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ABSTRACT

The present article points out dementia diagnosis, dementia mechanisms, advancements in Alzheimer's disease therapy, symptom management, lifestyle and non-pharmacological mediations, genetic and biomarker research, pathophysiological aspects, biomarkers, new drug release systems, neuroprotective agents, and several aspects of immunotherapy and gene treatment. Data on these topics have led to the conclusion that although it was not possible to cure this disease through chemotherapy, significant progress was found in it. According to this review, new therapies featured by extreme efficiency, low toxicity and low-cost feasibility will soon come up.

Keywords: Dementia. Alzheimer, immunotherapy, biomarker.

INTRODUCTION

Alzheimer damages the neurons in the brain. Injured neurons first show Alzheimer´s disease (AD) symptoms when the part of the brain responsible for cognition, memory and language is affected. Assumingly, these symptoms affect and start changing individuals' brains approximately two decades before they start showing up. Fortunately, over the years, before the symptoms come up, the brain balances these changes by employing alternate neuron networks to allow patients to remain as functional as they used to be. A person is diagnosed with dementia whenever the brain is no longer able to respond due to cognitive impairments that hinder the patient's ability to perform normal daily activities.

Cerebrospinal fluid analysis or other assays show that brain variations are produced by AD. In this case, patients are diagnosed with dementia due to Alzheimer's disease or Alzheimer's dementia. AD is an on-going illness, and its progress changes from person to person.

In 2023, approximately 60 million people were diagnosed with dementia worldwide, and AD was the justification of it in 60% to 70% of cases. Every year, approximately 10 million new dementia patients are registered, and it leads to collapse in global health systems (Rajanna et al. 2025). Thise mates show that this number is expected to rise to approximately 140 million people by 2025 because of the population aging all over the globe. In India, about 4 million patients have several dementia types and AD is the most extensive type of it (Sharma et al. 2025).

A study on Alzheimer's disease cases showed death rate close to the values (value X 100.000 population): Finland, 54.65 cases; UK, 42.70; USA, 33.26; Canada, 27.87; Spain, 21.52; China, 17.36; Germany, 15.54; Russia, 15.07; Italy, 14.86; Brazil, 11.93; Argentina, 4.95; Mexico, 2.70 (WLE-2024).

Family members and specialist caregivers perform critical procedures to keep Alzheimer's patients safe, in good shape and involved in the most significant activities to them. It is necessary to fulfil significant caregiving demands when neuronal injury progressively increases and these neural injuries extend to special parts of the brain, which impair basic physical functions such as swallowing and walking. Individuals at this severe functional impairment stage caused by Alzheimer's require help to perform all daily living (ADLs) activities. Mobility loss, along with cognitive limitations, can demand 24/7 care. However, it's common for these patients to have short, temporary lucidity when they may be able to consistently communicate and recover some functional capabilities, even in Alzheimer's stages when individuals often have difficulty communicating verbally. Some on-going research is assessing these facts. AD is ultimately fatal, but many Alzheimer's patients die of older age issues. AD is the most common dementia type among all known types of it, although there are other definitions of it, such as (Adeyemi et al., 2025):

Alzheimer's disease (AD): Aggregation of protein β-amyloid exterior to the neurons and bended tau (τ) protein strands within neurons cause these neurons death and injuries in brain tissue, as well as brain tissue atrophy and inflammation.

Cerebrovascular disease (CV): Brain blood vessels and tissues are damaged by lack of oxygen, blood, or nutrients. People showing these changes are diagnosed with CV dementia.

Frontotemporal degeneration (FTD): Death of neurons in the brains' front and temporal lobes lead to lobes contraction or shrinkage, and to cortex superior layers smoothing. In this case, the number of proteins τ or of transmissive replicate DNA-binding protein (TDP-43) significantly rises.

Hippocampal sclerosis (HS): Tissue contraction and stiffening in the brain's hippocampus impairs crucial functions for memory production. Brain alterations in HS cases are featured by misfolded proteinTDP-43.

Lewy body disease (DLB): Defective accumulation of protein α-synuclein in neural cells produced on cortex, which causes dementia.

Limbic-predominant age-related TDP-43 encephalopathy (LATE): Protein TDP-43 concentration in the brain helps nerve progression. LATE cases are often featured by this protein concentration in the brain region linked to the limbic system (memory, behavior, mood, and emotion).

Mixed pathologies (MP): Even if one of the brain alterations caused dementia, MP seemed like the reason for it. If specific pathologies lead to dementia symptoms throughout life, it is described as mixed etiology dementia.

Parkinson's disease (PD): PD is defined as the accumulation of protein α-synuclein in the substantia nigra. These proteins degrade the neurons that generate dopamine.

Research has shown that patients over 65 years stay alive for 4 to 8 years post AD diagnosis, on average, although some patients can live for more than 20 years. There is no way to prove how to prevent AD and there is not actually remediation to it. Moreover, there are many accessible therapies to help with symptoms, and two of them change the essential biology of Alzheimer's and moderate disease advancement, such as therapy based on administering medicines such as lecanemab (Leqembi®) and donanemab (KisunlaTM), which reach and detach beta-amyloid from the brain. Currently, several on-going studies aim at spreading and varying accessible therapies, as well as at enhancing the quality of life of dementia patients (Adeyemi et al., 2025).

DEMENTIA DETECTION

Dementia clinical diagnosis is likely made by primary care experts through patients' clinical assessment (Hafiz et al., 2023). Montreal Cognitive Assessment (MoCA) is often adopted to detect mild cognitive decline and initial dementia signs (Rosenzweig 2025; Nelson and Racelis, 2025). Neuropsychological evaluation plays basic role in signalizing cognitive decline at different dementia levels; furthermore, neuroimaging, biomarkers and digital instruments are possibly used by medical practitioners (Alzola et al., 2024). It is critical to provide prompt action and disease maneuver, and to detect instruments and the right methodology at primary dementia detection stage, so the symptoms can be notably improved (Azizan et al., 2025). Diagnostic assessments are first achieved from a clinical viewpoint, although neuroimaging has also markedly developed over the years (Hassan et al, 2025). Newly discovered neuroimaging techniques such as diffusion tensor imaging (DTI), which detects changes in the structural binding of white matter sections (Zhao et al, 2025); functional MRI (fMRI), which detects changes in brain activity standards that assumingly point toward functional changes in the brain) (Alarjani and Almarri, 2025); PET (positron emission tomography) (Leuzy et al., 2025; Raham, 2025) and SPECT (single-photon emission computed tomography) (Mulumba et al., 2025), have been showing to provide relevant information for dementia detection. PET and SPECT are available to detect changes in brain metabolism and blood fluidity; they enhance dementia detection accuracy. New research has assessed the application of new PET tracers to reach specific pathological dementia dementia aspects, i.e., β-amyloid and tau proteins (Landau,2025). New aspects of machine learning algorithms aimed at assessing neuroimaging data have also been updated to help dementia detection (Martin et al. 2025).

New research has assessed the use of blood-based biomarkers, mainly NfL (neurofilament light chain) (Meng et al., 2025) and p-tau (plasma phosphorylated tau) (Palmqvist et al., 2025) for brain neurodegeneration diagnosis. Higher levels of these biomarkers are significant since they show dementia presence, even before the symptoms are detected. Blood biomarkers' application is highly helpful in detecting AD pathological features (Hasselbalch, 2025). Moreover, blood-based biomarkers and CSF (cerebrospinal fluid) biomarkers (i.e., amyloid beta, tau and phosphorylated tau) have been

enhancing AD detection accuracy (Oh and Wyss-Coray, 2025). Retinal nerve fiber layer thickness and macular volume (as retinal biomarkers) have also been investigated as potential biomarkers for early dementia detection (Kastelan et al., 2025).

Currently, the healthcare industry has supported technological progress to enhance precaution provisions. Digital instruments, such as artificial intelligence (AI) machine learning algorithms, wearable devices and smartphone apps have led to upgrades in dementia detection. These instruments can monitor subtle changes in cognitive and conduct roles, and these changes can assumingly suggest dementia presence. AI algorithms can accurately predict AD onset, even before its effects show up. It can be done by monitoring neuroimaging data. Smartphone apps, such as Sea Hero Quest (Glitchers, Edinburgh, Scotland), have been updating spatial navigation expertise analyses that are often engaged at the primary dementia stage. Smartwatches and fitness trackers are following changes in both sleep patterns and physical activity, since these factors are relevant as potential primary dementia markers. BrainCheck Inc. (Austin, Texas, United States) has developed five games based on gold-standard neurocognitive assays The app plots a graph to highlight the cognitive function label important for users' executive action, cognitive processing, immediate memory, visual attention and delayed recall skills based on these games' results. Primary dementia diagnosis is crucial for the disease's prompt interventions, control and management (Hafiz et al., 2023).

DEMENTIA MECHANISM

Two years ago, it was recorded that approximately 55 million people in the world had dementia, and AD accounted for 60% to 70% of these cases. Its exact mechanism is not fully understood since AD etiology is extremely complex. Furthermore, Aβ and tau essential function and the spectrum of other factors can contribute to AD pathology; in other words, acetylcholine deficiency, neuro-inflammation, oxidative stress, biometal dyshomeostasis, glutamate imbalance, insulin resistance, gut microbiome abnormalities, cholesterol homeostasis disruption, mitochondrial dysfunction, and autophagy anomaly (Fig. 1).

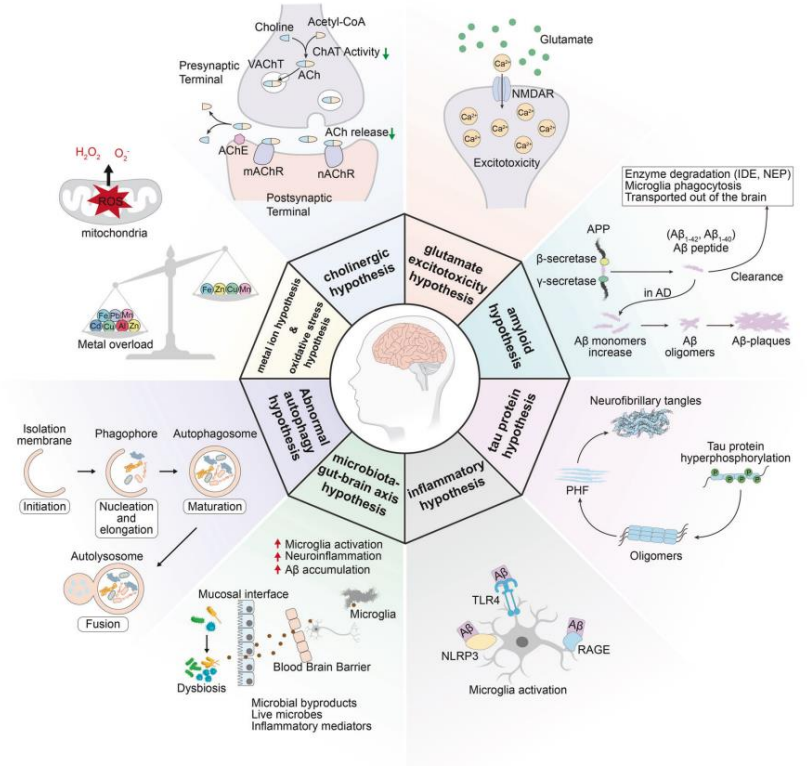

Fig. 1 Diagram for the pathogenesis of AD, including the cholinergic hypothesis, the glutamatergic hypothesis, the amyloid hypothesis, the tau protein hypothesis, the inflammatory hypothesis, the microbiota-gut-brain axis hypothesis, the oxidative stress hypothesis, the metal ion hypothesis, and the abnormal autophagy hypothesis from Zhan et al. (2024), (approved by Springer Nature under a Creative Commons Attribution 4.0 International License).

All these elements feature dementia clinical detection and therapeutic attempts. Biomarkers are relevant because they can characterize individuals at initial disease stages, as well as follow their progression and assess medication efficiency. Although the hypotheses about these pathogenic indicators provide potential targets for medicine advancements, the progress of efficient AD medicines has been supported by pure narratives. Tacrine was mainly ruled out from the market due to its hepatotoxicity. Medicines such as donepezil, galantamine, rivastigmine, memantine and namzaric have been administered by clinical recommendation; however, these drugs can mitigate or control symptoms in the short run, but they are not capable to pausing AD's long-term progress, despite their likely associated side effects. New medications, including sodium oligomannate and aducanumab, which were firstly approved by FDA, but that had their production later canceled by its manufacturer-Biogen); lecanemab and donanemab, whose sales remain under review for approval, helped to the development of proposals for disease-modifying treatments that act against AD progress (Zhang et al., 2024; Rajanna et al., 2025; Sharma et al., 2025).

PROGRESSES IN ALZHEIMER'S DISEASE THERAPY

Current AD's endorsed DMTs (disease-modifying treatments) involve mAbs (anti-amyloid monoclonal antibodies) and Lecanemab (Leqembi®) and

Donanemab (Kisunla™) are the ratified medicines. The mAbs share some similarities, but, at the same time, they show different features. From the MoA (action mechanism) viewpoint, all these treatments select high molecular weight fibrillar Aβ associates, and it leads to significant Aβ reduction based on amyloid PET exploration in combination to ARIA (amyloid-related imaging abnormalities). Studies involved patients with primary AD described as MCI (mild cognitive impairment) due to mild AD dementia. It is worth highlighting that the initial AD classification covers mAb assessments, and it could have impact on individuals' therapy selection (Rajanna et al., 2025).

The mABs lecanemab targets amyloid-beta plaques. It binds to protofibrils, which are an amyloid-beta type known to be especially harmful to neurons. Clinical trials have shown that Lecanemab effectively decreases amyloid plaque development and slows down cognitive decline in individuals with mild cognitive impairment or early AD. Ongoing research aims at validating these results and at further exploring Lecanemab's therapeutic benefits (Ameen et al., 2025). FDA has approved its traditional license for donanemab use as therapy in early AD, mainly in MCI patients or in those with mild dementia caused by AD due to proven high beta-amyloid rates in the brain. Donanemab can slow Alzheimer's progress at its primary stage, give patients longer daily action gain time, and help them keep their autonomy. Individuals are encouraged to discuss with their healthcare provider to expand a personalized Alzheimer's therapeutic plan by taking in account the profits and hazards of all authorized drugs and treatments (Rajanna et al., 2025).

SYMPTOMS MANGEMENT

Cholinesterase inhibitors, such as donepezil, galantamine and rivastigmine, have been typical AD golden therapy. These medicine types play key role in suppressing acetylcholinesterase. They disrupt acetylcholine, which is an important neurotransmitter for schooling and the mind. Cholinesterase inhibitors likely help upgrade cognitive roles and delay symptoms deterioration at low to moderate AD by increasing acetylcholine content in the brain. Nevertheless, although these medicines do not have any effect on this disease's fundamental process, they provide efficient typical help to several individuals (Gajendra et al., 2025).

Memantine is a N-methyl-D-aspartate (NMDA) seen as antagonist receptor. It is an important treatment to be administered to improve Alzheimer's symptoms. Its mechanisms lie in controlling the action of glutamate, which is a neurotransmitter linked to schooling and mind; furthermore, its glutamate action can lead to neuronal injury and cognitive reduction (Puranik and Song, 2024). Memantine can normalize glutamate action and, consequently, protect neurons and enhance the cognitive role. It is combined to a cholinesterase inhibitor to enhance overall therapy efficacy and increase its efficiency.

As previously observed, AD complexity points out the need of a multidisciplinary attempt to achieve effective treatments. Combining amyloid-targeting medicines like donanemab to symptomatic therapies, such as inhibitors like cholinesterase and receptor antagonist NMDA, for example, assumingly lead to more effective benefits. In addition, the association of medicines aiming amyloid-beta with those targeting the tau protein is a fruitful and active field of research. The goal of associating treatments is to simultaneously approach multiple pathological

procedures to possibly reach high cognitive role enhancement and delay disease progression (Da Mesquita et al, 2021; Angioni et al., 2025).

WAY OF LIFE AND NON-MEDICAL OR NON-PHARMACOLOGICAL INTERVENTIONS

Cognitive teaching plans are related to structured mental tasks selected to improve especial cognitive functions such as memory, attention and problem-solving. This planning can be split into computer-based exercises, individual therapy sessions or group activities. According to the outcomes, normal cognitive schooling can help support or even enhance cognitive capabilities in AD patients. Furthermore, cognitive exercises can improve the brain's plasticity by helping it to adapt and compensate the neuronal injury (Reddy, 2025).

Diet and exercise play key role in keeping brain sanity and in potentially reducing AD risk. The Mediterranean diet (fruits, vegetables, whole grains, fish and healthy fats) has been related to lower risk of cognitive decrease and AD. Overall, exercising (aerobic exercises, i.e., swimming, walking, and dancing) has been showing to enhance the cognitive role and to reduce hazardous Alzheimer's progress. This activity type increases blood fluidity to the brain to achieve neurotrophic indices capable of improving the health of neural cells and of helping to reduce oxidative stress and inflammation. Social activities and mental motivation deriving from hobbies, as well as social activities help achieving cognitive resistance and full brain sanity.

Surface-based morphometry techniques were applied to assess cortical density and speech-related volume, and AD-related brain sections. Brain stores in language-related regions was not proven. Diminished hippocampal volume was measured in AD monolingual adults, rather than in bilingual ones. Therefore, bilingualism is supposed to add to brain preservation in the AD reference frame (Coulter and Phillips, 2024).

NEW VISION ON GENETIC AND BIOMARKER INVESTIGATION

The basis of genetic investigation lies on featuring several genes relate to increased AD hazard as the APOE4 (Apolipoproteína E4) allele, which is the one of the well-known genetic hazardous factors. Patients charge one or, sometimes, two copies of this allele, and it pointed out significantly higher hazardous AD progression. This knowledge field has shown that Alzheimer's genetic aspects can lead to specific or personalized medicine attempts whose therapies are designed to a specific genetic profile of the individual. This attempt could enhance therapy efficiency and reduce its negative effects (Kucwaj-Brysz et al., 2021; Ataei et al., 2024)

Biomarkers' progress dramatically changes AD detection and follow up. Imaging methodologies, such as PET scans, allow seeing amyloid-beta and tau precipitates in the brain (Chen et al., 2022). Fluid biomarkers, including CSF and blood assays, help assess the content or level of amyloid-beta, tau and of other AD-related proteins. The use of these biomarkers enables exact diagnosis at the first stage, such as AD progression follow up and therapy effectiveness (Jack et al., 2024). Currently, investigation targets the validation and enhancement of these biomarkers in a largely accessible and less invasive way (Schneider, 2024).

ALZHEIMER'S DISEASE BIOMARKERS: PATHOLOGICAL BASIS

AD pathogenesis is defined by imprint pathological features, namely: extracellular amyloid-beta (Aβ) plaques, intracellular NFTs (neurofibrillary tangles) composed of neuro-inflammation and hyperphosphorylated tau (Simões-Pires et al., 2025). Biomarkers reflecting these processes are useful detection or diagnostic and prognosis indicators (Doke et al., 2024).

Pathology biomarkers Aβ, such as CSF Aβ42: Aβ40 ratio, are quite important. Decrease in this ratio clearly points out the Aβ plaque content in the brain. Search based on PET imaging with amyloid tracers, such as florbetapir, is another way to observe this process (Vandenberghe et al., 2025). It showed that individuals with low CSF Aβ42 levels had higher brain amyloid precipitation, and it explains the cognitive decay.

Amyloid PET Imaging as PET tracers 11C-PiB (Pittsburgh compound B) has emphasized amyloid deposition *in vivo*, and this finding supports differential AD diagnosis in comparison to other dementia types (Wu et al., 2025).

According to CSF t-tau (total Tau) and p-tau (phosphorylated Tau), high t-tau levels suggest neuronal damage, but enhanced p-tau is related to NFT diseases or pathology (Rajanna et al., 2025). High CSF p-tau contents were connected to fast cognitive damage when it was used as precursory hallmarked in MCI (mild cognitive impairment) individuals (Wang et al., 2025).

High NfL (neurofilament light chain) levels in blood and CSF point toward axonal injury and depict AD neurodegeneration, as well as other neurodegenerative disorders (Nakamura et al, 2024).

Structural magnetic resonance imaging (MRI) is a golden standard to find hippocampal atrophy for neurodegradation (Ayedemi et al., 2025) measuring purpose.

Increased YKL-40 levels in CSF and plasma as biomarker of astrocytosis and microglial stimulation are found in AD (Pelkmans et al., 2024).

PET imaging with transpositional protein (TSPO) tracers present microglial stimulation and neuro-inflammation in AD brain (Wijesinghe et al., 2025).

Progress in highly sensitive sensor techniques, such as SIMOA (single-molecule array), can improve blood-based biomarkers by proposing a minor invasive and cost-effective possibility to CSF biomarkers (Dong et al., 2024).

Plasma ratio Aβ42:Aβ40 show amyloid precipitation and excellent correlation to amyloid PET findings (Trelle et 2025).

Plasma p-tau181 and p-tau217 have recorded favorable accuracy determination related to CSF and imaging biomarkers. Plasma p-tau217 showed higher accuracy in differentiating AD from non-AD dementias (Blennow et al., 2018).

However, these biomarkers had excellent updates in AD handling; however, its high cost inhibits its normalization. New methods such as artificial intelligence and multiomics, aim at enhancing biomarker inventions and administration. Multiomics attempts involving proteomics, metabolomics and transcriptomics are featuring new biomarker applicants, such as lipids and metabolites related to AD or to its pathology (Sanches et al., 2024).

DRUG DELIVERY SYSTEMS: INNOVATION

Techniques of classical medicine release often involve confrontation with agents accounting for efficiency releasing therapies to the brain due to BBB (blood-brain barrier). New medicine release systems help solve these questions. Methodologies such as nasal sprays can deliver medicines straight to the brain

through olfactory bypass and BBB crossing. An interesting technique focused on ultrasound is associated with microbubbles (Fisher et al., 2025) that can temporarily open BBB and make these medicines highly efficiently go to the brain (Abbot, 2025). These progressed release methods have the potential to improve Alzheimer's therapies efficiency by guaranteeing that higher levels of therapy agents will get to their aims in the brain (Kucwaj-Brysz et al., 2021).

IMMUNOTHERAPY

Immunotherapy (vaccines) is a growing field in Alzheimer's investigation. Experimental vaccines focus on activating the immune system to recognize and clear amyloid-beta or tau proteins. Alive immunotherapy concerns administering a modified form of the protein to get an immune response in patients, whereas passive immunotherapy focuses the direct administration of antibodies. Primary trials of Alzheimer's vaccines have engaged in reducing amyloid-beta levels (Budd Haeberlein et al., 2022) and in slowing down cognitive decay. However, confrontation, such as ensuring the security and efficiency of these vaccines is needed before they are expected to become highly accessible.

GENE AND STEM CELL TREATMENTS

Gene therapy is a potential strategy to communicate AD genetic sustains. Methods such as CRISPR/Cas9 allow accurate editing genes related to Alzheimer's such as APOE4 (Rottner, et al. 2025). Modifying these genes is a way to reduce disease hazard or severity. Gene therapies have the potential to release therapeutic genes that codify proteins to protect neural cells or to improve the brain role. Gene treatment provides a favoring frontier for Alzheimer's therapy at its primary stages given the possibility of stopping or even of reversing disease progress (Liu-Seifert et al., 2018).

Sten cell therapy can act in replacing lost neural cells and in renovating their role; however, this field remains in its primary investigation stages (Abbott, 2023, 2025; Uwishema et al., 2025).

AGENTS FOR NEUROPROTECTION

Compounds that protect neural cells (neurons) from injury and help their role are called neuroprotective agents. Investigations on these agent types are still going, and some of them are shown in preclinical research (Pekdemir, et al., 2024). Examples of them are antioxidants that are likely to reduce oxidation stress, which causes AD neuronal injury. In addition, anti-inflammatory compounds can mitigate the neuro-inflammation process, which is another important Alzheimer's pathological aspect. Moreover, drugs that improve the mitochondrial role and energy generation in neural cells are under investigation. Neuroprotective drugs could be associated with other therapies to maintain neuronal healthiness and its role whenever they prove themselves effective (Mafi et al., 2021; McDade et al., 2021).

A list of new medicines applied in clinical trials expanded to AD was released by Howard et al. (2023), Troutwine et al. (2022) and Rajanna et al. (2025) (Table 1).

Table 1. List of new drugs under clinical trials, developed to treat Alzheimer's disease (modified from Rajanna et al., 2025; Sharma et al., 2025; Zhang et al., 2024).

DRUG	THERAPEUTIC TARGET
Lecanemab:	Soluble Aβ protofibrils. Approved by FDA. ARIA, infusion-related reactions, headache
Donanemab	:Amyloid β. Approved by FDA. ARIA, infusion reactions, brain swelling
Semaglutide	: GLP-1 receptor. Ongoing trials; initial results promising. Nausea, vomiting, gastrointestinal issues
Simufilam	: Filamin A (modifies tau and Aβ42 interaction). Phase III trials underway; promising early results. Headache, fatigue, gastrointestinal issues
Gantenerumab:	Amyloid-β (Aβ) plaques. Ongoing clinical trials ARIA, infusion-related reactions, headache
Solanezumab	: Amyloid-β (Aβ) monomers. Ongoing clinical trials. Infusion-related reactions, ARIA
Memantine	: NMDA receptor antagonist. FDA approved, well established safety profile. dizziness, headache, constipation
Troriluzole:	Glutamate modulation Phase II/III trials underway. Dizziness, headache, fatigue
Tideglusib	: GSK-3 inhibitor (tau phosphorylation) Phase II trials showed mixed results. Nausea, diarrhea, fatigue
LMTX	: Tau aggregation inhibitor Phase 3 trials underway. Gastrointestinal issues, fatigue
ANAVEX2-73:	Sigma-1 receptor agonist Phase II/III trials underway. Dizziness, headache, diarrhea
Blarcamesine	: Sigma-1 receptor and muscarinic receptor. Ongoing clinical trials. Dizziness, headache, gastrointestinal issues
Elamipretide	: Mitochondrial dysfunction. Ongoing clinical trials. Headache, nausea, fatigue
E2814	: Tau propagation inhibitor. Ongoing clinical trials. Headache, fatigue, gastrointestinal issues
ALZ-801	: Amyloid oligomers Phase 3 trials underway. Nausea, headache, fatigue
Edaravone:	Oxidative stress FDA approved for ALS; trials for AD underway. Bruising, gait disturbance, headache.
ALZT-OP1[cromolyn +(R) ibuprofen]	: Facilitate the elimination of Aβ or its aggregates. Oral. Phase III
Nasal insulin	: Restructuring synapses and utilization of glucose. Intranasal, Phase III
Donapezil	: Transdermal patch, named Adlarity, was FDA-approved for treating mild, moderate, and severe dementia of the Alzheimer type. Its weekly dosing frequency showed bioequivalence to daily oral administration at the same dosage while presenting fewer gastrointestinal adverse events than oral administration
Galantamine	: Cholinesterase inhibitor. Widely used, well-established safety profile. Nausea, vomiting, diarrhea, weight loss. Second-generation AChEIs, including donepezil, rivastigmine), Galantamine is more selective. They exhibited fewer side effects or improved pharmacokinetic profiles, stablishing them as first-line drugs for AD. Although these drugs have been widely used, ongoing research focuses on optimizing dose, dosage form, routes of administration, and combination therapies to minimize adverse. Furthermore, the combination use of appropriate cholinesterase inhibitors, such as donepezil and galantamine, or the combination of cholinesterase inhibitors with other neurologic drugs, metal chelators, or antioxidants, may yield surprising effects in the management of cholinergic drugs in AD, including efficacy, tolerability, and safety.
Namzaric	: Namzaric (fixed-dose combination memantine extended-release/donepezil) also provides another treatment option for patients with moderate to severe AD. These drugs primarily function by modulating neurotransmitter levels but cannot alter the course of the disease, which are instructive for designing new drugs
Sodium GV-971	: Sodium oligomannate (9, GV-971), an oligosaccharide extracted from marine algae, was conditionally approved in China in 2019 amidst ongoing debates regarding its mechanism of action and therapeutic efficacy. GV-971 was postulated to counteract AD by inhibiting neuroinflammation triggered by gut dysbiosis and disrupting the formation of Aβ fibrils altering. This modulation influenced microbial metabolism and peripheral inflammation, regulated the activation state and functionality of microglia, and thereby reduced

neuroinflammation and amyloidosis. Currently, two phase IV clinical trials are ongoing to further investigate its efficacy and safety, with an expected continuation until 2025.
Rivastigmime: Rivastigmine patch and its cholinesterase inhibitors qualities through intranasal administration, intra venous injection, and other methods are possible. Furthermore, the combination use of appropriate cholinesterase inhibitors, such as galantamine, or the combination of cholinesterase inhibitors with other neurologic drugs, may yield surprising effects in the management of cholinergic drugs in AD, including efficacy, tolerability, and safety
Brexpiprazole: Commonly prescribed for depression and schizophrenia, targets serotonin, dopamine, and norepinephrine receptors. It is known to help mitigate agitation in individuals with AD. These innovative medicines delve deeper into AD mechanisms and present diverse target choices, holding the potential to halt or reverse AD progression. Further studies are needed to understand drug mechanisms, assess long term efficacy, and ensure safety. These drugs are noted for their extensive safety and tolerance profiles, as well as their potential for multiple uses.

Modified from Rajanna et al, 2025, Sharma et al., 2025, Zhang et al., 2024; Abbreviations: FDA, Food and Drug Administration; ARIA, Amyloid-related imaging abnormalities; ALS, amyotrophic lateral sclerosis.

Table 2 describes the brief safety profile of new treatments in AD.

Table 2 provides a brief security profile of new AD therapies.

Drug	Adverse effects	Key risk factors for complications
Lecanemab	ARIA (edema and hemorrhages), headache.	APOE ε4 genotype, microhemorrhages, anticoagulant use.
Donanemab	ARIA (27% incidence), confusion.	APOE ε4 genotype, advanced amyloid plaque burden, prior microhemorrhages
Semorinemab.	Cognitive worsening, inflammation.	Advanced tau pathology, older age.
Gantenerumab.	ARIA, nausea, infusion reactions.	APOE ε4 genotype, comorbid vascular conditions, treatment dose.
Verubecestat (BACE inhibitor).	Liver toxicity, cognitive decline.	Dose-dependent effects, genetic predisposition, older.
ACI-35 (Anti-Tau vaccine).	Mild inflammation, behavioral changes.	Interaction with other therapies, comorbidities (e.g., vascular issues).
Bepranemab.	The drug was safe, with no signs of ARIA.	Incidences of brain hemorrhagic events and inflammatory changes.
Remternetug.	ARIA-E, ARIA-H (small brain hemorrhage) at high dose.	There were also no macrohemorrhages observed in any study group.
Trontinemab.	Amyloid-related imaging abnormalities-edema/effusion (ARIA-E) were observed in <5% (n=3/114) of participants.	Developed ARIA-E, which was mild and asymptomatic.

Abbreviation: ARIA, Amyloid-related imaging abnormalities. Modified from Rajanna et all, 2025; Alzheimer's and Dementia Weekly https://alzheimersweekly.com/whats-ahead-for-alzheimers-drugs-in-2025/; https://biologyinsights.com/bepranemab-potential-impact-on-neurodegenerative-diseases/; https://www.fiercebiotech.com/biotech/lilly-sneak-peek-next-gen-alzheimers-drug-shows-rapid-and-robust-amyloid-reduction-familiar; https://www.alzforum.org/therapeutics/ trontinemab),

CONCLUSION

The AD therapy setting was quickly developed and showed important progress through numerous front lines. The current article highlights disease-modifying therapies, genetic research, new drugs, and several lifestyle mediation proposals aimed at changing the route of this damaging disease. The progress of new biomarkers, association treatments, genes, and stem cell treatments, as

well as individual or personalized medicine attempts are in progress. The relevance of biomarkers at primary diagnosis leads to research on early intervention, on important aspects to reduce disease progress and to maintain the cognitive role. These outbreaks can improve therapy access to and the global life aspects of AD individuals, besides helping their custodians or caregivers. When it comes to AD mechanistic aspects, synaptic dysfunction, neuro-inflammation and mitochondrial deterioration are crucial elements to the progress of new treatments and to action planning. It is worth observing that future AD therapies lie in a holistic attempt that associates pharmacological applications with lifestyle changes, along with cognitive therapies and supportive care. Advanced investigation and clinical trials are essential to translate this progress into efficient therapies and to, after all, improve the quality of life of both Alzheimer's patients and their companions.

This review made it clear that single-target medicines are often not enough due to AD's multifocal pathology. Several confronting AD features were reinforced, such as single targets, multiple hypotheses and MTDLs (multi-target-directed ligand), metal chelators, Aβ aggregation inhibitors and neuroprotective mechanistic aspects that emerge to support MTDLs, as assumed to hold an important function in handling AD. Finally, although AD remedy over chemotherapy has not yet been proven, significant advancements have been observed in it. The current review pointed out that new therapies accounting for extreme efficiency, low toxicity effects and economic feasibility will come up soon.

Author contributions

ND, WJF, GN: Formal analysis, Investigation, Methodology, Supervision, Validation, Visualization, Writing - original draft, Data, collection and analyses, Formal analysis, supervision of manuscript. Final editing manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaração de Disponibilidade de Dados

The research data is contained within the article text.

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