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Review Article

A systematic review on application of nano-carriers loaded with drug in the treatment of neurological disorders

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ABSTRACT

The central nervous system disorders represent a worldwide public health problem. Neuro-degeneration is associated with many transitions in brain including synaptic disorder and neuro-cognition decline. It is shielded by a barrier which controls the entry of compounds into the brain known as blood brain barrier (BBB), there by regulating brain homeostasis. In achieving a therapeutic amount of drug to the proper site of action in the body and then maintaining the desired amount of drug concentration for a sufficient time interval to be clinically effective for treatment. Particularly, neurodegenerative diseases such as Parkinson's disease (PD) and Alzheimer's disease (AD) are becoming further established in the elderly inhabitants of the society. These ailments usually encompass advanced degeneration & neuronal loss, rendering these disorders spread and difficult to treat. There are various types of pharmaceutical approaches to treat the neurological disorders. The drug loaded Nano-carriers are one of them. In this review, we will address the different applications of drug loaded Nano-carriers in the treatment of various neurological disorders. The Nano-carriers developed to enhance drug delivery across the BBB include micelles, exosomes, liposomes, nanotubes, nanoparticle, Nano emulsions, dendrimers, Nano gels, and quantum dots, etc. The recent developments in Nano-carriers' implementation through size/charge optimization and surface modifications like PE Gylation, targeting delivery, and coating with surfactants have been discussed, and a detailed description of the Nano-scaled pharmaceutical delivery devices employed for the treatment of central nervous system disorders has also been defined. This review provides a brief overview of the variety of carriers employed for central nervous system drug and diagnostic probes delivery.

1. Introduction

A central nervous system (CNS) problem may be present in up to 1.5 billion people worldwide at any given moment, according to estimates.[1] Researchers are still trying to solve the puzzle of what causes neurodegenerative illness. These problems are widespread and challenging to treat because neurodegenerative diseases like Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS)[2] typically involve gradual degeneration and neuronal death. Because nano-carriers have the potential to enhance the therapeutic efficacy of medications and lessen their negative effects, they are ideal instruments for delivering treatments and/or diagnostic probes to the brain. A central nervous system (CNS) disorder is estimated to be present in 1.5 billion persons worldwide at any given time.[1] Investigations are being made to learn the cause of neurodegenerative disease. Examples of neurodegenerative diseases include Alzheimer's disease (AD), Parkinson's

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disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS).[2] These conditions are common and difficult to treat because they typically involve gradual neuronal death and degeneration. These technologies are useful for delivering pharmaceuticals and/or diagnostic probes to the brain since nano-carriers can improve the therapeutic efficacy of medications and reduce their side effects.[3]

The central nervous system (CNS), which is made up of the brain and spinal cord and is regarded as the body's central processing station, is one of two major systems that make up the nervous system (NS), which is a complex that is in charge of establishing the body's fundamental functions as well as regulating and coordinating its activities. The second is known as the peripheral nervous system (PNS), which consists of all other neural components and is responsible for sending sensory data from the rest of the body to the brain via the muscles, tissues, and nerves. The phrase "neurological condition" is used to describe a CNS disease that results from physical damage to the brain or nerves, or, to put it another way, affects the central or peripheral nervous system.[4] Blood-brain barrier (BBB) protects the central nervous system, one of the most fragile micro environments in the body, and controls its homeostasis.[5] Because they are dangerous, expensive, and inappropriate for treating less localised brain illnesses, brain medication delivery techniques are not commonly employed.[6] Under normal circumstances, the blood-to-brain delivery technique that involves increasing BBB permeability of medications or drug-carrier conjugates can decrease the aforementioned negative effects.[7,8] In this review paper, we cover the many types of nanomaterials for blood-to-brain drug administration through the intact BBB, the processes of nanomaterials-mediated drug transport across the BBB, and the future directions of this ground-breaking field of study.

Only low molecular weight (400–500 Da) and small lipophilic molecules can enter the brain with several folds more competence than large molecules because the passage of molecules via BBB depends on their structure, surface characteristics, and chemical makeup.[9] In neurodegenerative illnesses, the structure and function of the BBB can change, but the barrier function of the BBB is still typically stable during treatment.[10,11] The cationic vehicle crosses the BBB via absorption-mediated transcytosis, making it of utmost importance to research various vehicles that can improve the BBB transportability of therapeutic medications to target area. Liposomes, nanoparticles, nanomicelles, and exosomes are a few types of frequently utilised nano-carriers. The bioavailability, stability, and peripheral toxicity of medicines may all be improved by utilising nano-carriers for drug delivery.[12] The ability to comprehend, work with, and regulate matter at the atomic and molecular level is what nanotechnology symbolizes.[13] Consequently, the use of nanotechnology to the creation of non-invasive drug delivery methods may result in the development of new and enhanced formulations to facilitate the transport of therapeutic substances across the blood-brain barrier. The investigation of drug delivery systems based on nanotechnology, such as nanoparticles, liposomes, dendrimers, carbon nanotubes, and micelles, has received a lot of attention in recent years. These systems may be able to deliver the required dose of a drug to the brain.[14–16]

1.1. Barriers to drug delivery for the CNS-Disease

Being able to pass the blood-brain barrier is what determines a drug's CNS permeability (BBB). Of all the organs in living things, the brain is one of the most complicated and vital. Therefore, it is essential to safeguard it from contaminating substances from the environment and foreign substances that could alter the concentrations of neuronal cells on the inside and outside of the body, which would then impair nerve conduction and cause problems with the body's regulatory systems.[17] Systemic drug distribution is challenging since the brain is a particularly protected organ and lives within the bony constraints of the skull. Blood brain barrier, blood cerebrospinal fluid barrier, choroids plexus barrier, and arachnoids layer of the meanings are the three interfaces where barriers are established (blood–arachnoids layer)[18,19] (Figure 1).

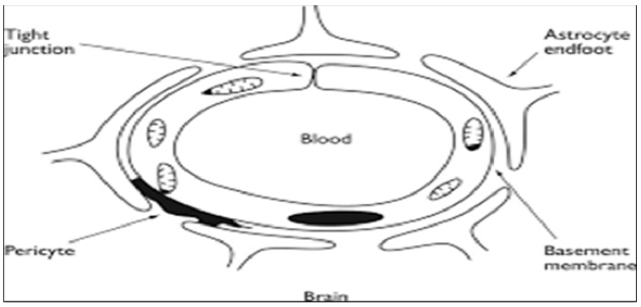

Fig. 1: Schematic diagram of blood brain barrier.

The blood-brain barrier, which serves as a local entry point against circulating poisons and cells through a mechanism of selective permeability, is what keeps the brain safe. As one of the functional units of the BBB that maintains the homeostasis of the brain micro environment, brain capillary endothelial cells (BMEC), astrocytes, pericytes, neurons, and the basal lamina make up the neurovascular unit.[20] Small particles known as nano-carriers are used to deliver pharmaceutical active ingredients under controlled conditions. These active ingredients are encapsulated inside the aforementioned nano-carriers and adsorbed or conjugated onto their surfaces.[21]

2. Nanoparticle for Drug Delivery to the Brain

The Blood Brain Barrier (BBB) is a physical barrier that separates the blood from the brain, and medication molecules are transported over it utilising nanoparticles. These medications penetrate the BBB and carry medications to the brain for the therapeutic treatment of neurological illnesses. Parkinson's disease, Alzheimer's disease, schizophrenia, depression, and brain tumours are some of these conditions. The fact that there is currently no truly effective way for medications to penetrate the BBB contributes to the difficulties of treating certain central nervous system (CNS) illnesses. However, studies have shown that some drugs can now cross the BBB, and some even exhibit low toxicity and reduce adverse effects throughout the body. Examples of molecules that cannot pass the BBB alone[22] include antibiotics, anti-neoplastic agents, and a variety of CNS-active drugs, especially neuropeptides. Because high toxicity levels in the body could injure the patient by affecting other organs and impairing their function, toxicity is a key concept in pharmacology.[23] Additionally, the BBB serves as more than just a barrier to drug delivery to the brain. Other biological elements influence how medications enter the body and how they find their target tissues. There are numerous barriers that make creating a reliable delivery system challenging, but nanoparticles offer a promising mechanism for drug transport to the CNS. Some of these pathophysiological factors include blood flow changes, edoema and elevated intracranial pressure, metabolic perturbations, and altered gene expression and protein synthesis.[24]

Small, enclosed particles known as nano-carriers are employed for the regulated distribution of pharmacological substances that have been adsorbed or conjugated onto the surfaces of the aforementioned nano-carriers.[25] Several substances can be utilised as nano-carriers, including carbon nanotubes, liposomes, micelles, polymeric and lipid-based nanoparticles, dendrimers, and micelles.[26] Human body cells typically range in size from 10 to 20 micrometres, hence it is conceivable for cells to adsorb or absorb nano-sized drug-carrier conjugates, opening up the possibility of drug delivery into cells. Nano-carriers have the ability to transport pharmaceuticals via carbon nanotubes and the BBB because they can have their surfaces functionalized with targeted ligands. (Figure 2).

3. Liposomes: Classic Dosage form to Penetrate BBB

Unilamellar or multilamellar phospholipid bilayers envelope an aqueous inner core in nanoscale vesicles known as liposomes. The systemic administration of medications using liposomes has been extensively studied.[27] The delivery mechanism known as a liposome (LP) has the ability to encapsulate a wide range of

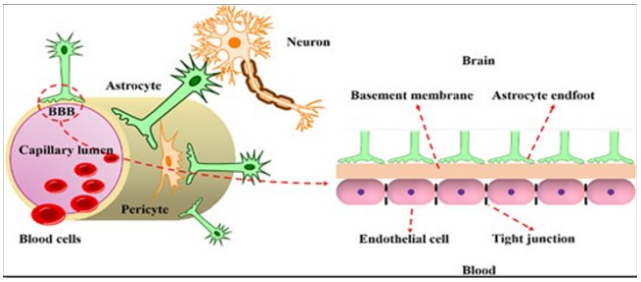

Fig. 2: Crossing the blood brain barrier with nanoparticles

medications and imaging agents. LPs' structural design enables the application of a load that is either loaded in the aqueous compartment or embedded in the lipid bilayers. They represented the initial wave of cutting-edge medication delivery vehicles.[28] Liposomes, which have a structure resembling that of a cell membrane, are biodegradable colloids that can be used to transport a variety of hydrophobic and hydrophilic pharmaceuticals, including small molecules, peptides, proteins, and RNAs, without altering their function and shielding them from immune responses and degradation (Figure 3). The ligands' glucose moiety gave the liposome a unique affinity for BBB endothelial cells, which improved the transport rate. The BBB was successfully penetrated and brain tumours were successfully targeted by doxorubicin liposomes conjugated with both foliate and transferrin.[29] Liposomes are poorly stable and have a tough time attaching ligands to their surface because of the scarcity of accessible surface groups and steric hindrance.

The inability to provide sustained drug release and moderate efficiency for the entrapment of lipophilic compounds are just a few of the limitations of liposomes.[30] Other drawbacks include fast systemic elimination, rapid metabolic degradation of the phospholipids, stability issues after extended storage, and inability to provide sustained release of drugs. Early experiments trying to transport medications over the BBB used very big liposomes with little success. When fluorescein or trepan blue were enclosed in liposomes and administered intravenously, they only stained the luminal side of the vasculature and not the luminal side or brain parenchyma, showing that the liposomes had failed to cross the BBB.[31] Small unilamellar vesicles (SUVs), with a diameter of 0.025 to 0.1 m, were developed as liposomes when it was discovered that their comparatively large size, i.e., 0.2-1.0 m, was the cause of the RES cells' rapid ingestion of liposomes, notably in the liver and spleen.[32] Comparing the usage of SUV liposomes to big vesicles, it was discovered that the rate of removal from circulation was significantly slowed. Therefore, the majority of the study on liposomes for BBB delivery has concentrated on the utilisation of these SUVs.

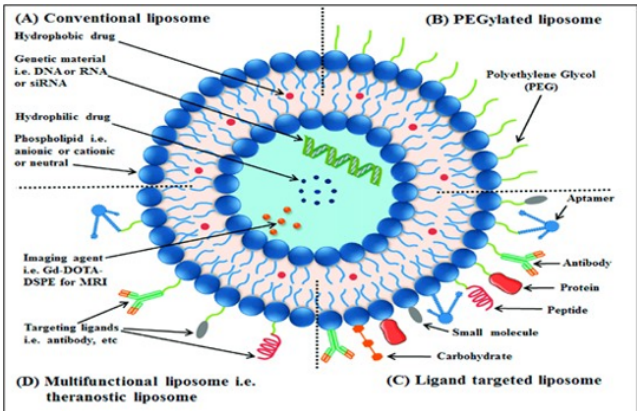

Fig. 3: Surface of Liposomes: Conventional liposomes are made of phospholipids (A); PEGylated/stealth liposomes contain a layer of polyethylene glycol (PEG) at the su posomes (B); targeted liposomes contain a specific targeting ligand to target a cancer site (C); and multifunctional such as theranostic liposomes, which can be used for diagnosis and treatment of solid tumors (D).

For the treatment of cerebral ischemia, several studies have shown the value of liposomes in penetrating the BBB. In these research, ATP, Calpain inhibitors, antioxidants (ascorbic acid and -tocopherol), CDP-choline, citicholine, and superoxide dismutase were all encapsulated in liposomes to see how well they prevented ischemia-induced neuronal injury when compared to free drug delivery. For the treatment of cerebral ischemia, several studies have shown the value of liposomes in penetrating the BBB. In these research, ATP, Calpain inhibitors, antioxidants (ascorbic acid and -tocopherol), CDP-choline, citicholine, and superoxide dismutase were all encapsulated in liposomes to see how well they prevented ischemia-induced neuronal injury when compared to free drug delivery.(Figure 3)

4. Transferrin Modified Liposomes

For the delivery of therapeutic drugs across the BBB to improve the targeting effectiveness, transferrin receptors, one of the receptors, have a particular grip. The receptor is a transmembrane glycoprotein that has two 90 kDa subunits that are connected by a disulfide bridge. Each of these subunits can bind to one molecule of the transferring substance (Figure 4). Transferrin has various issues that need to be addressed as a target drug delivery system. In addition to the BBB, the intestinal choroid plexus cells, hepatocytes, monocytes, erythrocytes, and neurons all express transferrin. As a result, liver and kidneys likewise contain substantial concentrations of transferrin-targeted liposomes.[33] The brain parenchyma's ability to absorb iron is controlled by the transferrin receptor. The presence of transferrin-functionalized fluorescein-loaded magnetic NPs (FMNs) in dendrites, synapses, cytoplasm, and axons of neurons suggests that these particles can successfully traverse the intact BBB through transferrin.

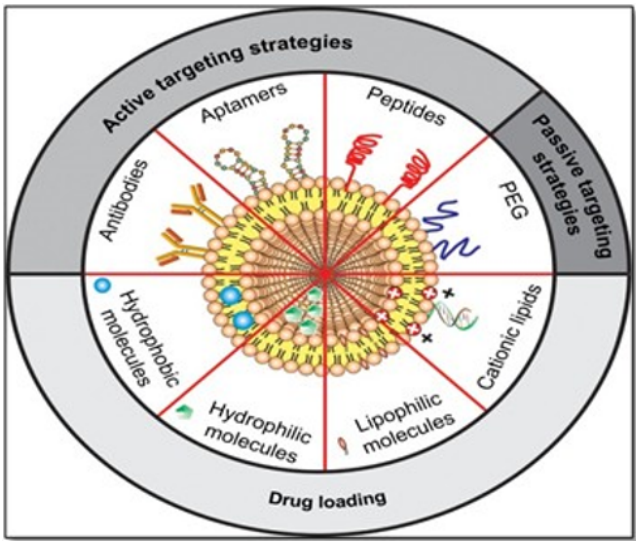

Fig. 4: Pathways for crossing the blood-brain barrier (BBB)

5. Micelles

Candidates for delivery to the brain have been identified as polymeric micelles. Since they have certain physical and biochemical advantages over other forms of Nano-carriers, their use as targeted delivery medications and as diagnostic-imaging agents has attracted considerable interest.[34]

These amphiphilic polymers typically have particle sizes between 10 and 100 nm, and the majority of them are biodegradable and biocompatible. Due to their capacity to solubilize hydrophobic pharmaceuticals, stop drug degradation, increase drug solubility in water, prolong drug circulation time, and have lesser negative side effects, micelles are ideal pharmaceutical carriers.[35] A shell and a core are present in amphiphilic surfactant molecules that spontaneously assemble in water to form spherical vesicles. The most researched micelles for nano-carriers are poloxamers, which are composed of Pluronic block copolymers.[36] Micelle fictionalisations, which increase their stability and lengthen their duration in circulation, can prevent the early drug release from the micelle Nano system before it reaches its particular targets.[37]

6. Nanoparticle

Nanoparticles are colloidal systems with compact structures in which the therapeutic substance is either coated on the particle surface by conjugation or adsorption or trapped within the colloid matrix. Because they exhibit the following distinctive qualities, nanoparticles are commonly used in the treatment of neurodegenerative diseases:

1. Due to their small size and relatively high drug loading, nanoparticles are able to transport active ingredients to a given site at a steady and controlled rate.
2. Nanoparticles, particularly inorganic ones, perform exceptionally well in imaging.

These nano-carriers fall into two categories: polymeric NPs and lipid-based NPs. The term "nanoparticle" refers to solid colloidal particles made of polymeric materials that have a size between 1 and 1000 nm.[38–40] They are employed as drug delivery systems for active ingredients that are dissolved, entrapped, encapsulated, and/or adsorbed or adhered to. Acrylic copolymers, poly (D, L-lactide-co-glycoside), poly (methyl methacrylate), poly (alkylcynoacrylate), and poly (lactide) are a few examples of synthetic polymers that have been utilised to create nanoparticles.[41] Additionally, polysaccharides and naturally occurring proteins like albumin and gelatin have been used to make nanoparticles (dextran, starch, and chitosan). According to physicochemical studies, coating colloidal particles with block copolymers like poloxamers and polyamines reduced the adhesion of the particles to the surface of macrophages. This reduced phagocyte uptake and resulted in significantly higher levels in the blood and non-RES organs like the brain, intestine, and kidneys, among others.[42,43]

In the field of modified drug delivery technology, lipid-based NPs, such as solid lipid nanoparticles (SLNs), are a significant class of colloidal systems. A single solid lipid is used to create SLNs, whereas a mixture of lipids that are spatially dissimilar or a combination of a solid lipid and a liquid lipid (oil) is used to create NLCs.[44] SLNs are thought to be particularly appealing Nano vectors for delivering pharmaceuticals to the brain despite having a low hydrophilic drug loading capacity due to their higher biodegradability and lower toxicity. They typically consist of a drug-filled hydrophobic core that is either dissolved or disseminated.[45] SLN include commonly used emulsifiers such as lecithin, polysorbate, and other types of poloxamers, as well as widely used food lipids, waxes and bile salts.

Polymeric NPs cross the BBB by endocytosis and then transcytosis through the BMEC lining the brain's blood capillaries. 4 Polymeric NP-delivered medications are P-gp substrates, which are actively exported from the central nervous system. When treating Alzheimer's disease, the introduction of polymeric nanoparticles improves drug transport to the brain while lowering oxidative stress, inflammation, and plaque load.[46,47] Additionally, the in vivo experiment involving the simultaneous administration of the anti-oxidant Boliden and the chemotherapy drug Cisplatin employing poly (lactide-co-glycolic) Nano-carriers led to an efficient target-specific delivery for the treatment of brain cancer.[48] In a nutshell, any one or a combination of mechanisms may allow nanoparticles to transport pharmaceuticals over the BBB.

7. Dendrimers

Repeating monomer units are arranged around and connected to a central core to form the flexible, highly branching structures known as dendrimers. Dendrimers are excellent candidates for drug delivery because of their outstanding structural characteristics, which include small size, limited polydispersity, narrow molecular weight distribution, well-defined globular shape, and a relative ease in including targeting ligands.[49] In addition to targeting particular cells, such as tumour cells, dendrimers' surface groups can be coupled with ligands for transport across the BBB. As a result, dendrimers offer tailor-able delivery mechanisms for better medication absorption into the brain. The drug-dendrimers conjugate demonstrated a rapid drug release profile at mild acidic conditions and a stable state in physiological environments, as well as good BBB transport ability with a transporting ratio of 6.06% in 3h. Dendrimers' biocompatibility issue must be resolved before they can be used for drug delivery in the brain. For instance, PAMAM Dendrimers have been demonstrated to be cytotoxic and hemolytic.[50] According to some research findings, biotinylated PAMAM Dendrimers might end up being more harmful than PAMAM Dendrimers on their own.[51] The variety of release mechanisms is one of dendrimers' drawbacks; as a result, medicines frequently release before the dendrimers can get to their target sites. Their long-term safety profiles are also less well-established than those of other polymers.[52]

8. Exosomes New Emerging and Promising Nanocarriers

Exosomes are natural endogenous nanocarriers that range in size from 30 nm to 150 nm, with a normal lipid bilayers structure, and are often referred to as "drifting bottles" in living organisms. B cells, T cells, macrophages, and dendritic cells are just a few of the cells that release it.[53]

1. Exosomes stand apart from other types of transportation primarily due to two characteristics. The first is immunological privilege: as endogenous cellular carriers with endosomal tropism, exosomes can bypass the endosomal pathwa[54,55] and liposomal breakdown, reduce mononuclear phagocyte clearance, and boost drug delivery to target tissue, thus acting as a "invisibility cloak". Transport of proteins and nucleic acids, unstable therapeutic agents, is facilitated by intercellular communication over enormous distances. Although the use of exosomes as SiRNA vectors is still in its early stages, exosomes may represent a significant improvement in the field of macromolecular drug delivery and may be a key step in the therapeutic application of SiRNA. Exosomes

and the pathophysiology of AD and PD are associated, although the cause-and-effect relationship between the two is not yet obvious enough in the related study. Before they can be addressed in therapeutic practise, a number of issues exist:

2. (1) Safety concerns and potential risks must be emphasised and thoroughly assessed because exosomes' molecular components are so complicated.
3. (2) The importance of exosomes as a brain target vehicle for increasing medication concentration in the brain and preventing side effects cannot be overstated. Exosome-based brain drug delivery systems have achieved proof of concept; nevertheless, before clinical evaluation, a number of challenges, including the selection of exosome donor cells, drug loading techniques, and targeting peptides, need to be resolved.

8.1. Quantum dots

A metalloid crystalline core (like cadmium selenium) and an intermediary unimaginative metallic shell (like zinc sulphide) that protects the core make up the class of colloidal semiconductor micro crystals known as quantum dots.[56] Quantum dots can have their outer coating chemically functionalized to transport therapeutic compounds as well as bioactive molecules that support desirable bioactivity and water solubility.[57]

The kind of colloidal semiconductor micro crystals known as quantum dots is composed of a metalloid crystalline core that protects the core (such as cadmium selenium) and an inbetween thin metallic shell (such as zinc sulphide). In order to transport medicinal substances as well as bioactive chemicals that support desired bioactivity and water solubility, quantum dots' outer coating can be chemically functionalized.[57]

Nanoparticles can be successfully internalised when TAT, a cell membrane translocation peptide, is employed. According to studies, TAT-conjugated CdS/Mn/ZnS quantum dots may mark brain tissue after a few minutes of being intravenously administered to a rat brain without interfering with the BBB since they moved beyond the endothelial cell line and entered the brain parenchyma. The TAT peptide was necessary for the quantum dots to cross the BBB since the same quantum dots without it failed to mark the brain tissue.[58,59]

8.2. Nano emulsions

The diameter of the inner phase is lowered to a nanoscale length scale in nanoemulsions, which are heterogeneous dispersions of oil-in-water (O/W) or water-in-oil (W/O) formulations stabilised with surface-active agents. For biocompatibility purposes, Nano emulsions are typically made from edible oils, such as flaxseed oil, pine nut oil, hemp oil, fish oil, as well as safflower oil and wheat germ oil, along with water and biocompatible surfactants, such as egg phosphate dichloride, which is one of the components of cell membrane lipids. The variety of oils and surface modifiers that can be utilised is what gives Nano emulsions their versatility.[60]

Nano, ultrafine, submicron, transparent, and mini-emulsions are all terms used to describe emulsions with droplet sizes between 5 and 200 nm.[61] Systems called nano emulsions have been created for the controlled release and drug delivery of biologically active substances. They are potential systems for biotechnology, diagnostics, medication therapy, and cosmetics.[62] Additionally, they have enormous promise as an innovative method of delivering fatty acids, polyphenols, natural colours, and tastes to the food sector, particularly for the production of functional meals.[63] Since lipophilic active chemicals are poorly soluble in water, the food sector faces significant difficulties in incorporating them into foods and beverages. The solubility issue is resolved and the bioavailability of lipophilic active substances, such as vitamins and carotenoids, is increased by using nanoemulsions as a carrier system.[64]

8.3. Carbon nanotubes

Due to the wide range of characteristics and shapes they provide, carbon-based materials like fullerenes and nanotubes might be useful in biotechnological applications.[65] With a diameter in the nanoscale range and a cylinder shape, carbon nanotubes (CNTs) are generated by graphite sheets; as a result, their passage through the BBB is made easier. This process is well-known to be crucial to the toxicity of the nano-carrier. Knowing the target organ's transport system inside and out is essential for functionalization.[66]

Single-walled and multi-walled carbon nanotubes are both possible, as are ends that are either left open or sealed with fullerene caps.[67] A co-culture model made up of primary rat astrocytes and primary porcine brain endothelial cells was used to study the permeation of amino-functionalized multi-walled carbon nanotubes through the blood-brain barrier in vitro, and systemic dosing of mice was used to study the process in vivo. The study's findings may open the door to the use of carbon nanotubes for the safe transport of medicines and biologics to the brain.[68]

8.4. Nano gels

The possibility of medication delivery across the intact BBB is provided by nano gels, an unique formulation of nanoparticles. In order to transport the drugs doxorubicin and insulin across the blood-brain barrier, Gil and Lowe created polysaccharide-based nanogels containing poly (B-amino ester) and B-cyclodextrin. These cationic nanogels increased the permeability of insulin across the in vitro

BBB model by 20%.[69] Since it has been demonstrated in the literature that lipophilic molecules cross the blood brain barrier more quickly than hydrophilic ones, surface functionalization of nanogels towards lipophilicity has been proposed as a means of accelerating the transport of encapsulated drugs across the blood brain barrier. Methotrexate (MTX)-loaded nanogels were created by Azadia[70] utilising an ionic gelation technique, chitosan, and sodium tripolyphosphate (TPP) as raw ingredients. To enhance drug delivery to the brain, polysorbate 80 was used to modify the surfaces of the MTX-loaded nanogels..

9. Limitations of Brain Targeted Nanoparticles

Even while nano-carriers have a number of benefits, such as the ability to carry medications across the blood-brain barrier and longer circulatory system retention times, their use in clinical settings is constrained by a number of drawbacks. The harmful effects of excessive exposure to nanomaterials, such as polymers, are of primary concern. Polymers may build in the CNS as a result of the repeated administration of Nano-carriers due to the major compositional percentage of Nano-drugs. Both toxicity and immunogenicity are possible side effects. Therefore, strict experimental protocol regimes are needed to both address and reduce these issues before they have clinical repercussions. The long-term toxicity profile of NPs in the brain must be thoroughly investigated since it may restrict the use of nanoparticle drugs in clinical settings. Second, it's crucial to maintain the encapsulation efficiency rate as the Nano-drug formulation process is scaled up from laboratory to industrial production. The formulation and physicochemical characteristics used to conjugate or encapsulate pharmaceuticals can affect the therapeutic efficacy of nano-drugs. Therefore, sustaining the rate of encapsulation efficiency under physiological settings depends on the formulation process optimization for large-scale production. Additionally, the procedure is constrained by the high expense of scaling up the synthesis of Nano-drugs and the usage of organic solvents in that process. Finding alternatives is therefore necessary in order to produce Nano materials that are both affordable and environmentally beneficial. Another drawback is that using FITC or other pH-dependent fluorescent tags to identify exocytose nanoparticles may cause interference. Another drawback is that the data may be difficult to interpret when exocytose nanoparticles are detected using pH-dependent fluorescent tags, such as FITC. Natively fluorescent (quantum dots, Nano diamonds), luminous (gold), and paramagnetic (ferrous oxide) materials can all provide significant benefits to get around this limitation.

10. Conclusion

The use of nano-carriers as drug delivery systems for delivering medications to specific tissues and organs has received extensive study. Given that it prevents the CNS from receiving numerous potentially beneficial therapeutic and diagnostic chemicals, the BBB is acknowledged as the main barrier to treating neurological illnesses. A great alternative to the current surgical and conventional methods, these nano-systems are demonstrating a great potential as drug carriers to the brain. This is due to many benefits associated with their use. To produce CNS treatments with increased activity and greater BBB permeability, however, and to further optimise the architecture of nanosystems.

Only drug-carrier conjugates' penetration into the brain parenchyma via transcytosis or endocytosis, according to the numerous modes of drug transport across the blood-brain barrier by Nano-carriers, exhibits suitable for all kinds of brain medications. The creation of a flexible delivery platform should therefore concentrate on its capability as well as its efficacy to be transcytosis or endocytosis in order to achieve a viable delivery platform for brain medications, it is stated here.

Finally, the drug transport efficiency across the BBB by Nano-carriers should be increased in order to reach the least effective drug concentration in brain parenchyma while maintaining the maximal safety drug concentration in other organs. In light of this, new methods for facilitating the endocytosis of Nano-carriers by brain capillary endothelial cells must be investigated. However, in the brain parenchyma, the effectiveness of drug accumulation is also influenced by BBB crossing, which is relatively simple to engineer.

11. Source of Funding

None.

12. Conflict of Interest

None.

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