this paper is to highlight advancements in nanotechnology that has enabled the clinician to cross blood brain barrier and to target the brain and CNS of the patient with multiple sclerosis. We have focused on application of nanotechnology having therapeutic and imaging components to improve tissue imaging, targeted interactions at molecular level, nerve protection and regeneration therapy. We have also discussed the pathophysiology of the disease and nanotechnology based new strategies to deliver the therapeutic candidates for the diagnosis and treatment of MS. Future advances in the development of new practical treatment modalities for the treatment of MS is currently a potential area of research.

Introduction

MS is a complex disease with a variety of physiologic and pathologic processes and pathways. The immune system targets the myelin sheath that protects nerve cells in the brain, spinal cord, and optic nerve in MS patients. The nerve cells are unable to conduct electrical signals adequately due to the damaged and impaired nerve membrane, resulting in limb numbness, paralysis, blindness, and other neurological diseases. The primary goal of this paper is to highlight recent advances in nanotechnology that have allowed clinicians to overcome the blood-brain barrier and target the brain and CNS of multiple sclerosis patients.

We've concentrated on using nanotechnology with therapeutic and imaging components to improve tissue imaging, molecular targeting, nerve protection, and regeneration therapy. We also talked about the disease's pathophysiology and innovative nanotechnology-based ways for delivering therapeutic possibilities for MS diagnostics and treatment. Future advancements in the creation of novel practical therapy techniques for the treatment of MS are now being investigated.

Multiple sclerosis (MS) is also known as encephalomyelitis and disseminated sclerosis. It's an autoimmune and inflammatory disease in which the body's immune cells assault the nervous system, producing demyelization and the destruction of myelinated axons in the CNS, resulting in slowed nerve signals. The diagnosis of disease is made based on the patient's clinical symptoms as well as supportive data from MRI of the brain and cerebrospinal fluid investigation. Multiple sclerosis (MS) is also known as encephalomyelitis and disseminated sclerosis. It's an autoimmune and inflammatory disease in which the body's immune cells assault the nervous system, producing demyelization and the destruction of myelinated axons in the CNS, resulting in slowed nerve signals. The diagnosis of disease is made based on the patient's clinical symptoms as well as supportive data from MRI of the brain and cerebrospinal fluid investigation.

everal diagnostic methods are currently used for brain characterization, neuronal development and maturation ranging from a single neuronal observation at the intracellular level, to synchronic monitoring the activity of millions of neurons collectively. *In vivo* neuroimaging is a powerful technique and is used for observing biochemical, structural and functional changes within the brain. Advancements in the ability of CNS imaging at higher resolutions have illustrated several functional components behind.

Subjective Heading

The MS patients are grouped into four major categories based on the course and progression of the disease Relapsing–remitting MS (RRMS): It is the most common form of MS, which affects about 85% of MS patients. It is defined by attacks of new neurological symptoms of relapses or exacerbations and followed by periods of partial or complete remission.

Axonal damage in MS has been associated with inflammatory CNS injury. Antibody directed at amyloidal precursor protein show damaged axons in active areas of MS lesions. The active areas with MS lesions contain more transected axons compared to inactive areas in more chronic lesions. $CD8^+$ T lymphocytes can cause axonal damage via the release of cytotoxic granules, induction of apoptosis through activation of surface receptors, release of cytokines or direct transaction of axons.

Discussion

The present review will briefly give an overview of how nanotechnologies can be utilized to improve quality of life in MS patients. This paper principally focuses on the nano scale approaches which has a successful implementation in other CNS disorders like Alzheimer's disease, parkinsonism, amyotrophic lateral sclerosis etc and shows a significant potential in treatment and management of

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MS too There are various types of colloidal nano forms with successful surface modification strategies which can be used in molecular detection, targeted drug delivery, fabrication of implants and therapeutic monitoring, disease diagnosis in various neurodegenerative diseases The success of nanotechnology based approaches in diagnosis and treatment of MS is reviewed in this paper, it demonstrates the role of interdisciplinary nano science research for the early diagnosis along with possible cure and management of MS pathophysiology

Clinical disability in MS is mainly due to the destruction of the CNS myelin protein. Currently there are no biomarkers available for MS diagnosis (other than oligoclonal IgG, which helps in diagnosis of disease but requires an invasive procedure and its correlation with disease activity and response to therapy is not clear). The monitoring, diagnosis and treatment of MS is mainly governed with the help of magnetic resonance imaging (MRI) which is an expensive technique.

Nanomaterials have a wide range of application in diagnosis, treatment and management of disease as these materials are biocompatible and have ability to form biophysicochemical interaction with cells, cell membranes, proteins, D.N.A. and other organelles at nano-biointerface to assist for diagnosis and treatment of disease at cellular and molecular level There are several different types of nanostructures these include polymeric nanoparticles, nanocapsules, nanospheres, nanogels, nanosuspensions, nanomicelles, nanoliposomes, carbon nanotubes and nanofibers. The challenge for modern therapy is to identify mechanisms behind brain function, from gene expression to physiological changes, and to determine their role in the etiology and progression of CNS diseases

The main cause of harm in MS is inflammation of the central nervous system (CNS). MS is characterised by plaques of demyelinated nerve cells in the CNS. Incorporation of genetic variables, environmental factors, and infectious organisms can all influence the development of MS, according to studies, yet the fundamental factor causing inflammation remains unknown. The experimental autoimmune encephalomyelitis (EAE) animal model has been widely employed in immunological research to investigate the roles of multiple immune pathways involved in MS. MS patients' brains and spinal cords have been found to have abnormally high levels of iron and other redox elements.

Innate and adaptive immune responses are two forms of immune responses that both play a role in the course of this neurological condition. Microbial compounds trigger the innate immune response by activating particular toll-like receptors (TLR) in an antigen-agnostic way. The binding of these antigenic molecules to TLR causes an increase in the generation of cytokines, which modulates the adaptive immune response further. The innate system controls T and B cell effector function and has a role in illness start and progression. Dendritic cells begin to polarise CD4+ T cells to develop into Th1 as they mature. When T cells convert into a Th1 phenotype from Th2 or Th17 phenotypes, inflammation is encouraged The presence of lymphocytic cells within plaques and other surrounding areas shows that antigen-specific targeting of myelin protein and other CNS components is the primary mode of inflammatory destruction in MS. With the help of stronger contrast and better focused molecular imaging probes, nanotechnology-based systems are employed to improve neuroimaging power. It can also be integrated into modern biosensor systems within the brain to investigate circuit physiology principles. Current approaches for detecting debilitating CNS illnesses can be considerably improved by utilising the unique and better physical, chemical, and biological features of nanomaterials, and new insights into brain physiology can be exploited to generate novel therapy strategies.

Nanotechnology based systems is used for enhancing neuroimaging power with the help of higher contrast and better targeted molecular imaging probes. Additionally, it can be implemented into an advanced biosensor systems within the brain for probing the principles of circuit physiology. By exploiting the unique and improved physical, chemical, and biological properties of nanomaterial's, current methods for diagnosing debilitating CNS disorders can be significantly enhanced, and new insights into brain physiology can be applied to develop novel therapeutic strategies

In the last few decades various advances have been made in the field of drug delivery systems against . Various drugs have been approved for the management and treatment of the disease, but there is a vital need of advanced drug delivery system to deliver the drugs in the immediate environs of the required target site. Various colloidal DDSs such as liposomes, emulsomes, and solid lipid nanoparticles etc. have solved this problem to a great extent. The site-specific targeting of drug molecules could present a multitude of clinically viable strategies, which may provide in great appreciation the treatment and management of disease. Colloidal drug delivery systems that are used for the treatment of disease with fewer side effects and in a cost effective manner will have definite advantages. Advancement in nano diagnostic neuro imaging proved to have a significant potential for brain visualization. The ability to track the progression of disease at cellular and molecular level has considerable benefit in monitoring the progression of disease.

Over the next decade, nanotechnology will continue to play a vital role in diagnosis and treatment of neurological disorders. It will help in development of highly specific and sensitive biosensors and imaging probes By accelerating the growth and application of innovative nanotechnology to find the solutions for neuroimaging and electrophysiology researchers can find a full construct of brain development and physiological functions for the effective treatment of CNS disorders.

There are still several challenges that must be overcome to explore the application of nanotechnology in neuroscience. Proper care must be taken to understand and avoid the potential hazards by investigating the safety and biocompatibility of nano materials. The next decade will present a wide scope for delivering and developing pure transformed technologies.

Pomegranate seed oil was supplied in the form of micro droplet formulation in an animal study and showed promising results in multiple sclerosis and autoimmune encephalitis The use of carbon nanowires and nanotubes in neuronal repair and regeneration is currently being investigated. They have an effect on cellular signal transmission, and have shown promise in improving cerebrovascular dysfunction following brain tumours, diagnosing and treating brain disorders, and enhancing neuronal cell function inside brain tissues. The two general types of immune response are the innate and adaptive immune responses and both play a major role in progression of this neurological disease. The innate immune response is mainly initiated by microbial products which activate specific toll-like receptors (TLR) in an antigen nonspecific manner. Binding of these antigenic molecules to TLR increases the production of cytokines which further modulate the adaptive immune response. The innate system influences the effector function of T and B cells and plays a role in initiation and progression of disease. On maturation dendritic cells begin to polarize $CD4^+$ T cells to differentiate into Th1, Th2 phenotypes or Th17 phenotypes and when T cells differentiate into a Th1 phenotype, inflammation is promoted The

presence of lymphocytic cells within plaques and other bordering areas suggests that inflammatory destruction in MS is mainly by antigen specific targeting of myelin protein and other CNS components.

Lymphocytic presentation of specific antigen by antigen presenting cells (APCs) to T lymphocytes initiates adaptive response. T cells from MS patients can recognize a variety of myelin protein The adaptive immune responses by T lymphocytes are considered to mediate injury to myelin sheath and nerves within the CNS during progression of MS. The relevance of antigen specific CD4 T cell responses in MS was also reflected with the results of trials using an altered peptide ligand of MBP (myelin basic protein) designed for therapeutic suppression of CD4 T cell responses, which exacerbate the disease in MS. These antigen presenting cells could be B cells, dendritic cells, microgla or macrophages. Several types of T cells like $CD4^+$ and $CD8^+$ phenotype are activated by APCs Study of family and twin has shown that genetic factors also influence MS pathogenesis susceptibility among first degree relatives of MS patients

The present invention disclosed a composition for the treatment of MS which comprises of a first myelin basic protein (MBP) peptide linked to a vector. Compositions of immune dominant peptides of myelin basic protein are finally encapsulated in mannosylated liposomes. This invention is based on the discovery that some MBP peptides act as major B cell epitopes in patients suffering from MS. It was found that the administration of liposomal formulations comprising of these peptides, to rodent models of MS resulted in improved delivery of these peptides to immune cells thus statistically significant reduction in paralysis

Conclusion

Various developments in the field of MS medication delivery systems have been developed throughout the previous few decades. Although various medications have been approved for the management and treatment of the condition, an enhanced drug delivery system is necessary to deliver the drugs in the local vicinity of the required target site. This challenge has been partially handled by colloidal DDSs such as liposomes, emulsomes, and solid lipid nanoparticles. Clinical disability in MS is mainly due to the destruction of the CNS myelin protein. Currently there are no biomarkers available for MS diagnosis (other than oligoclonal IgG, which helps in diagnosis of disease but requires an invasive procedure and its correlation with disease activity and response to therapy is not clear). The monitoring, diagnosis and treatment of MS is mainly governed with the help of magnetic resonance imaging (MRI) which is an expensive technique. Nanomaterials have a wide range of application in diagnosis, treatment and management of disease as these materials are biocompatible and have ability to form biophysicochemical interaction with cells, cell membranes, proteins, D.N.A. and other organelles at nano-biointerface to assist for diagnosis and treatment of disease at cellular and molecular level. There are several different types of nanostructures these include polymeric nanoparticles, nanocapsules, nanospheres, nanogels, nanosuspensions, nanomicelles, nanoliposomes, carbon nanotubes and nanofibers. The challenge for modern therapy is to identify mechanisms behind brain function, from gene expression to physiological changes, and to determine their role in the etiology and progression of CNS diseases.

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Conflict of Interest

The authors declare that they are no conflict of interest**.**

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