RESEARCH PAPER

Recent Advances in the Treatment of Alzheimer's Disease Using Nanoparticle-Based Drug Delivery Systems

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ABSTRACT

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive and functional insufficiencies as well as communicative changes. The treatment of AD is mainly based on cholinesterase inhibitors and NMDA-receptor antagonists. In the present study, gold nanoparticles (NMEs) targeting amyloid-β (Aβ)-induced complex neurotoxicity have received considerable attention in the therapeutic and preventive treatments of AD. In this work, we designed a small-sized Pd hydride (PdH) NP as high-payload hydrogen carrier and Pd similar self-catalyst to realize the in situ sustained release of bio-reductive hydrogen for the first time. We found that PdH NP could selectively scavenge highly cytotoxic OH in AD model cells and could ameliorate mitochondria dysfunction and promote cellular energy metabolism, inhibiting cellular apoptosis, and inhibiting Aβ-mediated peroxidase activity and Aβ-induced cytotoxicity. In addition, we found that intravenous injection of DBP-PLGA nanoparticulate significantly attenuated the Aβ accumulation, neuroinflammation, neuronal loss and cognitive dysfunction in the 5XFAD mice. These results suggest that DBP-PLGA-based drug delivery system could be a promising approach to obtain desirable drug-like properties by altering the biopharmaceutics and toxicological properties of the molecule.

Keywords: Alzheimer's disease; Dementia; Amyloid beta; Nanoparticles; Cholinesterase inhibitors; Gold particles; Neuroinflammation; Neurodegenerative.

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➢ INTRODUCTION

The increasing severity andprevalence of Alzheimer'sdisease, the development of effective treatments for Alzheimer's disease has become an important imperative. Aggregation of amyloid-beta (Aβ) plaques and tau protein tangles in neuronal tissue of the brain are two of the most histopathological /pathophysiological manifestations. Another important factor involved in the pathogenesis of Alzheimer's disease is decreased acetylcholine (ACh) levels in the brain. Medications currently available to treat Alzheimer's disease, such as cholinesterase inhibitors and N-methyl-D-aspartate receptor blockers, may temporarily relieve symptoms of dementia, but they may not be as effective as the disease. Progress cannot be stopped or reversed. Additionally, several medicinal plants have been shown to alleviate thedegenerative properties associatedwith Alzheimer's disease either in their raw form or as isolated chemicals. And nanotechnology is also help in treatment of Alzheimer with the help of nanoparticles such lyposome, gold particle,titanium dioxide etc. the ability of crossing bb barriers help to treat root of disease.[1]

Alzheimer disease [AD] is a neurodegenerative disorder featuring gradually progressive cognitive and functional insufficiencies as well as communicative changes [2]. It is biological define by the manifestation of B-amyloid containing plaques and tau –containing neurofibrillary tangles [3]. With the expansion of the disease, macroscopic atrophy affects the area and hippocampus, amygdala, and associative sections of the neocortex [4]. These pathologies lead to neuronal death and consequently clinical symptoms such as memory loss, confusion, and impaired cognitive function [5]. The combination of increased autophagy induction and defective clearance of Aβ-generating autophagy vacuoles creates conditions favourable for Aβ accretion in Alzheimer disease

➢ EPIDEMIOLOGY

The global prevalence of dementia has been estimated to be as high as 24 million and is predicted to double every 20 years until at least 2040. In this review we discuss the prevalence and incidence rate, the established environmental risk factors, and the protective factors, and briefly review genetic variants predisposing to disease.[6] More than 25 million people in the world today are affected by Alzheimer disease.

In America estimated 6.2 million American's are affected from AD. This number can grow to 13.8 million by 2060.There are more than 121,499 deaths recorded due to the AD in 2019. Between 2000 and 2019, deaths from stroke, heart disease and HIV decreased, whereas reported deaths from AD increased more than 145% [7]. The number of people living with dementia in the European Union (EU27) is estimated to be 7,853,705 and in European countries represented by AE members, 9,780,678. Compared to its earlier estimates, this constitutes a significant reduction from 8,785,645 for the EU27 and from 10,935,444 for the broader European region.

- Women continue to be disproportionately affected by dementia with 6,650,228 women and 3,130,449 men living with dementia in Europe.
- The numbers of people with dementia in Europe will almost double by 2050 increasing to 14,298,671 in the European Union and 18,846,286 in the wider European region [8]

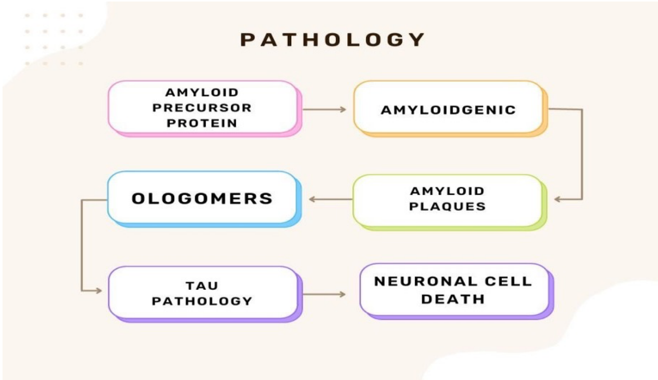
In India, the most of evidence indicates that neurodegenerative conditions are a significant public health issue wherein over 4 million Indian peoples have been affected. According to the Dementia India Report 2010 by the Alzheimer's and Related Disorders Society of India (ARDSI), there were around 3.7 million Indians with dementia in 2010 with the number projected to rise to 7.6 million by 2030.[9]

➢ PATHOPHYSIOLOGY

Neurotoxic Aβ is generated by cleaving of APP, and through the aggregation of soluble oligomers, occurs the formation of senile plaques, which is a major neuropathological marker of AD [10]. APP acts as a substrate for two enzymes as identified. They are α- secretase and β-secretase. These two enzymes cleave the extracellular domain of APP, which results in two soluble N-terminal peptides, namely APPsα and APPsβ respectively, as well as C-terminal fragments CTFα and CTFβ which are bound to the cell membrane. Next, proteolysis occurs. The transmembrane peptides CTFα and CTFβ are cleaved inside the membrane by a third enzyme, γ-secretase. This causes extracellular release of the p3 peptide from CTFα and of β-amyloid (Aβ) from CTFβ. The peptide p3 which is soluble, has no tendency to aggregate. conversly β-amyloid tends to aggregate[11-12].

β-amyloid may have 40-42 amino acids.This varies because of the variations of the site at which y-secreates cleaves the protein chain [13].The most neurotoxic form is AB.Which aggregates and bind to AMPA recepters and Ca+ levels thereby inceasing the influx of Ca is increases [14].This will leads to apoptosis of the neuronal cell an lead to cell deaths[15].Also,these aggregates leads to local inflammatory responses, which causes neuronal cell death[16].

During the accumulation process, Aβ produces hydrogen peroxide, which is potentiated by Fe^{2+} and Cu^{2+} ions. Cu^{2+} ions trapped within Aβ are electrochemically active and are capable of producing reactive oxygen species (ROS) [17]. These ROS cause peroxidation of lipids in neuronal cell membranes making the glucose transporters and ion channel ATPase's dysfunctional. This disturbance to cellular ion homeostasis and metabolism, caused by oxidative stress from Aβ, leaves the neurons susceptible to apoptosis [18]. Deposition of Aβ plaques initiates hyperphosphorylation of tau protein, which is a structural protein associated with the cytoskeleton of neurons, resulting in misfolding of tau protein and the formation of aggregates names nerifibirlliary angles (NFTs). These lead to impair communication between neurons and finally, death of the nueron cells [19].



RISK FACTORS

➢ AGE

Many epidemiology studies, agree that of various, agree that of the various demographic factors such as age, gender, race and social class, age is one of the most important risk factors for cognitive decline and AD [20]. With advancing age, the prevalence of AD increases to an estimated 19% in individuals 75-84 years of age [21] and to 30-35%, possibly up to 50% for those older than 85 years [22]. That AD could therefore be an accelerated form of normal aging is largely based on the observation that many of the pathological changes identified in AD are similar, apart from their severity to those present in normal aging. Hence, in cognitively normal brain, there is an age-related [23]

➢ HYPERTENSION.

Sixteen papers from ten studies reported on hypertension as a risk factor for AD. Nine papers from seven studies reported that hypertension was not a risk factor for AD [24]. According to two articles from the Kungsholmen Project, however, hypertension had the potential to become a risk factor depending on the parameters. The first article reported that a systolic blood pressure equal to or greater than 160 mm Hg did not affect risk significantly [25], while the second reported that a systolic blood pressure greater than 180 mm Hg significantly increased risk [26].Additionally, the first paper reported that a low diastolic blood pressure (less than 70 mm Hg) increased risk and the second reported that a very low diastolic blood pressure (less than or equal to 65 mm Hg) also increased risk of Alzheimer [27].

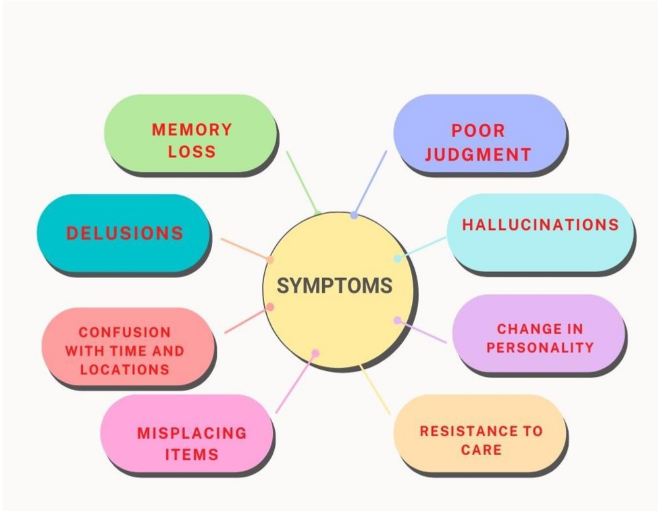
➢ CARDIOVASCULAR

Several studies consistently reported an increased risk of dementia and AD in association with vascular and metabolic risk factors, such as hypertension, hypercholesterolemia, obesity at midlife, diabetes mellitus, and atherosclerosis. Recognition that dementia and other chronic diseases share several risk factors has led international bodies, such as the World Health Organization (WHO), to promote broad preventive efforts. Evidence suggests that vascular pathological conditions promote the neuropathological hallmarks of AD. For example, vascular insufficiency causing decreased cerebral blood flow is thought to activate Aβ cleavage and its accumulation. Abnormalities in the blood brain barrier caused by vascular disease are associated with inflammatory and immune responses, which can initiate neurodegenerative pathways. Vascular risk factors are involved in the conversion from mild cognitive impairment (MCI) to AD because several studies have found that controlling vascular factors (such as hypertension and hypercholesterolemia) in patients with MCI delayed progression toward dementia. In this section, we review the main findings for vascular factors and their associated risk AD. [28].

➢ STRESS

Preclinical studies have suggested that manipulation of the glucocorticoid milieu can trigger cellular, molecular and behavioral derangement resembling the hallmarks of Alzheimer's Disease (AD). For example, stress or glucocorticoid. administration can increase amyloid ß precursor protein and tau phosphorylation which are involved in synaptic dysfunction and neuronal death associated with AD.[28]

➢ SYMPTOMS



➢ PSYCHOLOGICAL SYMPTOMS

1. **delusions** (prevalence ranges from 10% to 73%; delusion of persecution is the most common) [29]
2. **hallucinations** (12%-49%; visual hallucinations are the most common), misidentifications (affecting 16% of patients with AD)[30].
3. **depression** (diagnosis is very difficult in patients with dementia), apathy (one of the most common symptoms, with over 50% patients affected), and anxiety.

➢ Behavioural symptoms

1. **walkabout** (one of the most problematic), agitation/aggression,
2. **resistance to care**, inappropriate sexual behaviour, and catastrophic reactions (anger, verbal and physical aggression).

Although each type of dementia has different psychological symptoms, patients may also display symptoms that are not typical of the type of dementia that they have.[31]

➢ SOME COMMON SYMPTOMS

1. memory loss, for examples two items were uses to assess this symptoms, like continuous in remembering bring where the keys or glasses were placed.
2. Difficulty performing familiar tasks. One item was used to assess this symptom: 'Having difficulties completing everyday tasks.
3. Problems with language. One item was used to assess this symptom: 'Inability to remember simple words.
4. Disorientation to time and place. One item was included to assess this symptom: 'Inability to remember the way back home'.

5. Poor or impaired judgment. One item was used to assess this symptom: 'Having judgment problems, such as wearing a coat in a hot summer evening'.
6. Problems with abstract thinking. One item was used to assess this symptom: 'Having difficulties with light math calculations.
7. Changes in mood or behavior. Two items were used to assess this symptom: 'Having crying spells', and 'Having anger attacks.
8. Changes in personality. One item was used to assess this symptom: 'Having sudden changes in personality'.
9. Loss of initiative. One item was used to assess this symptom: 'Passivity [32].

➢ TREATMENT

The treatments of choice in Alzheimer's disease (AD) are cholinesterase inhibitors and NMDA-receptor antagonists, although doubts remain about the therapeutic effectiveness of these drugs. Herbal medicine products have been used in the treatment of Behavioral and Psychological Symptoms of Dementia (BPSD) but with various responses.[33]. The treatments of Alzheimer's disease are through cholinesterase inhibitors or NMDA-receptor antagonists, while doubts remain about the therapeutic efficacy of these drugs thus herbal medicine product have been used in the cure of Behavioral and Psychological Symptoms of Dementia. The genes play an important role in the development of Alzheimer's disease. Although some Food and Drug Administration approved drugs which are available for the treatment of Alzheimer's disease, the outcomes were not good enough, and there is a place for alternative medicine, that is, herbal medicine. Herbal remedies for Alzheimer's disease have become more and more popular in the recent years, some herbs that is Ginger, Turmeric, Liquorice, Ginseng, Sage, Rosemarry and etc mention below are useful for cognitive impairment of Alzheimer's disease. This paper reviews the clinical effects of a synthetic drugs and herbal medicines for the treatment of Alzheimer's disease.[34]

➢ *MEDICINAL DRUGS TO TREAT ALZHEIMER*

➢ *CurcumalongaL. (*Zingiberaceae*)*

Curcuma longa (Turmeric, Harida) has been used as a source of Curcumin (diferuloylmethane), an orange-yellow component of turmeric or curry powder. Studies have proved that Curcumin has anti-inflammatory and antioxidant activities, and it helps in combating Alzheimer's Disease (AD). Regular consumption of this herb helps in keeping the mind balanced. The dose of curcumin can be reduced by making it to colon targeting.[35]

➢ Matricariarecutita (Asteraceae)

German Chamomile is said to stimulate the brain, dispel weariness, calm the nerves, counteract insomnia, aid in digestion, break up mucus in the throat and lungs, and aid the immune system.[36]

➢ Collinsoniacanadensis (Lamiaceae)

Horsebalm (*Monarda*) has been reported to prevent the breakdown of acetylcholine. The chief chemical constituents of horsebalm are carvacol and thymol which are used for AD. Normally our body's protective blood-brain barrier helps prevent harmful substances in the blood from reaching the tissues of the brain. However, it can also prevent helpful medicines from reaching the brain. The horsebalm compounds seem to cross that great divide. Horsebalm is even used as an herbal shampoo by adding a few drops to your normal herbal shampooChamomile can relieve anxiety, and in higher doses, leads to drowsiness, according to the University of Maryland Medical Center.[37]

➢ Huperzine

A Huperzine A is a chemical derived from a particular type of club moss (Huperzia serrata). Like caffeine and cocaine, huperzine A is a medicinally active plantderived chemical that belongs to the class known as alkaloids. This substance is really more a drug than an herb, but it is sold over the counter as a dietary supplement for memory loss and mental impairment. According to three Chinese double-blind trials enrolling a total ofmore than 450 people, use of huperzine A can significantly improve symptoms of AD and other forms of dementia.Y5- 37 One double-blind trial failed to find evidence of benefit, but it was relatively small.[38] **Vinpocetine** is a chemical derived from *vincamine*, a constituent found in the leaves of *Catharanthusroseus*, common name periwinkle (Vinca minor) as well as the seed of various African plants. It is used as a treatment for memory loss and mental impairments. Studies have demonstrated that Vinpocetine posse's potential to enhance cerebral blood flow] and neuroprotective effects. It issued as a drug in Eastern Europe for the treatment of cerebrovascular disorders and age-related memory impairment [39]. Several double-blind studies have evaluated vinpocetine for the treatment of AD and related conditions. The clinical trials of Vinpocetine on 728 patients with AD have produced significant result in the improvement of Alzheimer's disease. Further, a 16-week double-blind placebo-controlled trial of Vinpocetine on 203 patients with mild to moderate dementia produced significant benefit in the treated group. Several clinical studies have also been conducted to prove the beneficial effects of this drug in the treatment of Alzheimer's and severe conditions., even this trial had several technical limitations, and the authors of their view concluded that vinpocetine cannot yet be regarded as a proven treatment. Currently, several better-quality trials are underway.[40]

➢ **TREATMENT OF AD USING DRUG THERAPY**

➢ **Donepezil**

Donepezil is a reversible, selective anticholinesterase that was approved for use in Alzheimer's disease in 1996. As compared with tacrine and physostigmine, donepezil has minimal peripheral anticholinesterase activity and a longer plasma half-life, allowing for once-daily administration.[41] Two 24-week clinical trials of donepezil including a total of 1291 patients with Alzheimer's disease who received either 5 mg or 10 mg of donepezil per day resulted in up to a 4.1 percent decrease in the score on the cognitive subscale of the Alzheimer's Disease Assessment Scale and a 6.3 percent decrease in the score on the Clinician's Interview-Based Impression of Change scale (Table 3).[42] Approximately 80 percent of patients receiving either dose of donepezil completed the studies. The most frequent adverse effects were nausea, diarrhea, and vomiting; insomnia occurred in up to 14 percent. The once-a-day regimen and the drug's reasonable tolerability and efficacy have made donepezil widely used in patients with Alzheimer's disease.[43]

➢ **Eptastigmine**

Epstastigmi is a carbamate derivative of physostigmine and a reversible inhibitor of anticholinesterase.24 In two 24-week trials, over 700 patients were randomly assigned to receive either a low dose (45 mg daily) or a high dose (60 mg daily) of eptastigmine or placebo.[44]The patients given 45 mg or 60 mg of eptastigmine had a 3 percent reduction in the score on the cognitive subscale of the Alzheimer's Disease Assessment Scale and a 5 percent reduction in the score on the Clinician InterviewBased Impression of Change scale (Table 3).Gastrointestinal adverse effects were similar in frequency in the eptastigmine and placebo groups, as was the frequency of discontinuation. Sinus bradycardia was more frequent in the eptastigmine group. A dose-dependent transient granulocytopenia occurred in 6 percent of the high-dose group, as compared with 2 percent in the low-dose and placebo groups. The adverse hematologic effects reported in these two studies [45] have resulted in the suspension of further clinical trials.

➢ **Metrifonate**

Metrifonate (trichlorfon), an anthelmintic drug with no anticholinesterase activity, undergoes nonenzymatic hydrolysis to dichlorvos, a pseudoirreversible inhibitor of anticholinesterase.[42] Its plasma half-life is longer than that of physostigmine or donepezil, and it rapidly enters the brain.[46] In two 12-week clinical trials in 530 patients, there was a 4 percent decrease in the score on the cognitive subscale of the Alzheimer's Disease Assessment Scale and the Clinician Interview-Based Impression of Change scale in patients treated with metrifonate.[47]In a 26-week trial in 408 patients given a higher dose, the improvement was similar.The most common adverse effects were diarrhea (18 to 19 percent of patients) and leg cramps (9 percent). Leg cramps and muscle weakness have occurred in phase 3 trials of this drug.[48].

➢ **\Nanotechnology**

A number of new molecular entities (NMEs) selected for full-scale development based on their safety and pharmacological data suffer from undesirable physicochemical and biopharmaceutical properties, which lead to poor pharmacokinetics and distribution after *in vivo* administration. An optimization of the preformulation studies to develop a dosage form with proper drug delivery system to achieve desirable pharmacokinetic and toxicological properties can aid in the accelerated development of these NMEs into therapies. Nanoparticulate drug delivery systems show a promising approach to obtain desirable druglike properties by altering the biopharmaceutics and pharmacokinetics properties of the molecule. Apart from the advantages of enhancing potential for systemic administration, nanoparticulate drug delivery systems can also be used for site-specific delivery, thus alleviating unwanted toxicity due to nonspecific distribution, improve patient compliance, and provide favorable clinical outcomes.[49] Recent nanotechnological advancements have the potential to offer large scale effective diagnostic and therapeutic options. Targeted drug (e.g., Rivastigmine) delivery with the help of nanoparticles (NPs) in the range of 1-100 nm diameters can effectively cross the blood brain barrier with minimized side effects. Moreover, biocompatible nanomaterials with increased magnetic and optical properties can act as excellent alternative agents for an early diagnosis. It is quite likely that this approach can end up providing remarkable breakthroughs in early stage diagnosis and therapy of AD. [50]

➢ **DRUG DELIVERY**

In order for a drug to have its maximum therapeutic effect, it is important for the drugs to retain its bioavailability, pharmacodynamics, and pharmacokinetics. Hence, the integration of a drug into or onto a polymeric and/or lipidic nanoparticle (NP) is aimed at greatly enhancing the pharmacotherapy effect of a drug. The use of nanoparticles is beneficial in drug delivery process as it increases the bioavailability of a drug by improving the aqueous solubility and increases the drug half-life which in turn reduces the rate of drug clearance as well as delivering the drug to its targeted site of action [51].

➢ Nanoparticles for AD treatment

BBB crossing NPs have been proposed as intriguing tools potentially able to solve the unmet problem of enhancing transports of drugs from the blood to brain, in particular by the functionalization of their surface with BBB targeting agents. Liposomes, solid lipid NPs (SLN), polymeric NPs and gold NPs are the most studied NPs for brain drug delivery, due to their common features of biocompatibility, stability, biodegradability, nontoxicity, limited antigenicity and suitability for surface functionalization. Moreover, they can incorporate both hydrophobic and hydrophilic drugs and a controlled drug release can be achieved.

Liposomes are spherical vesicles (20 nm–500 µm of size) in which an aqueous inner volume is enclosed by a membrane bilayer usually composed of naturally occurring phospholipids and cholesterol [52].

SLN are nanospheres (50–1000 nm of size) composed by lipids that are solid at physiological temperature, stabilized by physiologically compatible emulsifiers. SLN are very stable NPs that can be produced easily on a large scale [53].

Polymeric NPs are nanosized carriers (1–1000 nm), made of natural or synthetic polymers [54].

Gold NPs (1–150 nm of size) are the most stable metal NPs with unique optical, electronic and magnetic properties exhibited at nanoscale level. Interestingly, gold NPs have been shown to reach the brain and accumulate in neurons even in the absence of any specific functionalization, with a mechanism that is still to be understood.[55]

STERLIZATION USING NANOPARTICLE

Silver nanoparticles have been used extensively in the medical field such as medical devices and drug formulations. The citrate-stabilized silver NP size ranges from 20 to 80 nm can be sterilized directly via γ-radiation and autoclave. The silver NPs were introduced to a compound producer of hydroxy radicals, enabling the replication of the sterilization-based changes in size and morphology which inferred a free radical mechanism of action. Additionally, it was observed that the sterilized silver NPs have a likelihood of causing platelet accumulation, which is an in vitro indicator thrombogenicity, in comparison to the unsterilized silver NPs that were used as controls [56].

➢ INORGANIC NANOPARTICLES

Gold nanoparticles- Targeting amyloid-b (Ab)-induced complex neurotoxicity has received considerable attention in the therapeutic and preventive treatment of Alzheimer's disease (AD). The complex pathogenesis of AD suggests that it requires comprehensive treatment, and drugs with multiple functions against AD are more desirable. Herein, AuNPs@POMD- pep (AuNPs: gold nanoparticles, POMD: polyoxometalate with Wells–Dawson structure, pep: peptide) were designed as a novel multifunctional Ab inhibitor. AuNPs@POMD-pep shows synergistic effects in inhibiting Ab aggregation, dissociating Ab fibrils and decreasing Ab-mediated peroxidase activity and Ab-induced cytotoxicity. By taking advantage of AuNPs as vehicles that can cross the blood–brain barrier (BBB), AuNPs@POMD-pep can cross the BBB and thus overcome the drawbacks of small-molecule anti-AD drugs.[57]

➢ PD HYDRIDE NANOPARTICLES

Therefore, how to realize the *in situ* sustained release of hydrogen is of key importance to enhance the efficacy of AD treatment.

In this work, we designed the small-sized Pd hydride (PdH) nanoparticle as highpayload hydrogen carrier and Pd-similar self-catalyst to realize the *in situ* sustained release of bio-reductive hydrogen for the first time. PdH nanoparticle could selectively

scavenge highly cytotoxic OH in AD model cells by releasing bio-reductive hydrogen in a self-catalysis way and could ameliorate mitochondria dysfunction and promote cellular energy metabolism, inhibiting cellular apoptosis. The administration of PdH nanoparticle suppressed the over-expression of APP, BACE1 and sAPPβ, and consequently reduced the over- generation of Aβ in AD model cells and mice, blocking the progression of AD. The PdH treatment of 3 × Tg-AD mice remarkably ameliorated the cognitive impairment, synaptic deficits and neuronal death.[58]

Amin et al. (2017) evaluated nanoparticle-based drug delivery approach for the treatment of Alzheimer's disease. In the study, fluorescent magnetic nanoparticles were exploited for delivery to the brain cells of normal mice under functionalized magnetic field. The fluorescent magnetic nanoparticles successfully crossed the blood–brain barrier and reached the brain cells. According to Wen et al. (2017), it is possible to deliver the drugs by different routes using nanotechnology-based drug delivery systems, and it can be considered as promising tools to improve patient compliance and achieve better therapeutic outcomes in patients suffering from Alzheimer's disease.[59]

- **Vitamin d loaded PGLA nanoparticles**

According to Seong Gak Jeon et al the aggregation and accumulation of amyloid beta (Aβ) peptide is believed to be the primary cause of Alzheimer's disease (AD) pathogenesis. Vitamin D-binding protein (DBP) can attenuate Aβ aggregation and accumulation. A biocompatible polymer poly (D, L-lactic acid-co-glycolic acid) (PLGA) can be loaded with therapeutic agents and control the rate of their release. In the present study, a PLGA-based drug delivery system was used to examine the therapeutic effects of DBP-PLGA nanoparticles in Aβ- overexpressing (5XFAD) mice. DBP was loaded into PLGA nanoparticles and the characteristics of the DBP-PLGA nanoparticles were analyzed. Using a thioflavin-T assay, we observed that DBPPLGA nanoparticles significantly inhibited Aβ aggregation in vitro. In addition, we found that intravenous injection of DBP-PLGA nanoparticles significantly attenuated the Aβ accumulation, neuroinflammation, neuronal loss and cognitive dysfunction in the 5XFAD mice. Collectively, they suggest that DBP-PLGA nanoparticles could be a promising therapeutic candidate for the treatment of AD. [60]

CONCLUSION

Liposomes, solid lipid NPs (SLN), polymeric NPs and gold NPs are the most studied NPs for brain drug delivery, due to their common features of biocompatibility, stability, biodegradability, nontoxicity, limited antigenicity and suitability for surface functionalization. The administration PdH nanoparticle suppressed the overexpression of APP, BACE1 and sAPPβ, and consequently reduced the overgeneration of Aβ in AD model cells and mice, blocking the progression of AD. Collectively, they suggest that DBP-PLGA nanoparticles could be a promising therapeutic candidate for the treatment of AD.

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