



Review Article

HERBAL DRUG LOADED NANOPARTICLES FOR TARGETED BRAIN DELIVERY THERAPY OF ALZHEIMER'S DISEASE

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ABSTRACT

Alzheimer's disease is a progressive neurodegenerative disorder characterized by cognitive decline and neuronal loss. It is common worldwide among older people. In this review, summarize the recent advancements in nanotechnology-based drug delivery systems for loaded herbal drugs such as Curcuma longa, quercetin, Bacopa monnieri (Brahmi), Withania somnifera (Ashwagandha), Ginkgo biloba, Salvia officinalis, etc. They possess anti-inflammatory, antioxidant, anti-amyloidogenic and neuron-protective properties. With the continuous increase in prevalence of Alzheimer's disease, there a growing need to better understand its pathogenesis, enhance diagnostics strategies, and develop more effective therapeutic interventions.

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INTRODUCTION

Alzheimer's disease is the most common cause of dementia in elderly individuals. According to the World Alzheimer Report 2025, there were 50 million people with dementia globally. Around 7.2 million older adults in the U.S. will have Alzheimer's disease in 2025. Currently in India, approximately 8.8 million people suffer from dementia. Most of the cases are in people aged 60 or above. Account for an estimated 60-70% of all dementia cases. As of the most recent date, China is ranked as the first country with the largest number of people living with Alzheimer's disease in the older age group. The reason behind its aging population, urbanized lifestyle, and chronic lifestyle.

Alzheimer's disease affects the brain with major changes— amyloid beta plaques and neurofibrillary tangles. Herbal drugs and plant-based compounds show strong neuro protective effects. ^[1] The blood-brain barrier is a major challenge in delivering drugs to the brain. Small engineered nanoparticles can cross the blood-brain barrier, helping drugs reach the brain and improve Alzheimer's disease treatment. For effective therapy a drug must have good bioavailability and proper pharmacokinetics. This approach improves drug solubility, extends half-life, and facilitates targeted delivery to the intended site of action.

Clinical symptoms of AD -

1. loss of memory
2. problem in abstract thinking
3. problems in speaking, reading & writing
4. Difficulty to elaborating thoughts

PATHOPHYSIOLOGY OF ALZHEIMER'S DISEASE

The understanding of Alzheimer's disease pathology is important for treatment strategies. Scientists are researching and studying changes that occur in Alzheimer's disease. At present, there is no cure for Alzheimer's disease, but there is ongoing research to better understand this disease. ^[2,3] The main pathological hallmarks of Alzheimer's disease are:

1. Amyloid plaque: abnormal deposits formed by amyloid beta(A β) protein outside neuron.
2. Neurofibrillary tangles: twisted fibers made of tau protein inside neurons.

The most extensively investigated hypothesis in Alzheimer's disease research includes:

1. Amyloid hypothesis – build-up of A β protein damages brain cells.
2. Tau hypothesis – abnormal tau protein forms tangles inside neurons.
3. Neuroinflammation hypothesis – long-term brain inflammation harms neurons.
4. Mitochondrial dysfunction hypothesis – Problem energy production leads to cell damage.

Recent research also shows that the **Gut-Brain axis** may play a role. Changes in gut bacteria can affect brain function and may influence memory and thinking ability in Alzheimer's disease.

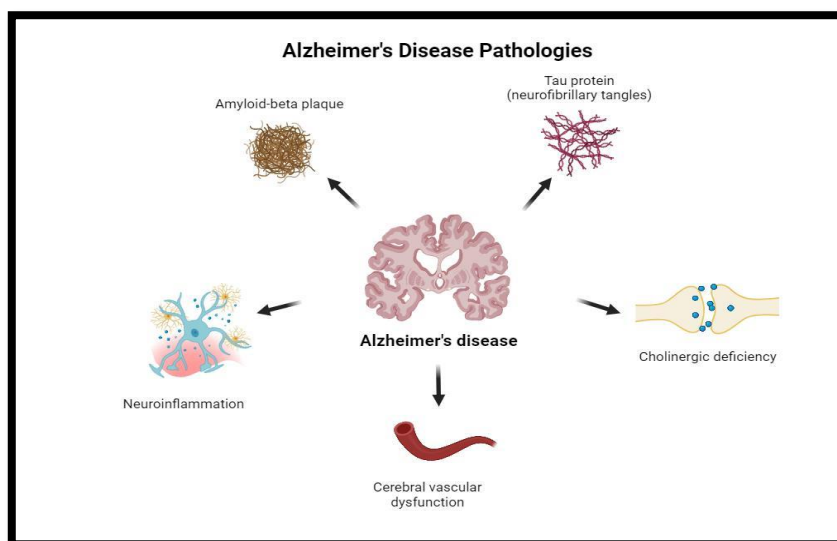


Figure no. 1 – Key hypothesis investigated by Alzheimer's Disease

Amyloid Hypothesis :

It suggests that amyloid beta protein builds up in the brain and forms plaques. This buildup of triggers inflammation, oxidative stress, and damage to synapses, leading to brain cell death and memory loss in Alzheimer's disease. ^[4] Recent identification of novel enzymes and pathways regulating A β production has expanded therapeutic targets.

Artificial intelligence (AI) is helping accelerate drug discovery in this area. ^[5]

Tau Hypothesis:

It states that abnormal tau protein accumulation in the brain plays a key role in Alzheimer's disease. Tau helps maintain neuron structure by stabilizing microtubules. In Alzheimer's disease, abnormal forms called neurofibrillary tangles, damage the cell transport systems and leading to neuronal death and cognitive decline. ^[6]

Future research focuses on developing tau -targeted therapies early diagnostic imaging techniques, and drugs to prevent tau aggregation. Understanding specific toxic tau forms may help to design more effective disease modifying treatments.

Neuroinflammation Hypothesis:

I suggest that chronic brain inflammation plays a major role in Alzheimer's disease progression. In AD, immune cells called microglia they overactivated due to amyloid- β and



abnormal tau releasing inflammatory molecules and oxidative stress factors that damage neurons. [7]

Focus on developing therapies that regulate microglial activity, reduce harmful inflammation target inflammatory cytokines and receptors, and modulate the gut–brain axis through microbiome-based intervention to slow or prevent disease progression. [8]

Mitochondrial Dysfunction Hypothesis:

The mitochondrial hypothesis suggests that impaired mitochondria contribute significantly to Alzheimer's disease. In AD, mitochondria reduced in number, structurally damaged and poor in energy production leading to oxidative stress, inflammation, and neuronal death. Copper imbalance further damages mitochondria by increasing reactive oxygen species and promoting amyloid- β and tau aggregation. [9]

Focus on therapies that restore mitochondrial health including antioxidants, copper chelates enhances mycophagy and stimulators of mitochondrial Targeting mitochondrial function may offer a promising disease-modifying strategy for slowing down AD progression. [10]

ALZHEIMER'S DISEASE THERAPEUTIC CHALLENGES

Blood-brain barrier and drug –

The blood brain plays central role in regulating drug permeability and maintaining the central nervous system. Structurally the BBB consists of tightly sealed endothelial cells with tight junctions, efflux transporters such as P-glycoprotein, and metabolizing enzymes that collectively limit drug permeability and reduce therapeutic efficacy. Nanotechnology-based drug delivery systems get strategies to overcome these limitations by receptor mediated transport, modulation of tight junctions and surface functionalization to enhance BBB. [11]

Future perspective of BBB as a therapeutic target for Alzheimer's Disease:

BBB Dysfunction In AD :

- Tight junction loss
- transporter dysfunction
- Increased permeability

AD Pathology :

- A β accumulation
- Neuroninflammation
- Neuronal injury

Nano - delivery strategies :

- targeted Nanoparticle
- Efflux pump evasion
- Nose to brain delivery

Future Precision Therapies :

- Herbal Nanoformulation
- Stage-specific treatment
- Theranostic Nanomedicine

Figure 2 BBB–targeted Nano therapies for Advanced Alzheimer’s Treatment [28,29,30,31]

LIMITATIONS OF CONVENTIONAL THERAPIES (CHOLINESTERASE INHIBITORS: DONEPEZIL, RIVASTIGMINE & GALANTAMINE)

Currently approved drugs for cognitive decline in Alzheimer’s disease such include cholinesterase inhibitors (donepezil, rivastigmine, galantamine) The NMDA receptor antagonist memantine. These agents enhance cholinergic neurotransmission by inhibiting acetylcholinesterase, by increasing acetylcholine levels the brain. Memantine, is recommended for patients with moderate to severe Alzheimer’s disease. These drugs provide symptomatic relief by improving neurotransmitter balance but do not cure and stop disease progression. [12]

Mechanism of action of cholinesterase inhibitor:

The inhibiting acetylcholinesterase in the case of rivastigmine by butyrylcholinesterase (BuChE). This inhibition prevents the breakdown of acetylcholine, a neurotransmitter essential for memory, learning, and attention. The galantamine also acts as allosteric modulator of the nicotinic acetylcholine receptor, further enhancing synaptic transmission.

Therapeutic Effects-

1. Enhanced memory & learning
2. Stabilization of cognitive symptoms

Future strategies for cholinesterase inhibitors focus on improving their effectiveness and safety. These include nanocarrier based delivery system to enhance brain penetration, multitarget drugs, combination therapy, novel receptor modulation techniques overall these developments providing both cognitive and neuroprotective benefits.

Herbal Phytochemicals with Neuroprotective Potential

Herbal phytochemicals exhibit significant neuroprotective potential in Alzheimer's Disease; their clinical translation is limited by poor solubility, low bioavailability, rapid metabolism, and restricted permeability across the BBB. Nanotechnology-based drug delivery systems have emerged as strategies to overcome these limitations by enhancing stability, targeted delivery, and controlled release of herbal bioactives.

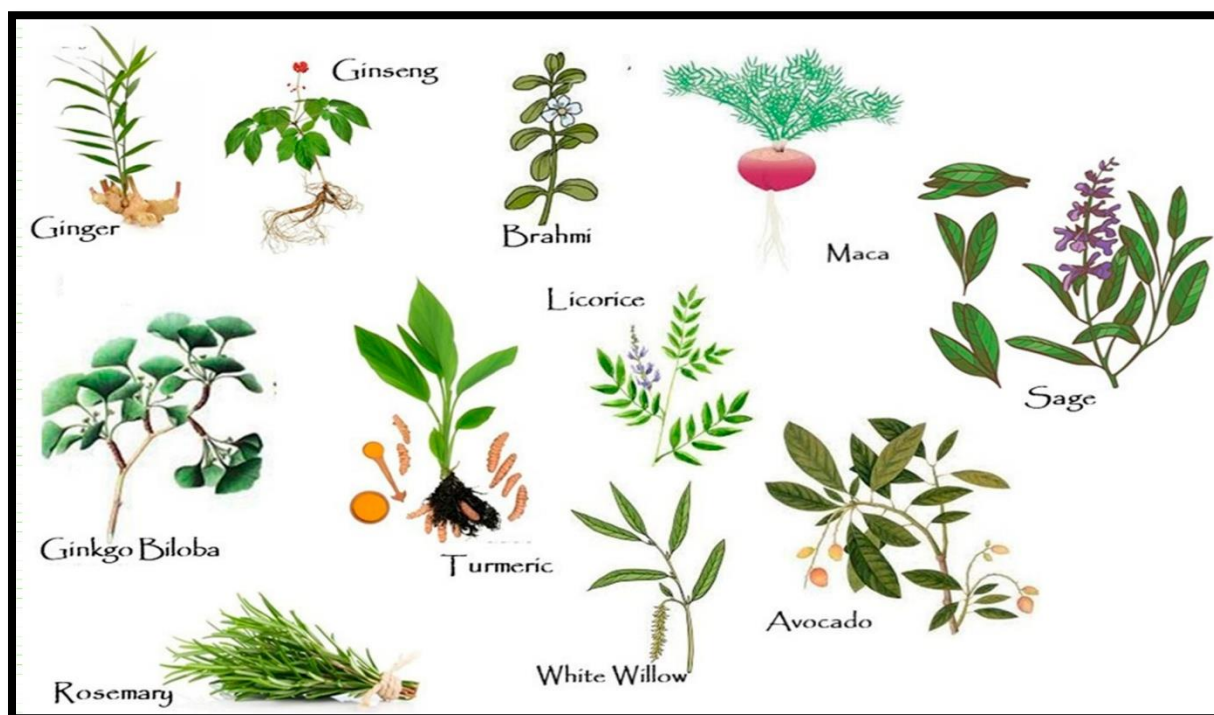


Figure 2- Herbs contribute treatment of Alzheimer's Disease [27]

This includes representative phytochemicals-

Curcumin – (*Curcuma longa*), Turmeric:

Curcumin shows strong potential as a therapeutic agent for Alzheimer's disease due to its multi-target actions. In preclinical studies it is demonstrated that curcumin reduces A β plaque deposition in both In-vitro and In vivo models. ^[13] Particularly when delivered via nanotechnology to overcome poor bioavailability and limited BBB permeability. Curcumin exhibits anti-amyloid, anti-inflammatory, and neuroprotective properties that target multiple AD pathways. ^[14]

Mechanism of curcumin formulation in AD:

Easy Mnemonic – **Brain**

	Meaning	What Curcumin Does	Overcome
B	BBB crossing	Nano formulations help curcumin reach the brain	Better drug delivery
R	Reduce plagues	Inhibit A β aggregation	Less brain damage
A	Antioxidant	Reduce oxidative stress	Protects neuros
I	Inflammation control	Lowers TNF- α , IL-1 β , calms microglia	Reduce neuroinflammation
N	Neuroprotection	Protects tau & synapses	Improved memory

Quercetin:

Quercetin is a plant-derived flavonoid widely used as one of the most potent natural antioxidants. Quercetin exhibits multiple beneficial effects on human health. It also acts as anti-carcinogenic, anti-infective and psychostimulant agent. Additionally, quercetin inhibits lipid peroxidation and platelet aggregation while promoting mitochondrial biogenesis it supports cellular energy metabolism and reduces oxidative stress. ^[15]

Several experimental studies have neuroprotective effects of quercetin in both In-vivo and In-vitro models. Emerging evidence suggests that quercetin may improve cognitive function through its anti-oxidant activity. Future research on quercetin for AD should prioritize improved brain delivery, advanced nanotechnology, and preclinical validation. Integration with precision medicine and preventive strategies may allow quercetin to emerge as disease modifying and neuroprotective agent.

Bacopa monnieri – (Brahmi)

Bacosides, the major active saponins in *Bacopa monnieri*, are promising for treating Alzheimer's disease because they reduce inflammation, fight oxidative stress, and prevent A β plaque formation. Preclinical studies demonstrate that bacosides exert anti-inflammatory and antioxidant effects, reduce pro-inflammatory cytokines and reactive oxygen species while enhancing endogenous antioxidant enzymes there by protecting neurons from oxidative stress-induced damage.^[16]

Clinical evidence is limited and variable in quality, including small randomized controlled trials comparing *B. Monnieri* extract place Boorst and t Collectively, these findings show that bacosides and *B. Monnieri* extract has therapeutic properties in AD, but well-designed, larger clinical trials are still needed to confirm efficacy and clarify safety profiles.

Resveratrol:

It is also called 3,5,4'-trihydroxystilbene is a natural polyphenol with a molecular weight 228.25g/mol. Its three hydroxyl groups are critical for its antioxidants, anti-inflammatory, antimicrobial and neuroprotective effect.^[17] These groups allow RSV to scavenge free radicals, chelate metals and interact with proteins, influencing biological activity and therapeutic potential. RSV is found in grapes, berries, peanuts, red wine. A plant-produced antimicrobial compound protects plants from stress, pathogens and UV damage.^[18]

Pharmacokinetics and Bioavailability:

It shows strong pharmacological effects RSV has low bioavailability, it is rapidly metabolized by enzymes like cytochrome P450 and glucuronosyltransferase. Over 20 RSV metabolites have been identified that may influence activity. Combining RSV with extra virgin olive oil has been shown to enhance antioxidant and anti-inflammatory effects potentially improving brain health and slowing age -related cognitive decline.

NANOPARTICLES AS DRUG CARRIERS IN ALZHEIMER'S DISEASE

Solid lipid nanoparticles

It is lipid based nanocarriers used for drug delivery. They commonly prepared high-pressure homogenization a solvent free, biocompatible and scalable method using water as the medium.^[19] SLNs encapsulate both hydrophilic and lipophilic drugs, protecting enzymatic or chemical degradation enhance drug stability. They improve drug bioavailability prolong blood circulation time and unable targeted delivery to the brain by cross BBB through receptor. Additionally, SLNs create drug concentration gradient, induce tight junction modulation and substained drug release making the promising carriers for CNS targeted therapies.^[20]

Liposomes:

Liposomes are spherical vesicles composed of lipid bilayer that encapsulates a hydrophilic core for deliver drugs. ^[21] The most liposome range 50 to 500 nm, which influence cellular uptake and tissue distribution. Liposomes can be surface functionalized with ligand; their lipid composition can be adjusted to achieve controlled or sustained drug release. They are biocompatible, biodegradable and improve drug stability and delivery across biological barriers. ^[22]

Polymeric nanoparticles:

NPs range from 1-1000 nm and synthesized from synthetic and natural material, allowing precise control of their size, shape and surface properties for specific applications. ^[23] For Alzheimer's disease, brain-targeting synthetic polymer like chitosan and PLGA are used. Surfactants can improve BBB penetration by increasing endothelial membrane fluidity. ^[24] Nasal administration is a route enhanced by PEGylation and antibodies to prolong residence time. (For example – poly (n-butyl cyanoacrylate) NPs coated with polysorbate 80 effectively delivered tacrine to the brain in mice) show better evidence. ^[25]

Nanoparticles as a herbal drug carriers in Alzheimer's disease:

1. Solid lipid nanoparticles -Curcumin- BBB crossing & sustained release –improved memory.
2. Liposomes - Quercetin – Targeted delivery – Reduce oxidative stress, improve cognitive function.
3. Polymeric NPs - Bacopa Monnieri – controlled release – neuroprotection, improved learning.

PRECLINICAL EVIDENCES

- **Curcumin** - Improved memory and learning in transgenic AD models, reduce A β plaque deposition.
- **Enhancement via nanoparticles** – deliver through SLNs and Nano emulsions that combine anti-amyloid, antioxidants optimize bioavailability for clinical translation in AD
- **Quercetin** – Reduced neuroinflammation, cognitive deficits in rodent AD models.
- **Resveratrol** – Reduced neuronal death and oxidative stress in rodent AD models.
- **Bacopa Monnieri** – Improved learning and memory, reduced neuronal oxidative damage.

Translational Challenges and Future prospects

Clinical trial gaps:

Although numerous nanoparticle formulations show efficacy in animal models of AD. (For example, lipid- based nanoparticles such as intranasal APH - 1105 have entered only early-phase clinical evaluation. ^[26]

Key barriers include:

- lack of clinical validation
- heterogeneous disease presentation

Bioavailability and pharmacokinetic barriers:

Systemic bioavailability and controlled release in humans remain challenging. Variability in particle size and surface chemistry influences pharmacokinetics and therapeutic outcomes.

The Challenge includes

The following Unpredictable in-vivo behavior:

Nanoparticles may undergo protein corona formation and rapid clearance by immune cells, impacting therapeutic efficacy.

Long term stability:

Physicochemical instability such as aggregation or gradation during storage, can reduce bioavailability.

Regulatory approval challenges:

Nanomedicine faces complex and evolving regulatory landscapes. Most regulatory frameworks such as U.S. Food and Drug Administration (FDA) and the European Medicines Agency, remain largely structured around conventional small molecule drugs.

Regulatory barriers include - 1) Physicochemical characterization 2) Safety and toxicology assessment.

Integrated future direction:

Personalized Nanomedicine – Involves tailoring nanoparticle design to individual patient characteristics such as genetic profile, disease stage, and biomarker status to enhance therapeutic efficacy and clinical trial success. By customizing parameters including nanocarrier size and surface drug combination, treatments can be optimized for targeted delivery and reduce systemic toxicity.

Emerging technologies – AI for predictive formulation design & high throughput screening

may optimize nanoparticle characteristics in development. Rapid evaluation of multiple nano formulations, reducing experimental time, cost, and resource use.

RESULTS

Nano-formulations significantly enhance the therapeutic potential of herbal drugs compared with their conventional forms. Traditional preparations of compounds such as curcumin, quercetin, bacosides, and resveratrol suffer from poor solubility, low bioavailability, rapid metabolism, and limited BBB penetration, resulting in modest clinical benefits. These enhancements lead to a greater reduction of A β plaques and oxidative stress, along with significant improvements in memory, learning, & overall cognitive function.

Herbal drug	Nanoparticle carrier	Model used	Results
Curcumin	SLNs, Nano-emulsion	Transgenic AD mice	A β plaque deposition, improved memory
Quercetin	Liposomes	Rodent AD models	Neuroinflammation
Bacopa monnieri	Polymeric NPs	Scopolamine induced rats	Enhanced learning and memory
Resveratrol	Gold/iron oxide	A β induced in mice	Neuronal death

CONCLUSION

Overall, herbal drug-loaded nanoparticles represent a promising and evolving therapeutic strategy for Alzheimer's disease with the potential to overcome current limitations and improve patient outcomes.

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Conflict of Interest

The authors declare that there is no conflict of interest.

REFERENCE

1. Ramer, L., Tremblay, M.-È., & V., (2023). Managing pathology burden and glial senescence build-up hypothesis for late-onset Alzheimer's disease. *Nature Communications*, 14, 167. <https://doi.org/10.1038/s41467-023-36141-9>
2. Agagündüz, D., Kocaadam-Bozkurt, B., Bozkurt, O., Sharma, H., Esposito, R., Özoğul, F., & Capasso, R. (2022). Microbiota alteration and modulation in Alzheimer's disease by gerobiotics: The gut–health axis for a good mind. *Biomedicine & Pharmacotherapy*, 153, 113430. <https://doi.org/10.1016/j.biopha.2022.113430>
3. Tamburini, B., Badami, G. D., Manna, M. P. L., Azgomi, M. S., Caccamo, N., & Dieli, F. (2023). Emerging roles of cells and molecules of innate immunity in Alzheimer's disease. *International Journal of Molecular Sciences*, 24(2), 1192. <https://doi.org/10.3390/ijms24021192>
4. Wang, H., Sun, M., Li, W., Liu, X., Zhu, M., & Qin, H. (2023). Biomarkers associated with the pathogenesis of Alzheimer's disease. *Frontiers in Cellular Neuroscience*, 17, 1270790. <https://doi.org/10.3389/fncel.2023.1270790>
<https://doi.org/10.3389/fncel.2023.127904>
5. Mehta, R.I.; Mehta, R.I. The Vascular-Immune Hypothesis of Alzheimer's Disease. *Biomedicines* 2023, 11,408. <https://doi.org/10.3390/biomedicines11020408>
6. Atoki, A. V., Aja, P. M., Ondari, E. N., & Shinkafi, T. S. (2023). Advances in Alzheimer's disease therapeutics: Biochemistry, exploring bioactive compounds and novel approaches. *International Journal of Food Properties*, 26(1), 2091–2127. <https://doi.org/10.1080/10942912.2023.2243140>
7. Ozsahin, I., Onakpojeruo, E. P., Uzun, B., Uzun Ozsahin, D., & Butler, T. A. (2023). A multi-criteria decision aid tool for radiopharmaceutical selection in tau PET imaging. *Pharmaceutics*, 15(5), 1304. <https://doi.org/10.3390/pharmaceutics15051304>
8. Merighi, S., Nigro, M., Travagli, A., & Gessi, S. (2022). Microglia and Alzheimer's disease. *International Journal of Molecular Sciences*, 23(21), 12990. <https://doi.org/10.3390/ijms232112990>
9. San-Millán, I. (2023). The key role of mitochondrial function in health and disease. *Antioxidants*, 12, 782. <https://doi.org/10.3390/antiox12030782>
10. Compagnoni, G. M., Di Fonzo, A., Corti, S., Comi, G. P., Bresolin, N., & Masliah, E. (2020). The role of mitochondria in neurodegenerative diseases: The lesson from Alzheimer's disease and Parkinson's disease. *Molecular Neurobiology*, 57(7), 2959–2980. <https://doi.org/10.1007/s12035-020-01929-9>
11. Liu, S., Jin, X., Ge, Y., et al. (2025). Advances in brain-targeted delivery strategies and natural product-mediated enhancement of blood–brain barrier permeability. *Journal of Nanobiotechnology*, 23(1), 382. <https://doi.org/10.1186/s12951-025-02082-0>
12. Dou, K.-X., Tan, M.-S., Tan, C.-C., Cao, X.-P., Hou, X.-H., Guo, Q.-H., Tan, L., Mok, V., & Yu, J.-T. (2018). Comparative safety and effectiveness of cholinesterase inhibitors

- and memantine for Alzheimer's disease: A network meta-analysis of 41 randomized controlled trials. *Alzheimer's Research & Therapy*, 10, 126. <https://doi.org/10.1186/s13195-018-0458-8>
13. Lim, G.P.; Chu, T.; Yang, F.; Beech, W.; Frautschy, S.A.; Cole, G.M. The Curry Spice Curcumin Reduces Oxidative Damage and Amyloid Pathology in an Alzheimer Transgenic Mouse. *J. Neuroscience*. 2001, 21, 8370–8377. <https://doi.org/10.1523/JNEUROSCI.21-21-08370.2001>
 14. Frautschy, S. A., Hu, W., Kim, P., Miller, S. A., Chu, T., Harris-White, M. E., & Cole, G. M. (2002). Phenolic anti-inflammatory antioxidant reversal of A β -induced cognitive deficits and neuropathology. *Neurobiology of Aging*, 23(6), 993–1005. [https://doi.org/10.1016/S0197-4580\(02\)00017-3](https://doi.org/10.1016/S0197-4580(02)00017-3)
 15. Brüll, V., Burak, C., Stoffel-Wagner, B., Wolffram, S., Nickenig, G., Müller, C., Langguth, P., Alteheld, B., Fimmers, R., & Naaf, S. (2015). Effects of a quercetin-rich onion skin extract on 24-hour ambulatory blood pressure and endothelial function in overweight-to-obese patients with (pre-)hypertension: A randomized double-blind placebo-controlled crossover trial. *British Journal of Nutrition*, 114(8), 1263–1277. <https://doi.org/10.1017/S0007114515002950>
 16. Rauf, K., Subhan, F., Al-Othman, A., Khan, I., Zarrelli, A., & Shah, M. (2013). Preclinical profile of bacosides from *Bacopa monnieri* (BM) as an emerging class of therapeutics for management of chronic pains. **Current !**Medicinal Chemistry*, 20(8), 1028–1037. <https://doi.org/10.2174/0929867311320080006>
 17. Salehi, B.; Mishra, A.P.; Nigam, M.; Sener, B.; Kilic, M.; Sharifi-Rad, M.; Fokou, P.V.T.; Martins, N.; Sharifi-Rad, J. Resveratrol: A Double-Edged Sword in Health Benefits. *Biomedicines* 2018, 6, 91 <https://doi.org/10.3390/biomedicines6030091>
 18. Gambini, J., Inglés, M., Olaso, G., Lopez-Grueso, R., Bonet-Costa, V., Gimeno-Mallench, L., Mas-Bargues, C., Abdelaziz, K. M., Gomez-Cabrera, M. C., Vina, J., et al. (2015). Properties of resveratrol: In vitro and in vivo studies about metabolism, bioavailability, and biological effects in animal models and humans. *Oxidative Medicine and Cellular Longevity*, 2015, 837042. <https://doi.org/10.1155/2015/837042>
 19. Wang, Y., et al. (2025). Targeted nanoparticles for drug delivery across the blood–brain barrier in early and late stages of Alzheimer's disease: A review. *Molecular Neurobiology*, 63(1), 75–?? <https://doi.org/10.1155/2015/837042>
 20. Fonseca-Santos B, Gremião MPD, Chorilli M. Nanotechnology-based Drug delivery systems for the treatment of Alzheimer's disease. *International journal Nano medicine* 2015 <https://doi.org/10.2147/IJN.S86279>
 21. Satapathy MK, Yen TL, Jan JS, Tang RD, Wang JY, Taliyan R Et al (2021) Solid lipid nanoparticles (SLNs): an advanced drug Delivery system targeting brain through BBB. *Pharmaceutics* 13(8):1183 <https://doi.org/10.3390/pharmaceutics13081183>



22. Mehnert W, Mäder K (2001) Solid lipid nanoparticles: production, characterization and applications. *Advanced Drug Delivery Review* 47(2–3):165–196. [https://doi.org/10.1016/S0169-409X\(01\)00105-3](https://doi.org/10.1016/S0169-409X(01)00105-3)
23. Mufamadi, M. S., Choonara, Y. E., Kumar, P., Modi, G., Naidoo, D., Van Vuuren, S., et al. (2013). Ligand-functionalized nanoliposomes for targeted delivery of galantamine. *International Journal of Pharmaceutics*, 448(1), 267–281. <https://doi.org/10.1016/j.ijpharm.2013.03.032>
24. Naqvi S, Panghal A, Flora SJS (2020) Nanotechnology: a promising approach for delivery of neuroprotective drugs. *Frontier Neuroscience* 14:498. <https://doi.org/10.3389/fnins.2020.00498>
25. Zhang J, Zhang Y, Wang J, Xia Y, Zhang J, Chen L. Recent advances in Alzheimer's disease: mechanisms, clinical trials and new drug development strategies. *Signal Transduction and Targeted Therapy*. 2024;9(1):68. Doi:10.1038/s41392-024-01764-2.
26. Zhang W, Mehta A, Tong Z, Esser L, Voelcker NH. Development of polymeric nanoparticles for blood–brain barrier transfer: strategies and challenges. *Advanced Science*. 2021;8(10):2002794. Doi:10.1002/advs.202002794.
27. Baranowska-Wójcik, E., Gajowniczek-Ałas, D., Pawlikowska-Pawlęga, B., & Sz wajgier, D. (2025). The potential role of phytochemicals in Alzheimer's disease. *Nutrients*, 17(4), 653. <https://doi.org/10.3390/nu17040653>
28. Iqbal I, Saqib F, Mubarak Z, Latif MF, Wahid M, Nasir B, et al. Alzheimer's disease and drug delivery across the blood–brain barrier: approaches and challenges. *European Journal of Medical Research*. 2024;29(1):313. Doi:10.1186/s40001-024-01859-0.
29. Nguyễn-Thi, P. T., Ho, T. T., Nguyen, T. T., & Vo, G. V. (2024). Nanotechnology-based drug delivery for Alzheimer's and Parkinson's diseases. *Current Drug Delivery*, 21(7), 917–931. <https://doi.org/10.2174/1567201820666230707113405>
30. Boyetey, M., Choi, Y., Lee, H., & Choi, J. (2024). Nanotechnology-based delivery of therapeutics through the intranasal pathway and the blood–brain barrier for Alzheimer's disease treatment. *Biomaterials Science*, 12, 2007–2025. <https://doi.org/10.1039/D3BM02003G>
31. Li, H., Shen, X., Zhang, B., et al. (2025). Brain-targeted intranasal delivery of biologics: A perspective for Alzheimer's disease treatment. *RSC Pharmaceutics*, 2, 1323–1348. <https://doi.org/10.1039/D5PM00148J>