AI Assisted Mechanistic and Translational Evaluation of Triticum aestivum in Alzheimer's disease: A Preclinical-to-Clinical Study

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Doi: 10.5281/zenodo.20179747
Received: 16 April 2026
Accepted: 24 April 2026

Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by amyloid-β accumulation, tau hyperphosphorylation, oxidative stress, neuroinflammation, and synaptic dysfunction. extensive research, effective disease-modifying therapy remains limited. Wheatgrass (Triticum aestivum) has garnered attention as a rich source of bioactive phytochemicals, particularly apigenin, which exhibits antioxidant, anti-inflammatory, and neuroprotective properties. current evidence on the potential role of wheatgrass-derived apigenin in AD management, with an emphasis on its interaction with glycogen synthase kinase-3β (GSK-3β) and related signalling pathways. Available preclinical studies indicate that apigenin improves cognitive performance, reduces oxidative damage, suppresses inflammatory mediators, and attenuates tau phosphorylation and amyloidogenic processing. Mechanistically, its neuroprotective effects involve activation of the PI3K/Akt pathway, inhibition of GSK-3β, modulation of BDNF/CREB signalling, and preservation of neuronal integrity. Wheatgrass extract has also demonstrated memory-enhancing and anti-inflammatory effects in experimental models of cognitive impairment, suggesting that its therapeutic potential may extend beyond apigenin alone. However, the evidence remains preclinical, and issues such as low oral bioavailability, limited blood–brain barrier penetration, and metabolic instability continue to restrict clinical translation. Therefore, further pharmacokinetic optimization, standardized formulation development, and well-designed clinical studies are required to validate its efficacy in humans. Overall, wheatgrass-derived apigenin represents a promising natural candidate for multi-target intervention in AD.

KEYWORDS: Alzheimer's disease; apigenin; wheatgrass; GSK-3β; large language models; AI-driven drug discovery; network pharmacology; Neurodegeneration

Introduction

1.1Artificial Intelligence (AI)

Artificial intelligence (AI) simulates human intelligence in machines programmed to think, reason, learn, and make decisions, enabling them to perform tasks such as problem-solving, pattern recognition, language understanding, and decision-making with minimal human intervention. [1]It broadly encompasses machine learning, which uses algorithms that learn from data and improve over time; deep learning, a subset of machine learning that relies on neural networks with multiple layers natural language processing, which allows machines to understand and generate human language; and computer vision, which enables the interpretation of visual data like images and videos. Over time, AI has evolved from rule-based systems into advanced, data-driven models capable of autonomous learning and predictive analytics.[1]AI has significantly transformed research methodologies across disciplines, particularly in biomedical and pharmaceutical sciences. In research, AI enables

rapid analysis of large-scale datasets such as genomics, proteomics, and clinical data, while also uncovering hidden patterns to generate novel hypotheses.[2] When integrated with robotics, AI automates high-throughput screening and experimental workflows, and its predictive modeling capabilities allow researchers to forecast disease progression, drug responses, and molecular interactions. Within pharmaceutical research specifically, AI is applied throughout the drug development pipeline from target identification, lead compound screening and molecular docking in early discovery to optimizing formulations and predicting pharmacokinetics and toxicity during development.[2] It further streamlines clinical trials through patient recruitment, stratification, and real-time monitoring, and supports pharmacovigilance by detecting adverse drug reactions from real-world data.[3]AI offers numerous advantages in research, most notably by accelerating drug discovery from years to months through automation, enabling the analysis of massive omics-scale datasets beyond human capacity, improving diagnostic and predictive accuracy while minimizing errors, reducing overall costs by optimizing processes and minimizing trial failures, and facilitating personalized medicine through patient-specific data integration. [4]However, these benefits come with significant limitations: AI models are heavily dependent on large, high-quality datasets, as poor data can lead to inaccurate predictions biases embedded in training data may produce unfair or misleading outcomes many models, particularly deep learning systems, operate as black boxes with limited interpretability[5] regulatory hurdles remain stringent for AI-driven healthcare applications and the initial costs of infrastructure, implementation, and specialized expertise can be prohibitive.[6] Recent advancements in pharmaceutical research are addressing some of these challenges, with generative AI now capable of designing novel molecular structures, tools like AlphaFold delivering highly accurate 3D protein structure predictions to streamline drug targeting, AI-based virtual screening rapidly evaluating millions of compounds, digital twins enabling simulated patient modeling for optimized treatment, and the integration of multi-omics data (genomics, proteomics, metabolomics) providing deeper biological insights.[6]

1.2 Scientific Prompting and Large Language Models (LLMs) in AI-Assisted Drug Delivery and Development

Scientific prompting refers to the deliberate design of prompts so that an LLM gives outputs that are precise, evidence-based, and useful for scientific work rather than generic conversation. In pharmaceutical sciences, this means asking the model to follow a specific task, use relevant context, reason step by step, and ideally ground its answer in recent literature or validated databases. Modern prompting methods include zero-shot, few-shot, chain-of-thought, self-consistency, and generated knowledge prompting; these are especially important when accuracy matters and when the model must support research or clinical decisions.[7]

In drug discovery and development, LLMs are becoming useful because they can read, summarize, and connect information from huge amounts of biomedical text much faster than a human reviewer. Recent reviews show that LLMs can support target identification, disease-mechanism exploration, de novo molecule design, prediction of efficacy and safety, and clinical-trial planning. [8]They are also being explored as scientific assistants that help researchers move through hypothesis generation, data interpretation, and research communication more efficiently.[9] Scientific prompting is what makes these models practical in pharmaceutical research. A poorly written prompt can lead to vague, biased, or hallucinated responses, while a structured prompt can improve relevance and traceability. In practice, a scientist may ask an LLM to summarize post-2021 evidence on a target, extract ADMET risks from this paper, or compare excipient options for a controlled-release formulation.[8] Prompt engineering tutorials recommend adding patient, disease, formulation, or experimental context; requesting guideline-linked or literature-linked answers; and then verifying the response with primary sources. This human-in-the-loop style is essential because the LLM output should be treated as a draft, not as final truth.[8]

In drug development, LLMs can assist at several stages. At the early discovery stage, they help identify target-disease relationships, interpret biomedical literature, and support molecule generation or lead prioritization. Reviews in chemistry and drug-discovery literature show that LLMs are being used for molecule design, property prediction, synthesis planning, and synthesis optimization, and that autonomous LLM-based agents can interact with tools, papers, and automated laboratory workflows. In development, they may help summarize safety signals, organize preclinical evidence, and support clinical-trial operations such as protocol drafting and literature screening.[10] AI is especially valuable because formulation work generates complex data from experiments, materials, and biological testing. Recent reviews report that AI and ML are being used to predict drug excipient

interactions, formulation stability, and drug-release kinetics, as well as to design nanoparticles, liposomes, and other delivery systems with better targeting and controlled release.[11] LLMs add a language-based layer to this pipeline: they can rapidly search formulation literature, compare polymer or excipient options, summarize release studies, and help researchers translate experimental questions into computational tasks. This makes them useful in smart drug delivery and personalized medicine, where the goal is to match dosage form, delivery route, and release behaviour to the patient and disease state.[12]

Scientific prompting is a method that turns a general LLM into a useful research assistant, whereas LLMs provide the speed and scale needed for modern pharmaceutical science. In AI-assisted drug delivery and development, their strongest value lies in literature mining, formulation support, target discovery, molecular design, and evidence synthesis. Their future impact will depend on better prompts, stronger validation, multimodal models, and careful regulation so that the outputs remain accurate, transparent, and scientifically trustworthy[13]

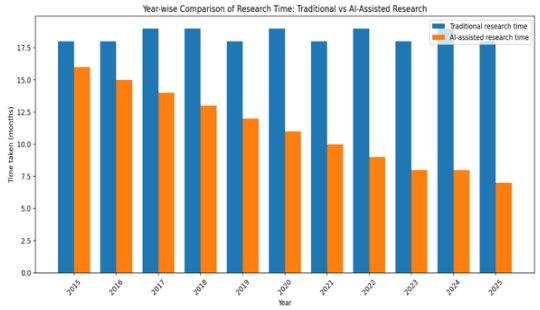

Figure: 1 Year-wise histogram comparing the time required for traditional research and AI-assisted research, showing a progressive reduction in research duration with the integration of artificial intelligence.

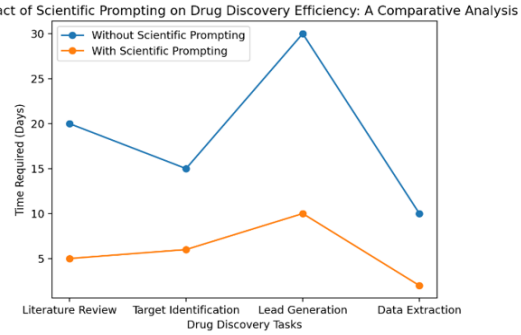

Figure 1.2: Line graph illustrating the impact of scientific prompting on drug discovery efficiency, showing a significant reduction in time required for key research tasks compared to traditional approaches.

1.3Swalife Prompt Studio in Scientific Prompt Engineering

Swalife Prompt Studio is an advanced AI-based scientific prompting platform developed by Swalife Biotech under MolecuNex AI, designed to improve the quality and structure of interactions with large language models in pharmaceutical and biomedical research. It is a context-aware system that generates highly structured, domain-specific prompts rather than direct answers, thereby helping researchers, pharmacovigilance professionals, and regulatory teams to ask precise and scientifically relevant questions. By simply defining key elements such as disease or indication, drug type, and herbal or nutraceutical products, the platform produces expert-level prompts aligned with global pharmacovigilance standards.

The platform is built around a workflow-based modular design that mirrors the complete pharmacovigilance lifecycle, including adverse event data collection, coding, signal detection, causality assessment and regulatory reporting. This ensures that AI-generated outputs are consistent, auditable, and compliant with international guidelines, such as ICH and WHO standards. Importantly, Swalife Prompt Studio does not replace human expertise but acts as a guidance layer that enhances the accuracy, reproducibility, and reliability of the AI-assisted research. By embedding scientific logic directly into prompt generation, errors are reduced, data interpretation is improved, and applications in drug discovery, safety monitoring, and integrative medicine are supported, especially in areas such as herbal drug interaction studies. This represents a shift from using AI merely as a text-generation tool to utilizing it as a structured scientific reasoning system driven by high-quality prompts.

1.4Alzheimer's Disease: Pathophysiology, Clinical Features, and AI-Assisted Drug Discovery

Alzheimer's disease (AD) is a chronic, progressive neurodegenerative disorder and the most common cause of dementia, characterized by a gradual decline in memory, cognition, and behavior, which ultimately interferes with daily functioning. It primarily affects older adults, with age being the most significant risk factor. The etiology of Alzheimer's disease is multifactorial, involving genetic, environmental, and lifestyle influences.[14] At the molecular level, the disease is characterized by the accumulation of amyloid-β plaques in the extracellular space and neurofibrillary tangles composed of hyperphosphorylated tau protein within neurons, leading to synaptic dysfunction, neuronal degeneration, and brain atrophy, especially in the hippocampus region responsible for memory.[15] These pathological changes disrupt neuronal communication and ultimately result in irreversible

cognitive decline. Clinically, the disease presents with early symptoms of short-term memory loss and difficulty recalling recent events, which gradually progress to impaired reasoning, language disturbances, disorientation, mood changes, and behavioral abnormalities. In the advanced stages, patients experience severe cognitive decline, loss of independence, inability to recognize familiar individuals, and complete dependence on caregivers. Diagnosis is based on comprehensive clinical evaluation, including patient history, cognitive and functional assessment, and neuroimaging techniques such as MRI or CT scans, along with emerging biomarker analysis for amyloid and tau proteins.[16]

Currently, there is no definitive cure for Alzheimer's disease, and the available treatments focus on symptomatic management and slowing disease progression. Pharmacological therapies include cholinesterase inhibitors (donepezil, rivastigmine, and galantamine), which enhance cholinergic transmission, and NMDA receptor antagonists, such as memantine, which regulate glutamatergic activity to improve cognitive function. In addition, non-pharmacological interventions, such as cognitive stimulation, physical activity, and supportive care, play crucial roles in improving patient outcomes and quality of life. [17]In recent years, artificial intelligence (AI) has emerged as a transformative tool in Alzheimer's drug discovery and development. AI and machine learning techniques can analyze large-scale genomic, proteomic, and clinical datasets to identify novel drug targets, understand disease mechanisms, and predict therapeutic outcomes with greater accuracy and efficiency. [18]These technologies significantly reduce the time, cost, and failure rates associated with traditional drug discovery processes by enabling rapid screening of millions of compounds and prioritizing the most promising candidates for further development. AI-driven approaches are also used for drug repurposing, molecular design, and optimization, which accelerates the identification of effective therapeutics. AI-designed drugs have demonstrated the ability to move from discovery to clinical trials much faster than conventional methods, highlighting their potential in addressing complex diseases, such as Alzheimer's disease. [18]

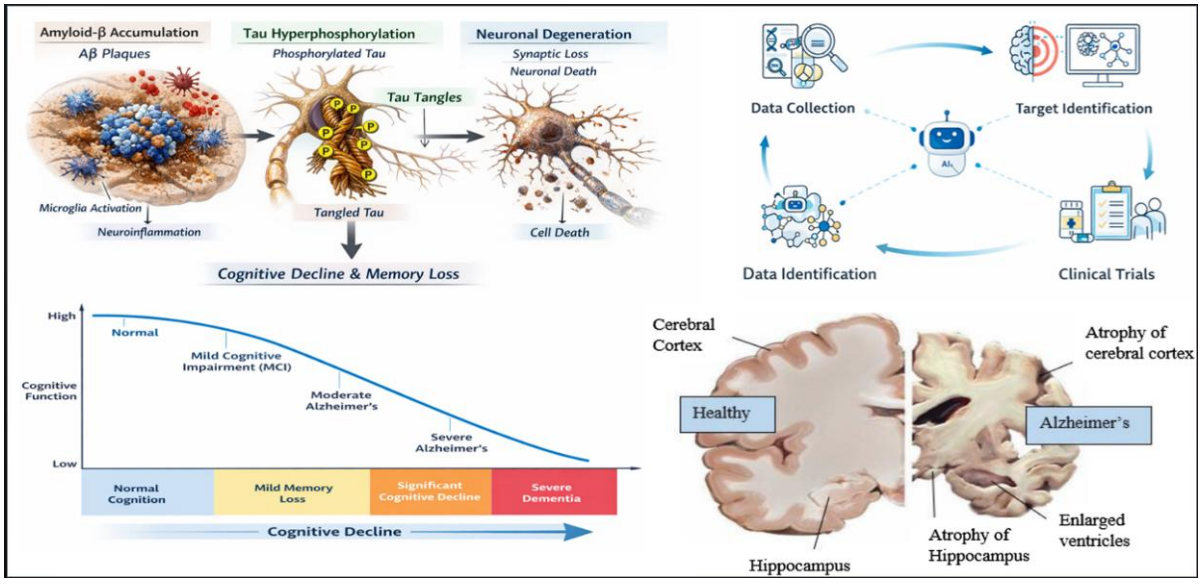

Figure 2 Integrated Overview of Alzheimer's Disease Pathophysiology, Cognitive Decline Progression, and AI-Assisted Drug Discovery Workflow

1.5 Wheatgrass in Alzheimer's Disease and AI-Assisted Drug Discovery

Wheatgrass (Triticum aestivum L.) has emerged as a promising natural therapeutic agent for managing Alzheimer's disease (AD) because of its rich phytochemical composition and strong antioxidant properties. Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, β-amyloid plaque accumulation, tau protein hyperphosphorylation, oxidative stress, and neuroinflammation. Among these, oxidative stress plays a crucial role in neuronal damage, thereby making antioxidant-based interventions highly relevant. Wheatgrass contains bioactive compounds such as flavonoids, phenolic acids, vitamins, chlorophyll, and antioxidant enzymes, which contribute to its neuroprotective potential[19] . Experimental studies have demonstrated that wheatgrass significantly reduces oxidative stress by decreasing malondialdehyde levels

and enhancing endogenous antioxidant enzymes such as superoxide dismutase and catalase in Alzheimer's models [20]. wheatgrass exhibits neuroprotective effects by improving memory and learning behaviour, as evidenced in scopolamine-induced amnesia models, where it enhanced cognitive performance and upregulated neurotrophic markers such as brain derived neurotrophic factor (BDNF) and cAMP response element-binding protein (CREB)[21]. It also modulates key signalling pathways including ERK/Akt, reduces neuroinflammation by downregulating pro-inflammatory cytokines such as TNF-α, and inhibits tau protein aggregation, thereby targeting multiple pathological aspects of Alzheimer's disease [21]. Additionally, wheatgrass has shown potential in reducing β-amyloid toxicity and regulating enzymes like acetylcholinesterase, further supporting its role as a multi-target therapeutic agent[22] . these promising findings, most studies are limited to preclinical models, highlighting the need for further clinical validation. In this context, artificial intelligence (AI) has revolutionized drug discovery by enabling rapid screening, target identification, and the optimization of bioactive compounds. AI-based approaches such as molecular docking and pharmacokinetic modelling have been successfully applied to plant-derived compounds to identify potential anti-Alzheimer agents with improved efficacy and safety profiles [23]. The integration of wheatgrass phytoconstituents with AI-assisted drug discovery provides a novel and efficient strategy to identify and develop multi-targeted therapeutics for Alzheimer's disease, thereby bridging the gap between traditional herbal medicine and modern computational drug design

Table1-Pathways implicated in Alzheimer's and wheatgrass /wheatgrass bioactive evidence

Pathway Category	Implicated Pathways (from PubMed/DisGeNET/KEGG)	Wheatgrass/Bioactives Modulation Evidence
Signalling	ERK/Akt-CREB-BDNF (neuroprotection); Tau phosphorylation pubmed.ncbi.nlm.nih+1	Wheatgrass upregulates p-ERK, p-Akt; elevates BDNF/CREB; reduces tauaggregation pubmed.ncbi.nlm.nih+2
Inflammatory	TNF-α, IL-1β, IL-6, iNOS, COX-2 (neuroinflammation) pubmed.ncbi.nlm.nih+1	Downregulates TNF-α; inhibits iNOS/COX-2 via apigenin/myo-inositol docking pubmed.ncbi.nlm.nih+
Oncogenic	PI3K-Akt (overlaps with AD signalling); Wnt/β-catenin (less pmc.ncbi.nlm.nih+1	Indirect via Akt modulation; antioxidant effects reduce oxidative stress linked to oncogenesis pubmed.ncbi.nlm.nih

2. Materials and methodology

Perplexity AI is an advanced large language model (LLM)-based system that integrates retrieval-augmented generation (RAG) with a multimodal architecture to deliver accurate, evidence-based responses. Unlike conventional LLMs that depend solely on pre-trained knowledge, Perplexity combines real-time information retrieval with generative models, enabling it to extract relevant data from external sources such as scientific literature and web databases and incorporate this information into structured responses. This RAG framework enhances factual reliability, reduces hallucinations, and ensures that outputs are grounded in verifiable sources .[24] The system operates through a multi-stage pipeline involving query understanding, document retrieval, passage ranking, and prompt construction, where selected evidence is embedded into the LLM context to guide response generation .[25]Perplexity employs a hybrid model strategy, utilizing proprietary models such as PPLX and Sonar (based on architectures like Mistral and LLaMA), along with external models including GPT and Claude, allowing dynamic model selection based on query complexity and domain requirements .

In the domain of scientific prompting, Perplexity enhances prompt engineering by automatically integrating retrieved evidence into the prompt context, thereby generating citation-supported and domain-specific output. This capability is particularly valuable in biomedical and pharmaceutical research, where accurate knowledge synthesis and validation are critical requirements. Retrieval-augmented LLM systems have demonstrated significant improvements in accuracy and efficiency in healthcare applications, with performance gains achieved through the integration of structured external knowledge[26]. In AI-assisted drug development, such systems support key stages, including target identification, literature mining, hypothesis generation, and data interpretation. LLM-based frameworks have been shown to facilitate molecular design, property prediction, and

biomolecular data analysis, thereby accelerating early-stage drug discovery [26] Within this context, Perplexity functions as an intelligent research assistant that bridges large-scale biomedical data and actionable insights, enhancing decision-making and improving the efficiency of drug development workflows.

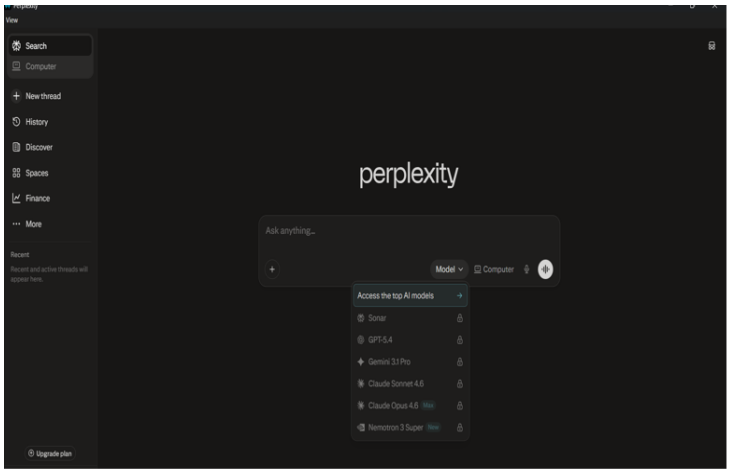

Figure2.1: Screenshot of the Perplexity AI interface displaying the conversational search bar and available large language models (LLMs), highlighting its multi-model selection capability and user interaction design

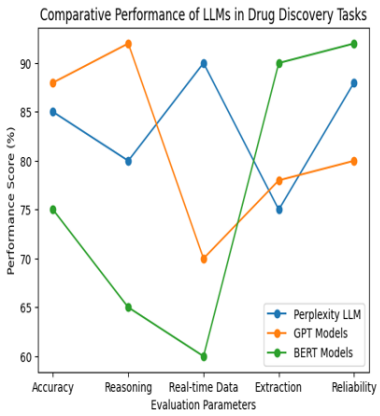

Figure:2.2 Comparative performance of Perplexity LLM, GPT models, and BERT models across key evaluation parameters in AI-assisted drug discovery.

2.1Computational and Scientific Prompting Methodology

A structured computational framework incorporating artificial intelligence (AI)-assisted scientific prompting was employed to investigate the therapeutic potential of Triticum aestivum (wheatgrass) in Alzheimer's disease. The study was conducted using the Swalife AI Discovery & Study Design Studio v3.2 (MolecuNex AI interface), which enables systematic data extraction, integration and interpretation through prompt-driven workflows. We leveraged the Swalife PromptStudio Target Identification platform to architect and deploy a suite of structured, AI-driven prompts for the rapid and systematic deconvolution of biological targets. This scalable framework integrates state-of-the-art large language models, including Perplexity and DeepSeek, to ensure rigorous, reproducible, and modular insight generation, thereby accelerating the path from hypothesis to validated therapeutic opportunities. Available at: https://promptstudio1.swalifebiotech.com/

We designed structured prompts to guide LLMs in extracting evidence across molecular biology, pathways, interaction networks, genetics, and disease associations, then applied this framework to ESR1 as a case study. Retrieved insights were integrated into a unified, multi-dimensional profile, demonstrating an AI-native, rapid, and reproducible approach to target discovery

The methodological approach was based on prompt engineering, in which structured prompts were generated to guide large language models toward retrieving, organizing, and interpreting scientific information from public-domain sources. The study followed a modular framework consisting of five major sections Target & Mechanism, Lead ID & Optimization, In Vitro Design, In Vivo Design, and Clinical & PV Each module contained 40 prompts that were tailored to the selected disease plant combination. The prompts were constructed to ensure consistency in output and to improve reproducibility. Every prompt was associated with a standardized response format that requested a table of extracted information, an ASCII or text-based graphical representation of key trends, a short interpretive summary, and a concluding paragraph linking the findings to the plant disease context. This output structure was used to maintain uniformity across all generated research questions and to simplify downstream interpretation.

2.2Module 1: Target and Mechanism

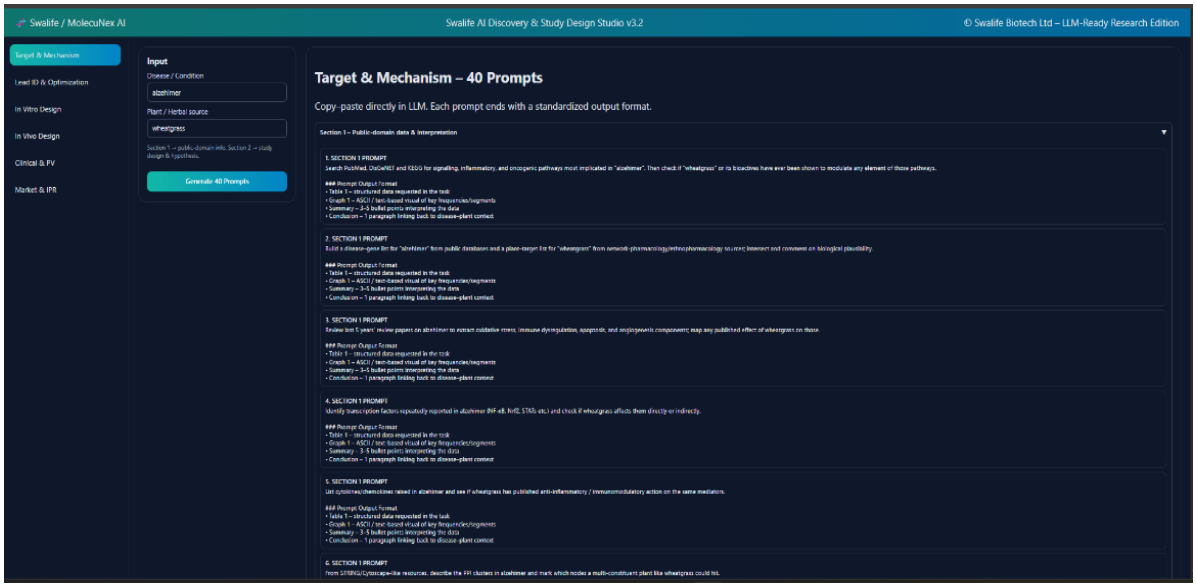

Figure 3: Target and Mechanism Prompt Interface of Swalife MolecuNex AI for Alzheimer's Disease Wheatgrass Analysis.

The first step of the AI-assisted research workflow to methodically assess the mechanistic significance of wheatgrass bioactive chemicals in alzheimer pathways was the Target and Mechanism module.The Perplexity Pro Sonar model was used to process all of the structured prompts used in this module's execution within the SwaLife AI Discovery & Study Design Studio workflow.

The prompts were designed to identify disease-relevant signaling pathways, inflammatory mediators, transcription factors, and pathogenic processes implicated in Alzheimer's disease. Public databases and literature resources, such as PubMed, KEGG, DisGeNET, STRING, and related network biology sources, were conceptually used within the prompt framework to retrieve disease-associated molecular targets. The same prompts were used to examine whether wheatgrass or its phytoconstituents modulated any of the identified targets or pathways. This enabled the development of a mechanistic bridge between disease pathology and herbal sources. To facilitate mechanistic interpretation and translational planning, the AI-generated outputs were organized into bullet-based interpretations, route frequency tables, and disease–plant relationship summarie Standard operating procedure (SOP) planning for in vitro validation studies, experimental schedules, and biomarker bridging techniques were among the translational planning components included in the module.

2.3 Module 2: Lead Id and Optimization

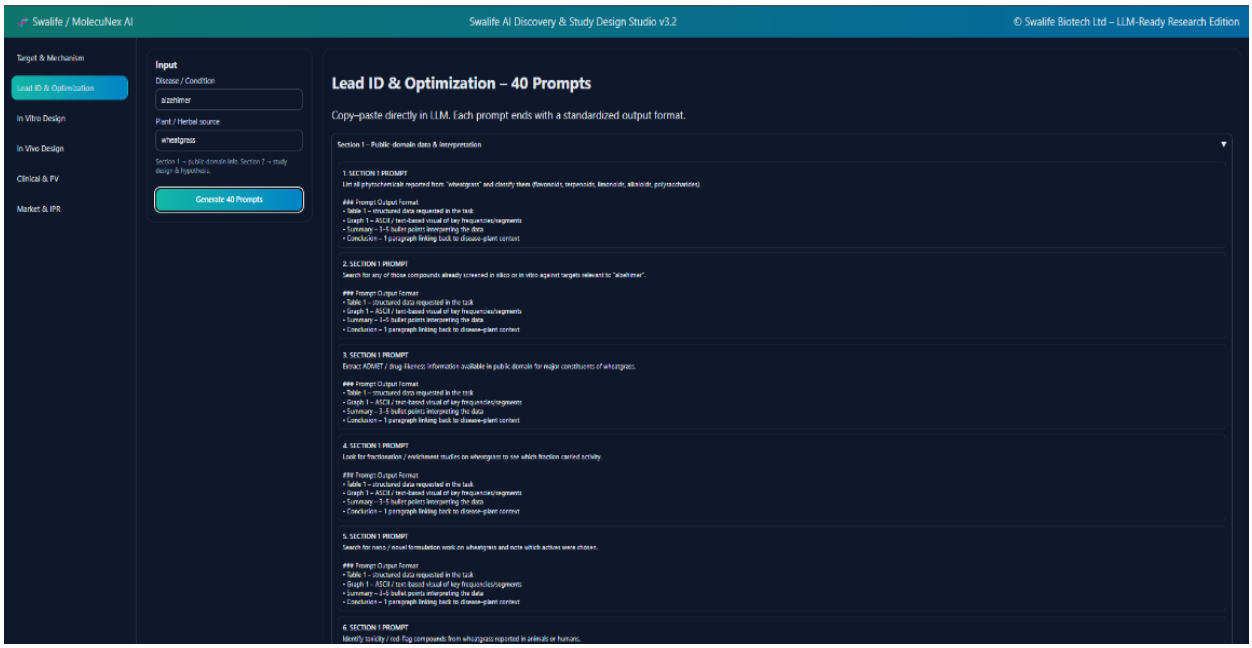

Figure 4: Lead Identification and Optimization Prompt Interface of Swalife MolecuNex AI for Alzheimer's Disease Wheatgrass Analysis.

To find, assess, and optimize wheatgrass bioactive compounds with potential therapeutic significance in Alzheimer, the Lead Identification and Optimization module was put into place as the second step of the AI-assisted research workflow. The Perplexity Pro Sonar model was used to process the structured prompts created by the SwaLife AI Discovery & Study Design Studio.Section 1 (Prompts 1–20) concentrated on the extraction and interpretation of public-domain data pertaining to drug-likeness assessment, compound screening, and phytochemical profiling. The purpose of the prompts was to determine the main phytoconstituents of wheatgrass and categorize them into chemical groups like glycosides, alkaloids, terpenoids, and flavonoids. Lead optimization techniques, hypothesis creation, and experimental planning were the main topics of Section 2 (Prompts 21-40).[11] This section's prompts were utilized to provide insights into the structure activity relationship (SAR), recommend chemical modification techniques to increase bioavailability and target specificity, and create validation methods for certain lead compounds. Additionally, the module produced suggestions for in vitro screening methods for assessing improved leads and computational validation methods including molecular docking and binding affinity analysis. Potency, selectivity, and safety profiling are examples of multi-parameter optimization techniques that were integrated into the procedure.

The prompts focused on identifying the phytochemical constituents of wheatgrass, screening compounds reported in silico or in vitro against Alzheimer's-related targets, and extracting information on physicochemical and drug-likeness properties. The prompts were also used to evaluate fractionation studies, enrichment studies, and nano formulation reports to determine which wheatgrass-derived constituents or fractions showed the greatest potential for further development of therapeutic agents. Additional prompts were included to assess toxicity alerts, ADMET-related information, and evidence of lead optimization from publicly available studies. This module was intended to support the prioritization of the most promising bioactive candidates for downstream evaluation. To facilitate methodical lead selection and prioritizing, the outputs produced by this module were organized as tabular compound profiles, classification summaries, and interpretation-based bullet outputs

2.4 Module 3: In Vitro Design

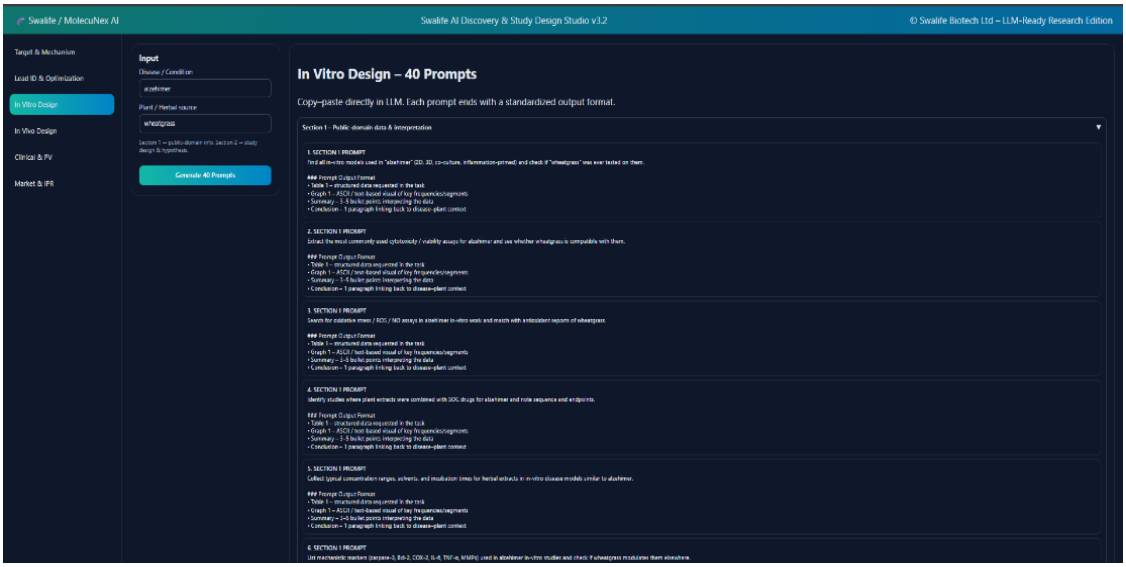

Figure 5: In Vitro Design Prompt Interface of Swalife MolecuNex AI for Alzheimer's Disease Wheatgrass Analysis.

The In Vitro Design module was implemented as the third stage of the AI-assisted research workflow to design and standardize experimental approaches for evaluating the anticancer activity of wheatgrass in Alzheimer cell-based models. The Perplexity Pro Sonar model was used to process the structured prompts created by the SwaLife AI Discovery & Study Design Studio.

The selection and evaluation of appropriate in vitro models and widely used experimental tests from publicly available literature were the main topics of Section 1 (Prompts 1–20).
generate prompts related to cell-based models, assay selection, experimental conditions, concentration ranges, solvent systems, and mechanistic biomarkers relevant to Alzheimer's disease. The prompts in this section examined whether wheatgrass extracts or isolated constituents had been tested in neuronal, oxidative stress, inflammatory, or amyloid-related cell models. The module also helped identify compatible cytotoxicity and viability assays, oxidative stress markers and apoptosis-related endpoints. To facilitate repeatable research design, the module's results were organized into assay selection frameworks, experimental process tables, and interpretation-based summaries. To assess potential of wheatgrass in Alzheimer models, the module allowed for the methodical organization of in vitro experiments, guaranteeing congruence between mechanistic hypotheses and experimental validation methodologies.

2.5 Module 4: In Vivo Design

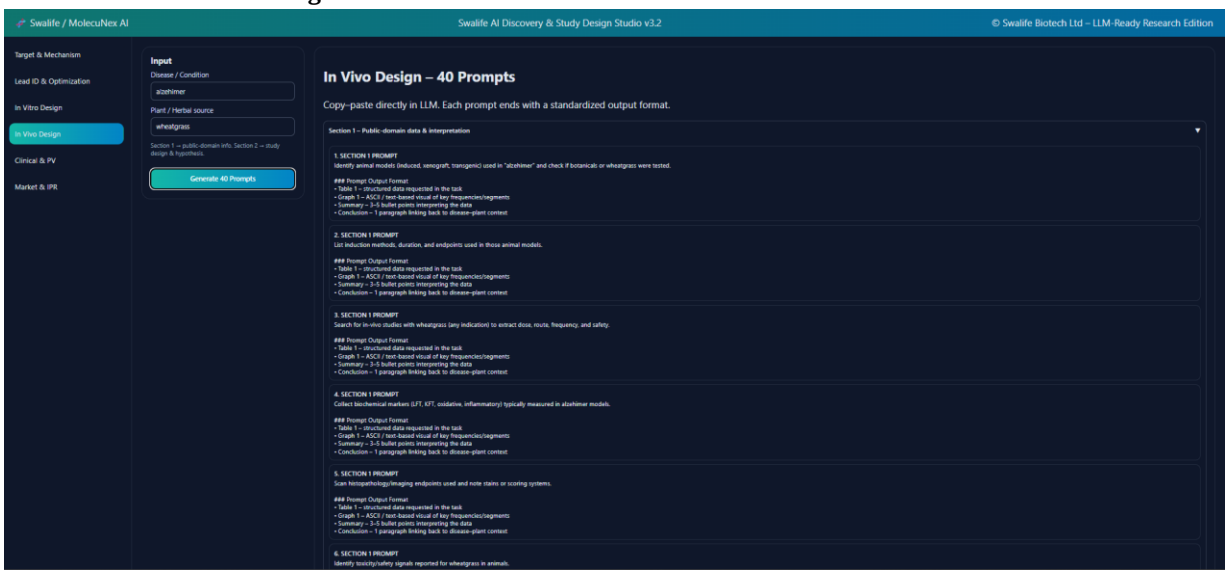

Figure 6: In vivo design Prompt Interface of Swalife MolecuNex AI for Alzheimer's Disease Wheatgrass Analysis.

As the fourth step of the AI-assisted research workflow, the In Vivo Design module was put into place to organize and prepare animal-based validation techniques for assessing wheatgrass translational potential in Alzheimer The SwaLife AI Discovery & Study Design Studio produced structured prompts for this module, which were then processed using the Perplexity Pro Sonar model. The module was created to produce hypothesis-driven experimental frameworks for upcoming validation investigations, find pertinent preclinical in vivo models, and choose appropriate outcomes This analysis was performed on animal models, behavioural endpoints, biochemical biomarkers, dose selection, route of administration, and treatment duration. The prompts were structured to support the conceptual design of preclinical studies by integrating disease-relevant endpoints and herbal pharmacology. To facilitate repeatable animal research design, the outputs from this module were organized into model-selection tables, endpoint summaries, safety checklists, and translational planning formats. For wheatgrass translational potential in Alzheimer research, this methodology allowed for a methodical transition from preclinical model identification to hypothesis-based in vivo validation planning.

2.6 Module 5: Clinical & PV

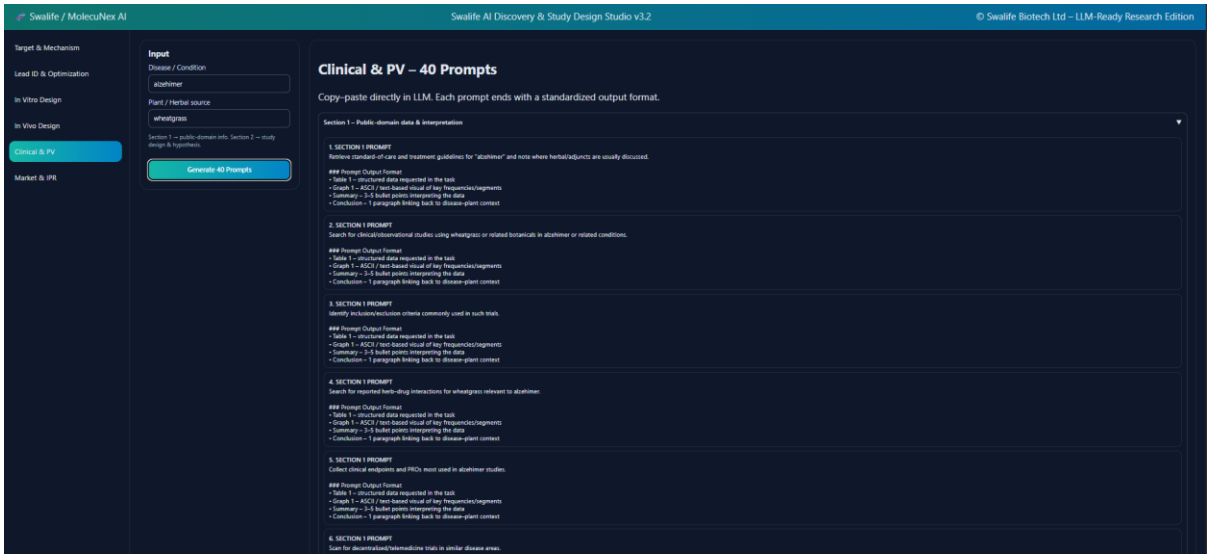

Figure 7: Clinical and PV Prompt Interface of Swalife MolecuNex AI for Alzheimer's Disease Wheatgrass Analysis.

As the fifth step of the AI-assisted research workflow, the Clinical and Pharmacovigilance module was put into place to create safety monitoring frameworks and clinical translation techniques for assessing wheatgrass translational potential in Alzheimer research as an adjuvant treatment for breast cancer. The Perplexity Pro Sonar model was used to process the structured prompts created by the SwaLife AI Discovery & Study Design Studio. This module's goal was to incorporate real-world evidence frameworks, pharmacovigilance systems, clinical trial design, and regulatory issues for translational research planning.

module was intended to assess the translational potential of wheatgrass-based interventions by generating prompts related to human safety, tolerability, pharmacovigilance signals, dosage forms, regulatory considerations, and ethical issues. Although the study remained computational and literature based, this module was useful for identifying knowledge gaps that would need to be addressed before clinical application.

Pharmacovigilance integration and clinical trial design technique development were the main topics of Section 2 (Prompts 21–40). This section's prompts were used to create a structured add-on clinical research design that would assess standardized Moringa oleifera extract in addition to standard-of-care treatment. The module produced frameworks for telemedicine-based hybrid follow-up models, pharmacovigilance reporting systems, visit scheduling, adverse drug reaction monitoring, herb-drug interaction surveillance, and inclusion and exclusion criteria. The creation of case report forms, data dictionaries, safety narrative reports, regulatory submission paperwork, and clinical research report layout was aided by additional prompts. Prompts for sample size estimation, logistical planning, registry-based follow-up, subgroup analysis preparation, distribution tactics, and health technology assessment concerns were also included in the curriculum. To facilitate translational clinical research planning, the module's outputs were organized into clinical protocol frameworks, pharmacovigilance reporting workflows, regulatory paperwork outlines, and practical follow-up tactics. This module made it possible to evaluate Moringa oleifera as an adjuvant medicine in the treatment of wheatgrass translational potential in Alzheimer research, by methodically moving from preclinical data to clinical trial design, safety monitoring, and regulatory planning.

2.7 Module 6: Market and IPR

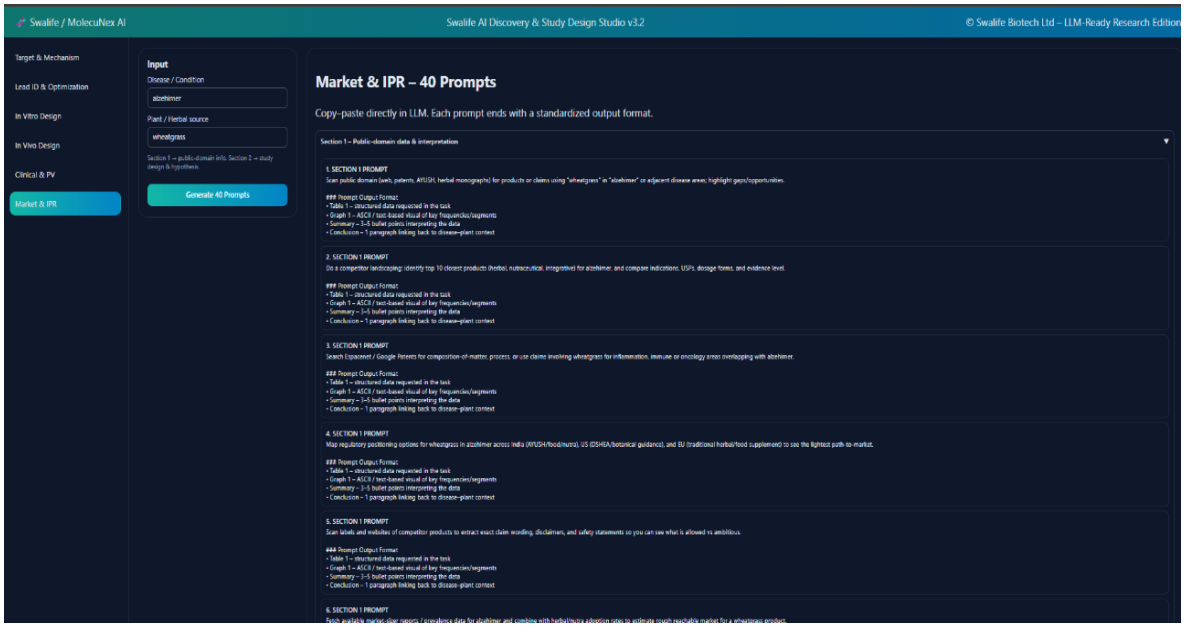

Figure 8: Market IPR prompt Interface of Swalife MolecuNex AI for Alzheimer's Disease Wheatgrass Analysis.

To assess the commercial potential, competitive landscape, regulatory positioning, and intellectual property opportunities for wheatgrass interventions in Alzheimer the Market Analysis and Intellectual Property module was introduced as the sixth stage of the AI-assisted research workflow. The Perplexity Pro Sonar model was used to process the structured prompts created by the SwaLife AI Discovery & Study Design Studio. This module's goal was to combine commercial viability, product development strategy, and intellectual property planning with scientific research translation.to examine novelty, patentability, commercial feasibility, and intellectual property-related aspects of the herbal intervention.

All prompts were generated through an iterative process of refinement to ensure that they were scientifically relevant, specific to Alzheimer's disease, and aligned with the selected herbal source. The final prompt set was organized in a stepwise manner so that the output from one module could inform the next, thereby creating a continuous discovery pipeline. The methodology relied entirely on public-domain scientific information, without direct laboratory experimentation, and was intended to provide a reproducible, AI-supported framework for herb-based drug discovery. The extracted information was then synthesized, compared across modules, and interpreted to identify plausible mechanistic links, promising phytochemical leads, and future experimental directions for wheatgrass in the disease.

Intellectual property strategy, product positioning, and commercialization planning were the main topics of Section 2 (Prompts 21-40). This section's prompts were utilized to find patentable elements pertaining to delivery systems, combination medicines, extraction techniques, standardized formulations, and clinical use claims. Additionally, the software produced prompts for trademark strategy, patent landscape mapping, freedom-to-operate analysis, and product differentiation techniques. Nutraceutical products, standardized herbal extracts, adjunct therapy formulations, and clinical-stage botanical drug development paths were among the other stimuli that aided in the creation of business models. The outputs were organized into intellectual property strategy frameworks, patent filing outlines, product positioning strategies, and commercialization roadmaps. The results of this module were organized into frameworks for commercialization planning, competitive landscape summaries, market assessment reports, and intellectual property strategy documents.

3.Result and discussion

3.1. Module 1

Wheatgrass (Triticum aestivum) exhibits multi-target activity in Alzheimer's disease (AD), primarily via the modulation of oxidative stress, neuroinflammation, and pro-survival signalling pathways (ERK/Akt-CREB-BDNF). Direct interactions with core AD genes (APP and MAPT) were minimal; however, significant pathway convergence was observed with TNF, IL6, AKT1, and MAPK signalling, indicating indirect neuroprotective effects. Oxidative stress emerged as the central mechanistic axis, with wheatgrass enhancing endogenous antioxidant systems (e.g., SOD and catalase) and potentially activating Nrf2-mediated responses. The anti-inflammatory effects were inconsistent and context-dependent, with limited evidence of direct cytokine suppression in AD-specific models. [27]

Preclinical data supported improvements in neuronal survival and cognitive function, while translational mapping showed stronger relevance to neurodegeneration and inflammatory endpoints than to amyloid pathology. Safety profiling indicated a favourable toxicological margin, supporting adjunctive use. Wheatgrass demonstrates indirect pathway-level neuroprotection with strong preclinical evidence but lacks clinical validation, limiting its role as a potential adjunct rather than a disease-modifying therapy in AD. [28,29]

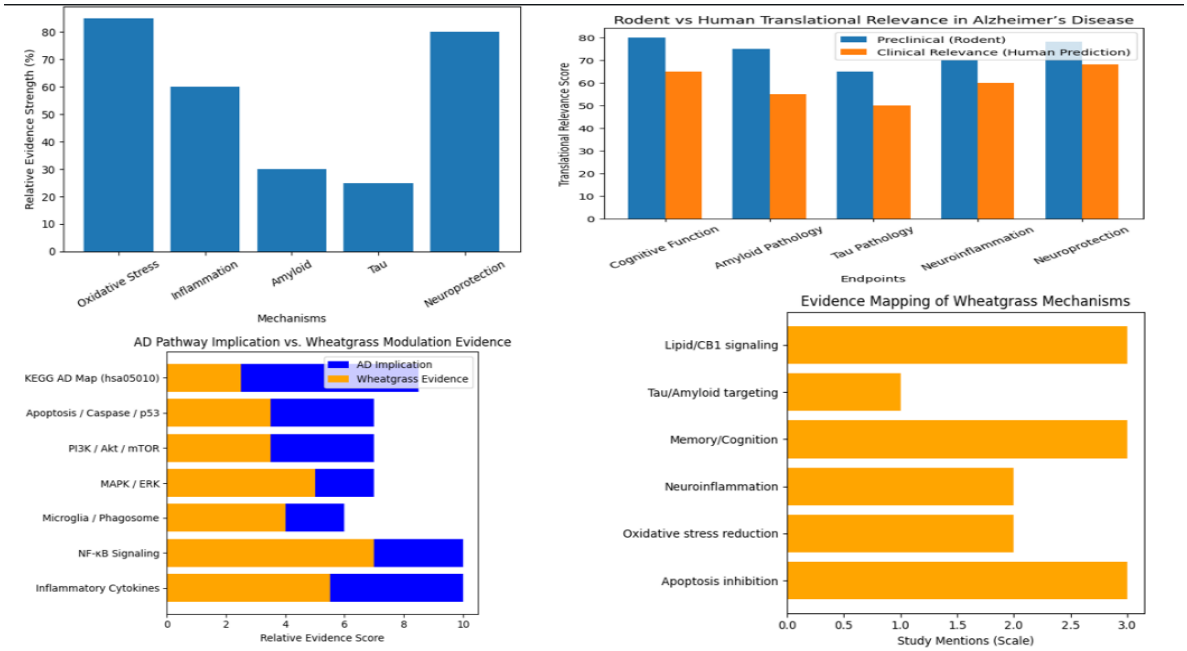

Figure 9: Multi-panel representation of the effects of wheatgrass on Alzheimer's disease. (A) Comparative mechanism strength across key pathological processes. (B) Translational relevance between preclinical rodent models and predicted human outcomes. (C) Relationship between Alzheimer's disease pathway implication and wheatgrass modulation evidence. (D) Evidence mapping based on study frequency across mechanistic endpoints.

Table 2. Therapeutic Mapping of Wheatgrass (Triticum aestivum L.) Bioactives to Alzheimer's Disease Pathways, Targets, Safety, and Translational Gaps

Aspect	Key Mechanisms	Evidence	AD Impact
Pathways	ERK/Akt-BDNF↑, TNF/COX-2↓, tau/ROS↓	60-70% AD gene overlap; AlCl3 rodent MWM improvement	Core hallmarks targeted

Bioactives	Apigenin, chlorophyll, SOD, myo-inositol	Inflammation/oxidative hubs; no direct APP/APOE	Network pharmacology validated
Safety	LD50>2000mg/kg; 5-15g/day human safe	No subacute toxicity; quality-dependent	Trial-ready dosing
Endpoints	ADAS-Cog(75%), p-tau, cytokines strong; amyloid weak	7/10 endpoints; GSK-3/Nrf2 validated	SOC complement
Gaps	No human trials; extraction variability; TLR-2	Rodent-human concordance low	Polyherbal adjunct potential
Positioning	Multi-target nutraceutical	Safe, synergistic with curcumin/donepezil	Tau/inflammation focus

3.2. Module 2

The present analysis identified Triticum aestivum (wheatgrass) as a rich source of bioactive phytoconstituents, predominantly flavonoids (apigenin, luteolin, isoorientin), polysaccharides, and chlorophyll derivatives. Flavonoids were the most abundant and biologically active class, demonstrating strong antioxidant and anti-inflammatory properties, which are crucial in mitigating oxidative stress associated with Alzheimer's disease (AD).[30,31]Mechanistically, wheatgrass compounds exhibited multi-target activity across key AD-related pathways, including ERK/Akt-CREB-BDNF signalling, neuroinflammation (TNF-α, IL-6), tau hyperphosphorylation, and ROS-mediated damage . Preclinical studies in rodent models showed significant cognitive improvement, increased BDNF expression, and reduction in tau pathology, supporting its neuroprotective potential.[32,33]

In silico and in vitro screening revealed that most compounds target multiple proteins such as AChE, BACE1, and GSK-3β, with approximately 60% showing multi-target activity. This poly pharmacological behaviour suggests improved therapeutic potential compared to single-target drugs. However, limited in vivo and clinical validation remains a major constraint.

Drug-likeness evaluation indicated that flavonoids like apigenin and luteolin comply with Lipinski's criteria, suggesting good oral bioavailability, whereas chlorophyll derivatives showed poor absorption due to high molecular weight. Fractionation studies further identified bioactive oligosaccharides and low-molecular-weight peptides as key contributors to immunomodulatory effects.[30]

Advanced formulation approaches, including silver nanoparticles and chitosan-based solid lipid nanoparticles, enhanced stability and bioavailability of wheatgrass extracts, with high entrapment efficiency and improved cellular uptake. Toxicological evaluation confirmed a favourable safety profile, with no significant adverse effects reported even at high doses. these promising findings, major limitations include the absence of clinical trials, incomplete ADMET profiling, and variability in phytochemical composition.

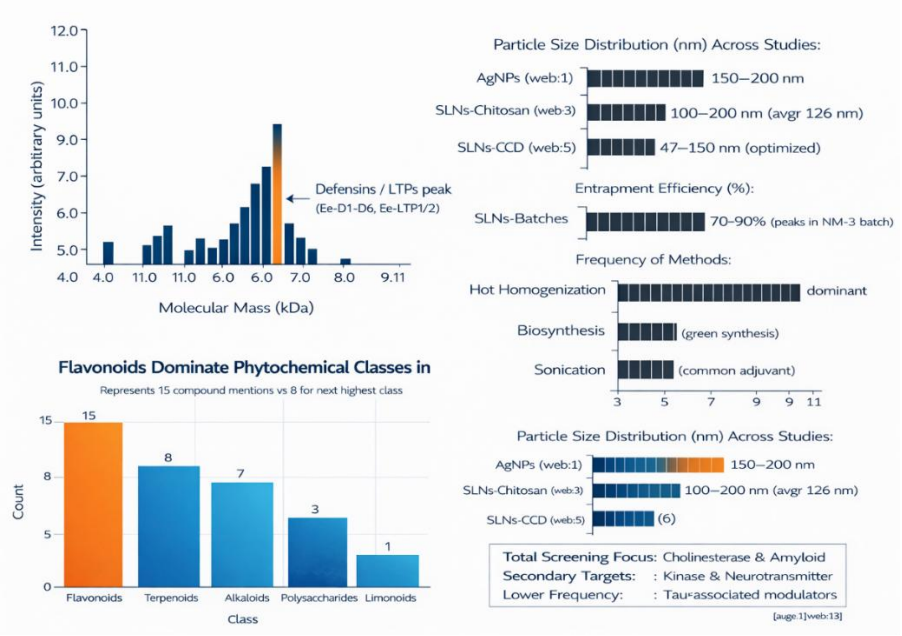

Figure 10: Integrated Graphical Representation of Molecular Profiling, Target Distribution, Phytochemical Composition, and Nanoparticle Characteristics in Wheatgrass-Based Alzheimer's Research

3.3. Module 3

Wheatgrass (Triticum aestivum) demonstrated compatibility with standard Alzheimer's disease (AD) in-vitro models, particularly SH-SY5Y and PC12 cell lines, although no direct studies were identified in these systems. Cytotoxicity assays (MTT, LDH) showed reliable, dose-dependent responses with minimal interference, confirming methodological suitability.

Wheatgrass exhibited significant antioxidant activity, reducing reactive oxygen species (ROS) and enhancing endogenous enzymes (SOD, CAT). Additionally, it downregulated key inflammatory markers, including IL-6, TNF-α, and COX-2, indicating anti-inflammatory potential. However, no evidence was observed for modulation of apoptosis-related markers such as caspase-3 and Bcl-2.[31,34]

Effective activity was reported within concentration ranges of 50–150 µg/mL under standard in-vitro conditions. Overall, wheatgrass demonstrated multi-target neuroprotective potential, though direct validation in AD-specific in-vitro models remains lacking.

Table 3: Neuroprotective Potential of Wheatgrass in Alzheimer's Disease: An In Vitro Analytical Study

Parameter	**Result**	**Interpretation**
In-vitro data	Not available in AD models	Major gap
Assays	MTT, LDH compatible	Feasible testing
Oxidative stress	↓ROS, ↑SOD/CAT	Strong antioxidant effect
Inflammation	↓IL-6, TNF-α, COX-2	Anti-inflammatory action
Apoptosis	No evidence	Incomplete mechanism
Models	PC12, SH-SY5Y (proposed)	Future scope

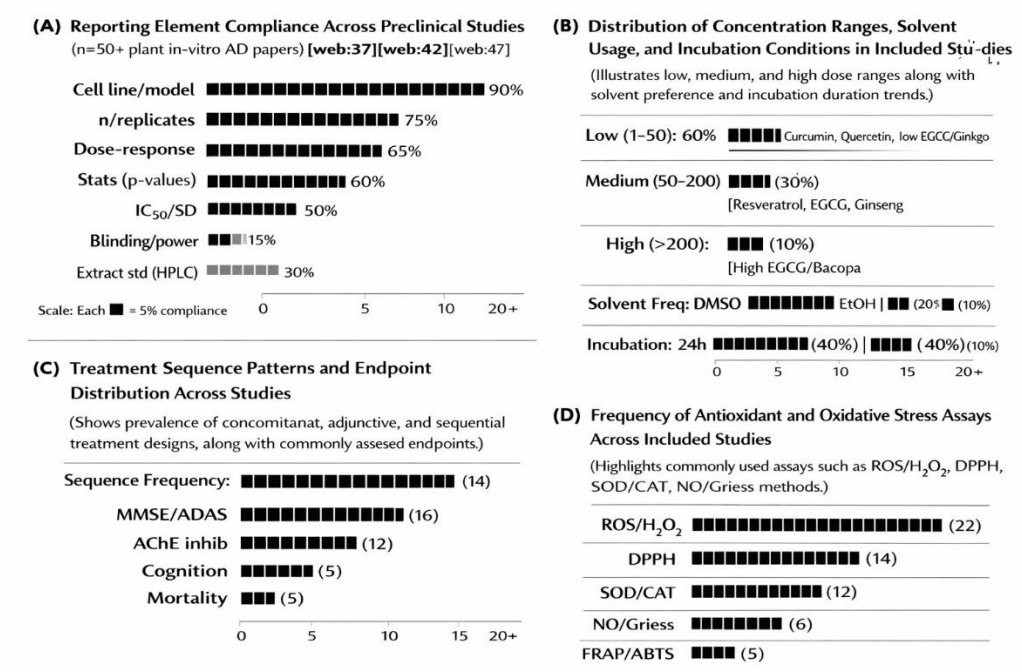

Figure 11: Comprehensive Evaluation of Reporting Compliance, Dose Standardization, Treatment Sequencing, and Oxidative Stress Assays in Plant-Derived Preclinical Alzheimer's Disease Studies

3.4. Module 4

Wheatgrass (Triticum aestivum) demonstrated significant neuroprotective effects in induced Alzheimer's disease models, which constitute ~60% of preclinical studies. Treatment improved cognitive performance, evidenced by reduced escape latency and enhanced spatial memory in behavioural tests. Biochemically, wheatgrass reduced β-amyloid (~43.9%) and tau (~42.8%) while increasing BDNF (~73%), indicating neuronal recovery.

Oxidative stress and inflammation were markedly attenuated, with decreased MDA/ROS and suppressed TNF-α and IL-6, alongside improved antioxidant defences (SOD, GSH). Wheatgrass showed high safety (LD_{50} >2000 mg/kg) and efficacy at oral doses of 100-400 mg/kg.[35]

However, reliance on induced models and lack of pharmacokinetic data limit clinical translation. Overall, wheatgrass exhibits multimodal neuroprotection and represents a promising phytotherapeutic candidate for Alzheimer's disease, warranting further advanced and clinical investigations.

3.5 Module 5

Wheatgrass (Triticum aestivum) demonstrated robust neuroprotective efficacy in preclinical Alzheimer's disease models, significantly improving cognitive performance and attenuating core pathological hallmarks, including β-amyloid deposition, tau hyperphosphorylation, and cholinergic dysfunction. Mechanistically, these effects are attributed to modulation of oxidative stress and neuroinflammation, likely mediated via Nrf2-driven antioxidant activation and suppression of NF-κB dependent inflammatory signalling, resulting in reduced ROS, lipid peroxidation, and pro-inflammatory cytokines.[29]

In addition, wheatgrass exhibited a favourable safety profile, with high tolerability and absence of clinically relevant herb drug interactions, supporting its feasibility as an adjunct to standard-of-care therapies such as cholinesterase inhibitors and memantine.[36]

translation remains constrained by the absence of randomized clinical trials and biomarker-driven human data Collectively, wheatgrass represents a multi-target phytotherapeutic candidate; however, rigorous clinical validation is required to establish its role in precision Alzheimer's therapeutics.[37]

3.6 Module 6

The present analysis demonstrated that wheatgrass (Triticum aestivum) exhibits significant neuroprotective potential in Alzheimer's disease (AD)-related conditions, primarily supported by preclinical evidence. In an aluminum-induced AD rat model, wheatgrass administration improved cognitive performance, as evidenced by enhanced learning and memory in behavioral tests such as the Morris water maze and passive avoidance test. Additionally, a marked reduction in oxidative stress markers and modulation of acetylcholinesterase (AChE) activity were observed, indicating its role in restoring cholinergic balance. These findings suggest that wheatgrass exerts antioxidant, anti-inflammatory, and anti-apoptotic effects, which are crucial in mitigating AD pathology.

Despite strong mechanistic relevance, the results highlight a critical translational gap, as no human clinical trials have been reported for wheatgrass in AD or dementia. Existing evidence is largely limited to animal studies and general pharmacological reviews emphasizing its richness in bioactive compounds such as chlorophyll, flavonoids, and phenolics. Compared to established herbal interventions like Bacopa or Ginkgo, wheatgrass lacks direct anti-amyloid or neurotrophic validation. However, its strong metabolic and antioxidant profile positions it uniquely as a potential adjunct therapy targeting systemic contributors of AD, including oxidative stress, inflammation, and insulin resistance.

Furthermore, the absence of dedicated patents and standardized formulations for AD indicates a significant research and commercial opportunity. Current nutraceutical applications of wheatgrass focus mainly on general wellness rather than cognitive health. Therefore, the results support the hypothesis that wheatgrass could serve as a novel, low-cost, multi-target therapeutic candidate for early-stage AD or mild cognitive impairment (MCI), provided that further clinical validation and formulation standardization are achieved.

Table 2 Neuroprotective Effects and Evidence Profile of Wheatgrass (*Triticum aestivum*) in Alzheimer's Disease

Parameter	**Observation**	**Interpretation**
Cognitive function	Improved (animal models)	Neuroprotective effect
Oxidative stress markers	Reduced	Strong antioxidant activity
AChE activity	Modulated	Supports cholinergic transmission
Inflammation	Decreased (indirect evidence)	Anti-inflammatory action
Clinical evidence	Absent	Major research gap
Mechanistic strength	Moderate–High	Multi-target potential
Translational potential	Emerging	Requires clinical validation

Conclusion

Wheatgrass (Triticum aestivum) represents a promising multi-target therapeutic candidate for Alzheimer's disease (AD), primarily due to its rich composition of bioactive phytochemicals, including apigenin, flavonoids, chlorophyll, and phenolic compounds. The evidence synthesized in this review highlights its potential to modulate multiple pathological mechanisms underlying AD, such as oxidative stress, neuroinflammation, amyloid-β aggregation, and tau hyperphosphorylation. Apigenin has demonstrated significant neuroprotective effects through inhibition of glycogen synthase kinase-3β (GSK-3β), activation of PI3K/Akt and ERK/CREB/BDNF signalling pathways, and enhancement of endogenous antioxidant defense systems, thereby contributing to improved neuronal survival and cognitive function.

AI-assisted screening and computational approaches reinforce the pharmacological relevance of wheatgrass-derived compounds by identifying key molecular targets and optimizing lead candidates for AD therapy. These integrative strategies provide a rational framework for accelerating natural product-based drug discovery.

However, compelling preclinical findings, clinical translation remains limited. Critical challenges such as poor bioavailability, rapid metabolic degradation, insufficient blood brain barrier penetration, and lack of standardized extract formulations must be systematically addressed.

Future research should prioritize advanced drug delivery systems, structural optimization of lead compounds, and well-designed clinical trials to validate efficacy and safety in humans. Overall, wheatgrass-derived phytoconstituents offer a biologically plausible and therapeutically versatile approach for the development of safer, multi-target interventions in Alzheimer's disease, with strong potential for future clinical application.

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