The role of lipid based nanoparticles in brain targeted drug delivery system: An overview

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Abstract---Recently, targeted drug delivery systems have gained muchimportance fordeliveringmany kinds of drugs as well as imagingagents,particularly to the targetedDisease cells or tissues. The diagnosis and treatment of brain disorders is an extremely challenging task. The blood-brain barrier (BBB) is the primary obstacle in conveying the chemotherapeutic and diagnostic agents that prompt the insufficient delivery of drug at the brain-targeted site. Many drug molecules are non-soluble in aqueous systems, unable to cross BBB, or present severe side effects. Lipid-based nanoparticle (LBNP) systems represent one of the most potential colloidal carriers. They are preferred over polymeric nanoparticles due to their high stability, excellent targeting ability,increased loading capacity, non-toxicity, low production costs, and ease of preparation. Combining drug with lipid
nanoparticles reduces the therapeutic dose and toxicity, decreases drug resistance, and increases drug levels in the targeted tissue. This review presents the different types of LBNPs developed in recent years and their application in brain disorders.

**Keywords**—blood-brain barrier, chemotherapeutic, lipid-based nanoparticles, tumour, Parkinson's disease.

**Introduction**

Nanotechnology has evolved rapidly in the past two decades and has been used mainly to diagnose and treat diseases. Nanoparticles (NPs) are about 1 and 1000 nm in size and enhance the bioavailability of drug drugs and the selectivity of drugs (García-Pinel et al., 2019). NPs provide many benefits, including improving solubility, protecting the load from enzyme destruction, and enhancing targeting efficiency. NPs in the area of medicine and research have also increased consideration (Gao, 2016).

Multiple sclerosis (MS), Alzheimer's disease, Parkinson's disease, stroke, and brain tumors are currently disordered by the Central Nervous System (CNS), with much consideration and focus. Chemotherapeutic agents, specifically for the brain, must be administered for successful diagnosis and treatment of brain tumors. However, only small lipophilic molecules (<500 da) can effectively cross the BBB and enter an appropriate brain concentration other than nutrients. Due to drug transportation restriction into the brain by blood-brain barriers (BBBs), different techniques have been developed using NPs as carriers (Pardridge, 2007). Several nanoformulations used here are lipid formulations since the preparation and replacement compositions have made incredible advances in recent years.

**Brain Drug Delivery Obstacles**

**Barrier to the Blood-Brain**

BBB is the most crucial obstacle in the delivery of brain-driven drugs. In 1885, Ehrlich discovered that intravenously infused dye could label most of the organ, except the brain. BBB consists of different cells, including brain endothelial cells, pericytes, astrocytes and neuronal cells. BBB consists of different cells. Consistent tight intersections between BCECs prevent paracellular transport from blood to mind. Moreover, these close intersections create very high
transendothelial electrical resistance (TEER) between blood and the brain and considerably reduce the passive dissemination of compounds. Despite the restriction, various carriers may interfere in entering or expelling multiple substances from the brain (Gao, 2016; Teleanu et al., 2018).

**Barrier to Blood Brain Tumor**

In brain tumors, the core of the BBB is undermined but is essential in the environment. The delivery of drugs to brain tumors is smaller than peripheral tumors. BBTB has a small pore size and a higher level of drug efflux pumps, including P-glycoprotein, multidrug resistance-related proteins, and the breast cancer resistance protein relative to the blood tumor barriers in peripheral tumors (Wolburg et al.,)

**Brain Barrier Nose**

The nasal cavity's structure, physiology and brain delivery path have all been measured. The respiratory and olfactory regions are responsible for the brain or blood absorption of the medicine. Some compounds may reach the systemic circulatory system via the respiratory mucosa and cross the BBB into the brain. Some can be directly transported to the brain through trigeminal nervous pathway or lamina propria adsorption from perivascular and lymphatic spaces. The olfactory mucosa pathway mediates medicine from the nasal cavity to the brain very rapidly (Gao, 2016).

**Barrier to Blood-Cerebrospinal Fluid (BCSFB)**

The BCSFB is an obstacle to the introduction of drugs into the CNS. It consists of the plexus epithelial cells that prevent molecules from entering. Due to the inconsistency between interstitial fluid and CSF, the CSF-brain barrier has been established. The presence of polarised endothelial cells connected by near junctions in BBB results in low permeability. It restricts medication delivery to the central nervous system (CNS) (Hangargekar et al., 2019).

**Approaches to overcome the BBB**

The BBB is the first barrier in the brain delivery of medicines. Researchers have developed different techniques to circumvent or bypass BBB, including cellular internalisation, opening, and intranasal delivery by BBB (Gao, 2016). Various brain transporters are listed in Table 1

<table>
<thead>
<tr>
<th>Receptor Transport</th>
<th>Mediated Transport</th>
<th>Active Efflux Mediated Transport</th>
<th>Transporter Mediated Transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transferin receptor</td>
<td>Adenosine triphosphate-binding cassette (ABC) transporter</td>
<td>Glucose transporter, member 1</td>
<td>Glucose transporter, member 1</td>
</tr>
<tr>
<td>Insulin Receptor</td>
<td>P-glycoprotein</td>
<td>Large neutral amino acid transporter</td>
<td>Large neutral amino acid transporter, member 1</td>
</tr>
<tr>
<td>Low-density lipoprotein</td>
<td>ABC transporter</td>
<td>Large neutral amino acid transporter</td>
<td>Large neutral amino acid transporter, member 1</td>
</tr>
</tbody>
</table>
Lipid-Based Nanoparticles

Lipid-based nanoparticles (LBNPs) is highly regarded in drug discovery and cancer treatment. These nanoparticles can transport hydrophobic and hydrophilic molecules, show very low to no toxicity, and increase drug action time through extended half-life and controlled drug release (García-Pinel et al., 2019).

Liposomes

Liposomes are the drug delivery system most studied due to their biocompatibility and biodegradability (García-Pinel et. al., 2019). These are synthetic and spherical cells composed of single amphiphilic lipid bilayers that may carry drugs, vaccines, nucleic acids, aptamers, antibodies and protein molecules (Teleanu et al., 2018). They develop vesicles in water, enhance drug solubility and stability, and encapsulate hydrophobic or hydrophilic drugs. Cholesterol-modified liposomes consist of a multiple bilayer with sizes between 0.5 nm and 10 nm, called Multilaminar Vesicles (MLVs); a single bilayer with sizes above 100 nm, called Large Unilamellar Vesicles (LUVs); and intermediate sizes (10–100 nm) called Small Unilamellar Vesicles (SUVs) (Yingchoncharoen et. al., 2016).

Nanocarrier vectorisation has two methods. One is passive targeting that occurs by molecular movement through the cell membrane, and the other is active targeting, where liposomes loaded with antibodies recognising disease cells. Temperature, pH or magnetic fields are parameters that can be altered by an external stimulus for controlled drug delivery (García-Pinel et al., 2019).
Liposomes are mostly used in target brain therapy, due to the ability of crossing the blood-brain barrier. Many studies have reported the use of liposomal formulations to deliver drugs, such as mitoxantrone, 5-fluorouracil, paclitaxel, doxorubicin, erlotinib, opioid peptide and monoclonal antibodies as summarised in Table 2.

Table 2: Liposomes Based Formulations for Brain Targeted Drug delivery System

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Lipid</th>
<th>Preparation Method</th>
<th>Drugs</th>
<th>Comments</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PFV-PEG(2000)-DSPE</td>
<td>Nucleophilic substitution reaction</td>
<td>Doxorubicin and Erlotinib</td>
<td>Higher translocation of dual functionalised liposomes across the BBB and delivering chemotherapeutic drugs to the glioblastoma tumor cells</td>
<td>Lakkadwala et al., 2019</td>
</tr>
<tr>
<td>2</td>
<td>PEG(2000)-DSPE</td>
<td>Thin-film hydration method</td>
<td>Temozolomide</td>
<td>Reduced tumour growth and significantly prolonged survival of glioma-bearing mice</td>
<td>Papachristodoulou et. al., 2019</td>
</tr>
<tr>
<td>3</td>
<td>DOPE DOTAP,</td>
<td>Thin lipid film hydration method</td>
<td>Penetratin</td>
<td>Multifunctional liposomes provide an excellent gene delivery platform for neurodegenerative diseases</td>
<td>Rodrigues et al., 2018</td>
</tr>
<tr>
<td>4</td>
<td>PEG-DSPE</td>
<td>Ethanol injection method</td>
<td>HAIYPRH</td>
<td>Potential targeted drug delivery system of ischemic stroke treatment</td>
<td>Wang et al., 2015</td>
</tr>
<tr>
<td>5</td>
<td>DMPC and EYPC</td>
<td>PEG</td>
<td>Antibody</td>
<td>Specific delivery of single domain antibody fragments over the BBB</td>
<td>Rotman et al., 2015</td>
</tr>
<tr>
<td>6</td>
<td>SPC, DSPE</td>
<td>Repeated freeze-thawing method</td>
<td>^{188}\text{Re}</td>
<td>Significantly prolong the lifespan of rats while maintaining</td>
<td>Huang et al., 2015</td>
</tr>
<tr>
<td>7</td>
<td>DPPC and PEG</td>
<td>Freeze-drying method:</td>
<td>Tacrolimus</td>
<td>Enhanced therapeutic Efficacy; promising neuroprotectant after cerebral stroke.</td>
<td>Ishii et al., 2013</td>
</tr>
<tr>
<td>8</td>
<td>PC-E</td>
<td>Lipid film hydration</td>
<td>Mitoxantrone</td>
<td>Significantly improve the therapy of brain metastasis</td>
<td>Orthmann et al., 2012</td>
</tr>
<tr>
<td>9</td>
<td>PEG</td>
<td>Opioid peptide DAMGO</td>
<td></td>
<td>Promising platform for enhancing and prolonging the delivery of drugs to the brain.</td>
<td>Lindqvist et al., 2012</td>
</tr>
<tr>
<td>10</td>
<td>DSPE-PEG2000 and DSPEPEG2000-maleimide</td>
<td>Monoclonal antibody</td>
<td></td>
<td>Sustained therapeutic effects are achieved. Both dose-response and time-responses are observed</td>
<td>Xia et al., 2008</td>
</tr>
</tbody>
</table>

DAMGO:H-TyrD-Ala-Gly-MePhe-Gly-ol; DOPE: Dioleoylsnglycerol3phosphoethanolamine; DOTAP: Dioleoyl-3-trimethylammoniumpropane chloride; DMPC: 1,2-dimyristoylsnglycerol-3-phosphocholine; DSPE:1,2-distearoyl-snglycerol-3-phosphoethanolamine-N[carboxy(polyethylene glycol)-2000]; DPPC:Dipalmitoylphosphatidylcholine ; EYPC: eggyolk phosphatidylcholine;PC-E: Phosphatidylcholine; PEG: Polyethylene Glycol; RGD: Arginine-lysine-aspartate; SPC: Soy phosphotidylcholine; T7-P-LPs: T7-conjugated PEGylated liposomes; Tf: Transferrin.

**Solid Lipid Nanoparticle**

In 1991, solid lipid nanoparticles (SLNs) were introduced as an alternative to conventional colloidal carriers such as emulsions, liposomes, polymeric-micro and nanoparticles. SLNs are consisting of physiological lipids that can be dissolved or spread in a solid-state at room and body temperature. These particles range from 50–1000 nm (Bagul et al., 2018).
The vital monolayer phospholipid forms a grid material for drug encapsulation, including mono-, di- or triglycerides, fatty acids and complex glyceride mixtures, balanced by surfactants or polymers that allow them to cross tight BBB endothelial cells and escape the reticuloendothelial system (RES). During manufacture, the soft lipids were combined with the medication and distributed by high-pressure homogenisation or micro-emulsification into an aqueous surfactant (Masserini, 2013; García-Pinel et al., 2019; Hangargekar et al., 2019).

SLNs have significant advantages such as site-specific targeting, the possibility of lyophilisation, increased stability, controlled release of lipophilic and hydrophilic drugs, no special requirement for solvents, low cost, fast preparation and non-toxic (García-Pinel et al. 2019; Hangargekar et al. 2019). SLNs have bad effects on human granulocytes. This all makes them an effective candidate for drug delivery systems. In comparison, SLNs have some drawbacks, such as moderate drug-loading ability, drug expulsion due to crystallisation under storage conditions, and particle growth (García-Pinel et al., 2019). Table 3 offers a few examples of SLN-based formulations for brain-targeted drug delivery.

Table 3: SLN Based Formulations for Brain Targeted Drug Delivery System

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Lipid</th>
<th>Preparation Method</th>
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<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Stearic acid, borneol, puerarin</td>
<td>Emulsification evaporation-low temperature solidification method</td>
<td><em>Pueraria</em> flavone</td>
<td>More pronounced accumulation and a promising therapeutic carrier for brain disease</td>
<td>Wang et. al., 2019</td>
</tr>
<tr>
<td>2</td>
<td>Tween 80</td>
<td>Solvent Injection Method</td>
<td>Nifedipine</td>
<td>Enhanced site-specific delivery to the brain</td>
<td>Bhargava et al., 2018</td>
</tr>
<tr>
<td>3</td>
<td>Gelucire 43/01 Geleol and Precirol</td>
<td>Emulsification solvent evaporation technique</td>
<td>Agomelatine</td>
<td>Effectively enhanced both the absolute bioavailability and the brain delivery</td>
<td>Ahmed et al., 2017</td>
</tr>
<tr>
<td>5</td>
<td>Cetyl Palmitate</td>
<td>centrifugation followed by homogenisation and ultrasonic technique</td>
<td>Resveratrol</td>
<td>Superior anti-proliferative action</td>
<td>Neves et. al., 2016</td>
</tr>
<tr>
<td>8</td>
<td>POPC, DSPE, CHO, DM</td>
<td>Detergent dialysis technique</td>
<td>siRNA</td>
<td>Higher uptake and gene knockdown efficacy with an increase in the uptake of the LNPs.</td>
<td>Brunn et al., 2015</td>
</tr>
<tr>
<td>9</td>
<td>Stearic acid, DDAB, Compritol 888</td>
<td>Solvent displacement technique</td>
<td>Vincristine and temozolomide</td>
<td>Outstanding drug delivery system to achieve excellent therapeutic efficiency</td>
<td>Wu et al., 2015</td>
</tr>
<tr>
<td>10</td>
<td>Compritol 888, Precitol</td>
<td>Modified emulsification-diffusion technique</td>
<td>Haloperidol</td>
<td>Effective drug delivery system for psychiatric conditions</td>
<td>Yasira et al., 2014</td>
</tr>
<tr>
<td>11</td>
<td>Glycerol tristearate</td>
<td>Thin-layer ultrasonication technique</td>
<td>5-fluoro-20-deoxyuridine</td>
<td>Increased penetration through the blood-brain barrier</td>
<td>Wang et al., 2002</td>
</tr>
</tbody>
</table>

CHO: Cholesterol; DO-FUdR: 3,5-dioctanoyl-5-fluoro-2-deoxyuridine; DM: Dimyristoyl; DSPE: 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[carboxy(polyethylene glycol)-2000]; DDAB: dimethyldioctadecylammonium bromide; DMPC: 1,2-dimyristoyl-sn-glycero-3-phosphocholine; Lf: Lactoferin; POPC: 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine; Tf: Transferin; TPM: Tripalmitin
Nanostructured carrier

Nanostructured lipid carriers (NLCs) are the recently formed colloidal lipid carriers that spread partly crystallised lipid nanoparticles in an aqueous dispersion medium. NLCs have higher drug load potential and resist lipid crystallisation due to the inclusion of liquid lipids in NLC formulation. NLCs are a mixture of lipids such as glyceryl tricaprylate, ethyl oleate, isopropyl myristate and glyceryl oleate. The mean particle sizes range from 10–1000 nm and are influenced by the design of the lipids and manufacturing process.

Figure 3: Nanostuctured Lipid Carrier

The key advantages of these nanoparticles are: they can be loaded with hydrophilic and hydrophobic drugs, surface-modified, site-specific targeting, drug-release regulation, and low in vivo toxicity. However, the drawbacks of these nanoparticles are low loading potential and drug expulsion after polymorphic lipid transfer from the nanocarrier matrix during storage (García-Pinel et al., 2019).

Because of its lipid nature, it can triumph over BBB’s barrier role in brain tumour therapy. The surface-modified NLCs display superior tumour targeting ability. Studies showed NLCs could be used to enhance drug bioavailability. Among the contributions recorded in recent years is paclitaxel, which, together with triolein in an NLC, may be used as a candidate for cancer therapy due to possible drug delivery to the brain (Emami et al., 2017). Table 4 summarises various NLC-based formulations.

Table 4: NLC Based Formulations for Brain Targeted Drug Delivery System

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>Span 80, PEG 400</td>
<td>Hot, high-pressure homogenisation technique</td>
<td>Indinavir</td>
<td>Displayed significantly higher and augmented concentrations in the brain</td>
<td>Nasiri et al., 2019</td>
</tr>
<tr>
<td>2</td>
<td>Span 80, PEG 400</td>
<td>Hot homogenisation, rapid ultrasonication</td>
<td>Quetiapine Fumarate</td>
<td>Potential drug delivery system through intranasal route</td>
<td>Sivadasu et al., 2019</td>
</tr>
<tr>
<td>3</td>
<td>CHO, triolein,</td>
<td>Solvent evaporation</td>
<td>Paclitaxel</td>
<td>The potential delivery system</td>
<td>Emami et al., 2017</td>
</tr>
<tr>
<td>4</td>
<td>DMSO</td>
<td>Solvent diffusion method</td>
<td>Temozolomide</td>
<td>Efficient in selective delivery into U87MG cells</td>
<td>Song et al., 2015</td>
</tr>
<tr>
<td>5</td>
<td>Tripalmitin, oleic acid, polysorbate 80</td>
<td>Hot high-pressure homogenisation technique</td>
<td>Curcumin</td>
<td>The plasmid concentration was highly increased via intraperitoneally after loaded with NLC.</td>
<td>Chen et al., 2015</td>
</tr>
</tbody>
</table>

CHO: Cholesterol; DMSO: Dimethyl Sulfoxide; PEG: Polyethylene Glycol; RGD: Arginine-glycine-aspartic acid peptide; Tf: Transferin.

SLNs and polymeric nanoparticles are favoured to supply anticancer drugs (Qu et al. in 2016 and Wu et al. in 2015). In a gliomatosis cerebri treatment trial, three separate nanocarriers (SLN, NLC, and polymeric nanoparticles) were developed to deliver temozolomide (TMZ). Unlike TMZ-SLN and TMZ-polymeric nanoparticles, the formed TMZ-NLCs showed prevalent apoptotic activity against glioblastoma multiforme (GBM) cells. TMZ-unrivaled NLC’s in vitro apoptotic activity was attributed to its simpler entry and higher drug load (Song et al., 2015).

Due to curcumin’s low bioavailability and hasty in vivo metabolism, its chemotherapeutic application became risky. Thus, curcumin-exemplified NLCs were formed with a 6.4-fold increase in plasma concentration. Because of increased bioavailability and tumour efficacy targeting, the brain and tumour performance was dramatically upgraded. Curcumin-stacked NLCs can be used in brain tumour targeting (Chen et al., 2016).

**Niosomes**

Niosomes are microscopic lamellar vesicles formed by alkyl or dialkyl polyglycerol ether (non-ionic surfactant) and cholesterol. These are structurally similar to liposomes, but the key difference is that they contain non-ionic surfactant rather than phospholipid. They offer various advantages such as compatibility, non-immunogenicity, the ability to integrate hydrophilic, lipophilic and amphiphilic drugs, brain-specific drug choices, reduced dose and dosage frequency, higher stability, better bioavailability and delayed clearance (Das & Palei, 2011). Thus, liposomes are better favoured (El Maghraby et al., 2009).

![Figure 4: Niosome](image)
Ferrociphenol (Fc-diOH), an organometallic complex has potent antitumor activity. Fc-diOH stacked LNCs encapsulated inside the marrow-isolated adult multilineage inducible (MIAMI) cells were developed for targeted delivery of Fc-diOH to the brain tumour cells. MIAMI cells can relocate to the synapses crossing through the BBB. Thus, utilising MIAMI cells as a carrier for lipid nanocapsule could support brain targeted delivery of the chemotherapeutic agent in the treatment of brain tumour. Cytotoxicity study revealed that internalisation of Fc-diOH-LNCs did not improve MIAMI cell death (Roger et al., 2012).

In another study, cannabidiol-decorated and an antidepressant loaded LNCs were developed and evaluated in an animal model. The LNCs were administered through i.v. injection. Healthy mice receiving coated LNCs were not observed to have any toxicity. This study widens with cannabinoids the yet scarce

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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Span 60 and cholesterol</td>
<td>Ethanol injection method</td>
<td>Bromocriptine Mesylate</td>
<td>Enhancement in brain distribution and improved pharmacodynamic behavior with 10 times dose reduction</td>
<td>Sita et al., 2020</td>
</tr>
<tr>
<td>2</td>
<td>Sorbitan esters and cholesterol</td>
<td>Film hydration method</td>
<td>Rivastigmine</td>
<td>A good candidate for new drug delivery system.</td>
<td>Estabragh et al., 2018</td>
</tr>
<tr>
<td>3</td>
<td>Cholesterol</td>
<td>Thin-film hydration method</td>
<td>Temozolomide</td>
<td>Enhanced permeation into brain because of surface modification</td>
<td>De et al., 2018</td>
</tr>
<tr>
<td>4</td>
<td>Span 20, 60, 80, tween 20, 80 and cholesterol</td>
<td>Lipid layer hydration technique</td>
<td>Folic acid</td>
<td>The release of drug followed anomalous diffusion and obeyed first order release kinetics.</td>
<td>Ravouru et al., 2013</td>
</tr>
</tbody>
</table>

**Lipid Nanocapsules**

These are the submicron particles comprised of lipid and mixed with polymer, vitamins, proteins, amino acids etc. Lipid nanocapsules (LNCs) are promising DDS for conventional small anticancer drug molecules.
Ferrociphenol (Fc-diOH), an organometallic complex has potent antitumor activity. Fc-diOH stacked LNCs encapsulated inside the marrow-isolated adult multilineage inducible (MIAMI) cells were developed for targeted delivery of Fc-diOH to the brain tumor cells. MIAMI cells can relocate to the synapses crossing through the BBB. Thus, utilising MIAMI cells as a carrier for lipid nanocapsule could support brain targeted delivery of the chemotherapeutic agent in the treatment of brain tumor. Cytotoxicity study revealed that internalisation of Fc-diOH-LNCs did not improve MIAMI cell death (Roger et. al., 2012).

In another study, cannabidiol-decorated and an antidepressant loaded LNCs were developed and evaluated in animal model. The LNCs were administered through i.v. injection. Healthy mice receiving coated LNCs were not observed to have any toxicity. This study widens with cannabinoids the yet scarce armamentarium of exogenous and nonimmunogenic ligands available for brain targeting. Finally, the consistency of the results served to validate a versatile screening method to evaluate the passage of nanocarriers across the BBB (Aparicio-Blanco et. al., 2019).

**Lipid Polymer Hybrid Nanocarrier**

These are hybrid lipid-polymeric system made up by mixing lipids and polymers and served as an efficient carrier for delivering drugs as well as genes. These were introduced to avoid drawbacks associated with colloidal lipid nanocarriers and other polymeric nanoparticles. LPNs consist of two major parts: polymer and the lipid component. A typical LPN has a center shell structure. The polymeric core is used for loading various small molecule drugs and diagnostic agents and the lipid shell is used to confer stability and suitable biocompatibility (Wakaskar et. al., 2018).

Combination therapy of chemotherapeutic agent and nucleic acid significantly solved multidrug resistance issues in cancer. Pemetrexed (PTD) and miR-21
antisense oligonucleotide (anti-miR-21) co-encapsulated in lipid-polymer hybrid nanoparticles (LPHN) were developed for targeted delivery to the brain for the treatment of glioblastoma. The LPHN showed superior antitumor activity by increasing the cellular uptake from 6% to 78%. Higher bioaccumulation of PTD and anti-miR-21 in U87MG cells were achieved upon administration of LPNs, which was essential for the treatment of glioblastoma (Küçüktürkmen et. al., 2017).

**Conclusion**

The combination of the principle of nanotechnology and colloidal lipid carrier systems has modernised the pattern of chemotherapeutic approaches in the treatment of numerous pathologies, especially in brain tumour cases. Though the current therapeutic approach using polymeric nanoparticle carriers for brain tumour cases is efficient, it is related to severe and disturbing side effects. In customised medicine, lipid-based nanocarriers have shown promising clinical outcomes as they can distinguish and screen mind tumour treatment adequately in an early stage.

Lipid-based nanoparticles open new channels for drug delivery to the brain like antitumour, antianxiety, antibiotics, antipsychotics etc. Liposomes are the most broadly utilised LBNPs because of their extraordinary biocompatibility. Recent achievements in operating SLNs and NLCs have also been increasing exceptional consideration. Niosomal carriers for intranasal administration are also promising approaches for delivering neurotherapeutic agents via direct nose to brain route.

More work is still needed to better understand the absorption enhancing mechanisms of lipids to fulfil regulatory guidelines for characterisation and stability enhancement of lipid-based formulations. This review suggested that lipid-based nanoparticles could be a more promising candidate than others for effective management of diagnosis and therapy of brain disorders.

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