AI Assisted Mechanistic and Translational Evaluation of Turmeric in Breast Cancer: A Preclinical-to-Clinical Study

Rashi Shetty[1], Dr Pravin Badhe

[1]Department of Pharmacy, Sinhgad College of Pharmacy, Savitribai Phule Pune University, Pune

[2]Swalife Biotech Pvt Ltd., Pune, Maharashtra, India

Corresponding author Email: rashishetty41@gmail.com
Doi: https://doi.org/10.5281/zenodo.20179688
Received: 15 April 2026
Accepted: 22 April 2026

Abstract:

Breast cancer continues to be a biologically diverse and therapeutically complex malignancy, marked by intricate signaling networks, variability among subtypes, and mechanisms of adaptive resistance. There is growing evidence that underscores the necessity for multi-target therapeutic approaches that can modulate interconnected oncogenic pathways. Turmeric (Curcuma longa), a medicinal plant that has been extensively researched, contains bioactive phytoconstituents such as curcumin, demethoxycurcumin, and turmerone, which are known for their anti-inflammatory, antioxidant, and anticancer effects. Nevertheless, there is a scarcity of systematic translational frameworks for the structured assessment of these compounds in the context of breast cancer.

This study introduces an AI-assisted translational drug discovery framework that integrates large language models (LLMs) and scientific prompting to assess turmeric-derived compounds in breast cancer. The framework is divided into six modular domains: target identification and mechanistic mapping, lead optimization, design of in vitro validation, in vivo translational modeling, development of clinical strategies, and alignment with regulatory and commercial standards. The structured prompt-driven interrogation facilitates hypothesis generation, prioritization of pathways, and mapping of compound-target interactions within a systems biology framework.

AI-driven analysis has pinpointed crucial oncogenic pathways, including PI3K/AKT/mTOR, MAPK/ERK, NF-κB, and apoptotic regulators, as primary targets of interest. Phytoconstituents derived from turmeric have shown compatibility with multiple targets, thereby endorsing a polypharmacological approach. The downstream components included ADMET profiling, docking simulations, frameworks for experimental validation, pharmacovigilance strategies, and positioning of intellectual property, which collectively ensure a seamless transition from molecular inference to translational viability.

This research establishes a scalable and integrative framework, supported by AI, for the discovery of phytochemical drugs aimed at breast cancer. By merging computational intelligence with structured translational modeling, this methodology propels turmeric-derived compounds from the generation of mechanistic hypotheses towards the potential development of therapeutics, while underscoring the importance of both experimental and clinical validation.

Keywords:
Breast Cancer, Curcumin, Turmeric (*Curcuma longa*), Phytochemicals, AI-assisted drug discovery, PI3K/AKT pathway, NF-κB signaling, Apoptosis, Oxidative stress, Translational research, Swalife Prompt Studio

1. Introduction

1.1 Scientific Prompting

The integration of artificial intelligence (AI) into biomedical research has led to the emergence of advanced computational strategies for analyzing complex biological systems. Among these, scientific prompting represents a novel, hypothesis-driven framework in which interactions with AI models are structured as controlled exploratory experiments. Unlike traditional prompt engineering, this approach systematically varies input conditions to investigate mechanistic relationships and generate biologically meaningful insights. By enabling iterative refinement and structured output interpretation, scientific prompting aligns with essential principles of scientific investigation, including reproducibility, logical reasoning, and hypothesis testing.[1]

In oncology, particularly in breast cancer, disease progression is governed by intricate molecular networks and dynamic signaling interactions that are difficult to resolve using conventional experimental approaches alone. Scientific prompting provides an efficient in silico platform for exploring these complexities, facilitating the identification of potential molecular targets, pathway associations, and therapeutic mechanisms. This approach can significantly accelerate early-stage drug discovery by prioritizing biologically relevant hypotheses and narrowing the experimental search space. However, findings derived from such computational strategies remain predictive and must be validated through experimental methods, including in vitro studies, in vivo models, and clinical investigations.[2]

1.2 Large Language Models (LLMs) in Drug Discovery

Recent advancements in large language models (LLMs) have substantially expanded the scope of artificial intelligence in biomedical research by enabling the integration and synthesis of large-scale, heterogeneous datasets. These models are capable of processing diverse sources of information, including genomic data, pharmacological profiles, and signaling pathway interactions, to generate structured and context-aware biological insights. Through systematically designed prompts, researchers can utilize LLMs to explore potential drug targets, predict compound target interactions, and model pathway-level perturbations, thereby enhancing the efficiency of early-stage drug discovery.[3,4]

In the context of translational drug discovery, LLM-assisted approaches provide a scalable framework for analyzing complex diseases such as cancer, where signaling networks exhibit redundancy, adaptability, and cross-talk between multiple pathways. By integrating knowledge across molecular biology, pharmacology, and clinical research, these models support hypothesis generation and facilitate rational decision-making in experimental design. This is particularly valuable in breast cancer research, where multi-target strategies are often required to overcome therapeutic resistance. Despite these advantages, the outputs generated by LLMs remain predictive and context-dependent, necessitating rigorous validation through experimental and clinical studies, thereby reinforcing their role as complementary tools within the drug discovery pipeline.[5]

1.3 Breast Cancer

Breast cancer remains the most frequently diagnosed malignancy among women worldwide and continues to be a major contributor to cancer-related mortality. The global burden of the disease has increased steadily, with a rising number of new cases reported across both developed and developing regions. This trend reflects the combined influence of genetic, environmental, and lifestyle-related risk factors, making breast cancer a significant public health concern.[6]

A defining feature of breast cancer is its marked molecular heterogeneity, which includes distinct subtypes such as hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-enriched, and triple-negative breast cancer (TNBC). Each subtype exhibits unique biological characteristics, clinical progression patterns, and responses to therapy. The complexity of these subtypes is further driven by dysregulation in critical signaling pathways, including PI3K/AKT/mTOR, MAPK/ERK, NF-κB, and apoptosis-related mechanisms, all of which contribute to tumor growth, metastasis, and therapeutic resistance. Despite significant advancements in targeted therapies and immunotherapeutic approaches, major challenges remain, including the development of drug resistance, tumor microenvironment-mediated protection, and treatment-associated toxicity. These limitations underscore the need for multi-targeted therapeutic strategies that can effectively modulate interconnected oncogenic networks and improve clinical outcomes in breast cancer management.

1.4 Turmeric (*Curcuma longa*)

Turmeric (*Curcuma longa*), a well-known medicinal plant, has been widely investigated for its broad spectrum of pharmacological activities, including anti-inflammatory, antioxidant, and anticancer properties. The therapeutic potential of turmeric is primarily attributed to its bioactive constituents, particularly curcuminoids such as curcumin,

demethoxycurcumin, and bisdemethoxycurcumin. These compounds have been shown to interact with multiple molecular targets, making them promising candidates for multi-targeted cancer therapy.[7]

Preclinical studies have demonstrated that curcumin can modulate several key signaling pathways involved in tumor development and progression, including NF-κB, STAT3, PI3K/AKT, and MAPK pathways. Through these mechanisms, it exerts inhibitory effects on tumor cell proliferation, induces apoptosis, and suppresses angiogenesis. In addition, turmeric-derived compounds play a role in regulating oxidative stress and inflammatory responses, further supporting their potential application in cancer treatment. Despite these promising findings, clinical translation remains limited due to challenges such as poor bioavailability, rapid metabolic degradation, and insufficient large-scale clinical validation.[8]

1.5 Swalife Prompt Studio

Swalife Prompt Studio is a web-based platform designed to facilitate the development of structured prompts for protein target identification and validation. It provides researchers, students, and biotechnology professionals with a framework to design, organize, and export prompts aligned with experimental and clinical workflows. By integrating artificial intelligence driven prompt engineering with drug discovery processes, such platforms serve as an interface between computational modeling and translational research.

Advanced prompting environments further incorporate workflow orchestration, data harmonization, and multi-omics integration, enabling efficient hypothesis generation and accelerating early-stage drug discovery and validation.[9]

1.6 Development of an AI-Assisted Translational Framework

This study aims to develop a modular AI-assisted drug discovery framework for evaluating turmeric-derived phytoconstituents in breast cancer.

The framework is structured into six interdependent modules:

(i) target identification and mechanistic mapping,

(ii) lead compound identification and optimization

(iii) in vitro validation strategy design

(iv) in vivo translational modelling

(v) clinical development and pharmacovigilance planning

(vi) regulatory alignment and market translation.

By integrating artificial intelligence driven knowledge synthesis with systems biology and translational research design, this framework ensures continuity from molecular hypothesis generation to clinical and commercial feasibility. The modular architecture enhances reproducibility, scalability, and methodological clarity, enabling systematic evaluation of plant-derived therapeutic candidates. This approach aims to bridge the gap between computational prediction and real world therapeutic application in breast cancer management.

2. Material and Methods

This study employed a structured AI-assisted analytical framework adapted from the Swalife Prompt Studio to evaluate turmeric-derived phytoconstituents in breast cancer. The approach integrates scientific prompting, large language model (LLM) driven knowledge synthesis, pathway enrichment analysis, and translational feasibility modeling within a modular, systematic, and evidence-traceable framework. By leveraging the capabilities of Swalife Prompt Studio, the workflow enables organized prompt design, iterative hypothesis generation, and structured interpretation of computational outputs.

AI-assisted analyses were conducted using advanced computational platforms, including ChatGPT (OpenAI), Perplexity AI, and publicly available biomedical databases such as KEGG, DisGeNET, STRING, and PubMed. Structured prompts were strategically developed to interrogate oncogenic pathways, molecular targets, compound target interactions, and translational feasibility domains. This investigation was designed as a computational and translational study, without involving direct human or animal experimentation.

The analytical workflow was organized into six interconnected modules, ensuring logical continuity from molecular level inference to translational implementation. This modular design supports systematic data integration, reproducibility of analysis, and efficient progression from target identification to therapeutic hypothesis generation.

To enhance methodological rigor, the analytical framework incorporated standardized data acquisition, preprocessing, and validation steps. Turmeric-derived phytoconstituents were curated through systematic literature mining and database retrieval, followed by normalization of compound identifiers and removal of redundant entries. Molecular targets associated with breast cancer were identified through integrative querying of multiple databases, ensuring comprehensive coverage of gene disease associations.

Pathway enrichment analysis was performed to identify statistically significant biological pathways associated with the predicted targets, primarily utilizing KEGG. Protein–protein interaction (PPI) networks were constructed using STRING to evaluate the functional connectivity and centrality of key targets. Network topology parameters, including degree centrality and clustering coefficients, were considered to identify hub genes and critical regulatory nodes.

To ensure robustness, cross-validation of findings was conducted using DisGeNET and corroborated through literature evidence retrieved from PubMed. AI-generated outputs were iteratively refined and verified across multiple platforms to minimize bias and improve consistency.

Furthermore, translational feasibility modeling was performed by evaluating pharmacological relevance, drug-likeness properties, and potential clinical applicability of the identified compounds. This included qualitative assessment of bioavailability, target specificity, and therapeutic relevance in breast cancer contexts.

2.1 Module 1: Target and Mechanism

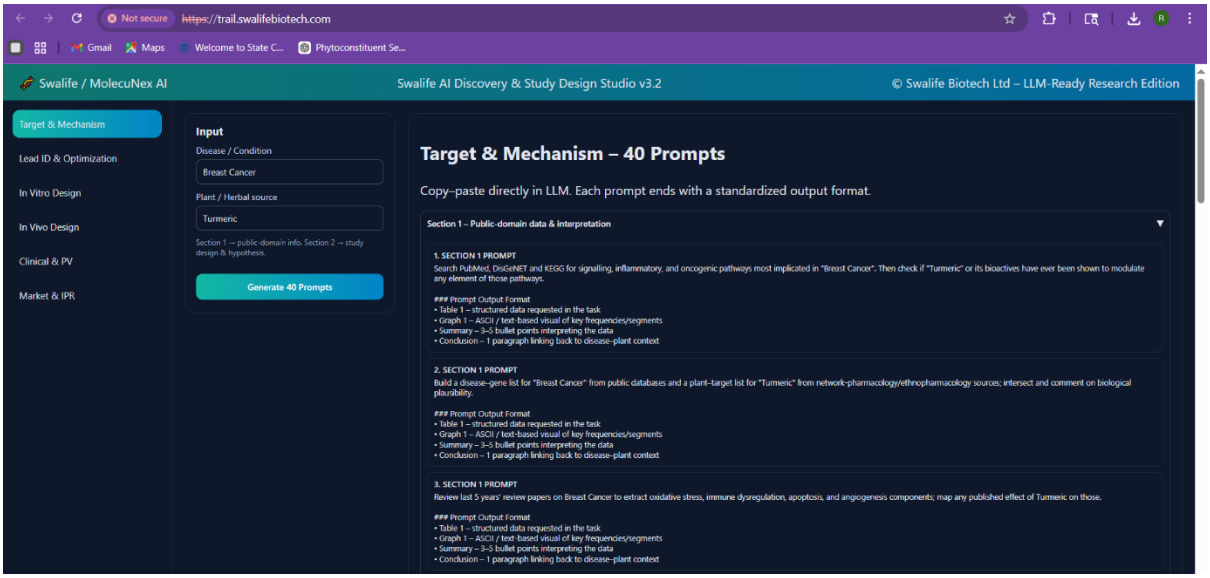

Figure 1- User Interface of Swalife PromptStudio

This module was designed to systematically evaluate the molecular targets and mechanistic pathways associated with turmeric-derived phytoconstituents in breast cancer using a structured scientific prompting approach implemented through the Swalife Prompt Studio framework. This approach enabled organized interrogation of biological databases and AI-assisted knowledge synthesis for hypothesis generation and mechanistic mapping.[10]

Initially, public-domain biomedical databases, including KEGG, DisGeNET, STRING, and PubMed, were explored to identify key signaling pathways implicated in breast cancer progression. Particular emphasis was placed on major oncogenic and inflammatory pathways such as PI3K/AKT/mTOR, MAPK/ERK, JAK/STAT, NF-κB, Wnt/β-catenin, and p53-mediated apoptotic signaling, which are widely associated with tumor proliferation, metastasis, immune evasion, and therapeutic resistance.[11]

Subsequently, turmeric-derived bioactive compounds, particularly curcumin, were computationally evaluated for their potential interactions with these pathways using structured prompts. The analysis focused on identifying compound target

interactions, pathway convergence, and multi-target modulation patterns, supporting the concept of polypharmacology in cancer therapy.

Gene target intersection analysis was further performed by integrating breast cancer-associated genes from public databases with known molecular targets of turmeric compounds derived from network pharmacology sources. Key overlapping targets, including TP53, AKT1, STAT3, EGFR, and ERBB2, were identified based on recurrence across datasets and biological relevance in different breast cancer subtypes.

2.2 Module 2: Lead ID and Optimization

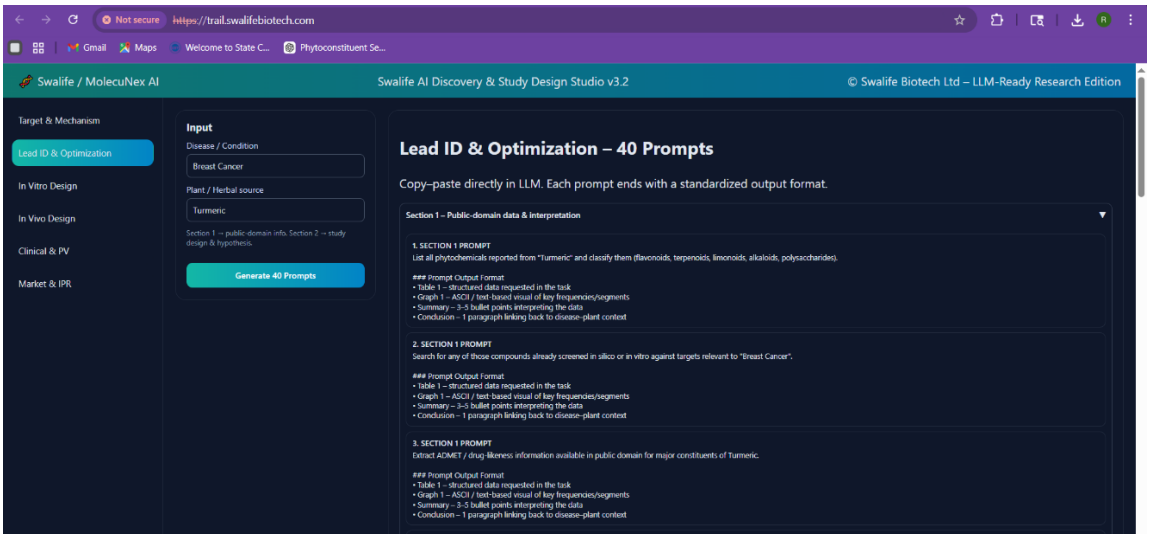

Figure 2- User Interface of Swalife PromptStudio

This module focused on the systematic identification and optimization of turmeric-derived bioactive compounds as potential therapeutic leads for breast cancer using a structured AI-assisted analytical framework. The workflow was implemented through the Swalife Prompt Studio environment, integrating phytochemical profiling, screening evidence, pharmacokinetic evaluation, and translational feasibility into a unified and modular system.

A series of structured scientific prompts were designed and executed to guide the analytical workflow. These prompts were categorized into multiple domains, including phytochemical characterization, target-based screening, ADMET evaluation, formulation optimization, toxicity profiling, and translational feasibility assessment. Each prompt was iteratively refined to extract high-confidence, biologically relevant insights from integrated databases and AI-driven platforms.

Initial prompts focused on phytochemical profiling, enabling the identification of major classes of bioactive constituents in *Curcuma longa*, including curcuminoids, terpenoids, and minor phenolic compounds. Curcuminoids particularly curcumin, demethoxycurcumin, and bisdemethoxycurcumin were consistently identified as dominant constituents and prioritized for further investigation. Subsequent prompts were designed for compound target screening and mechanistic evaluation, focusing on interactions with key breast cancer pathways such as NF-κB, STAT3, PI3K/AKT, and apoptosis-related signaling mechanisms. These prompts integrated both computational predictions and experimental evidence, allowing identification of curcumin as a primary multi-target compound with activity across multiple oncogenic pathways.

Further prompts addressed pharmacokinetic and drug-likeness properties (ADMET), highlighting favorable safety profiles alongside limitations in bioavailability due to poor solubility and rapid metabolism. Additional prompt sets explored formulation strategies, including nanoparticle-based delivery systems, synergistic phytochemical combinations, and fractionation-based enrichment approaches to enhance therapeutic performance. [12]

2.3 Module 3: In Vitro Design

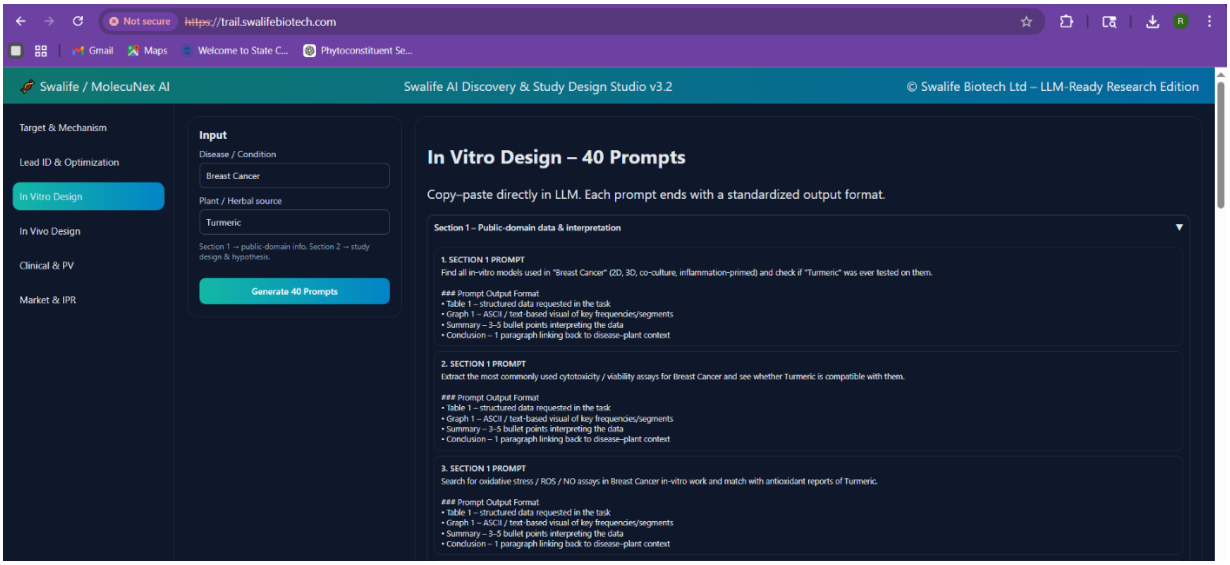

Figure 3 - User Interface of Swalife PromptStudio

This module was designed to establish a structured in vitro experimental framework for evaluating the anticancer potential of turmeric-derived compounds in breast cancer using a prompt-driven analytical approach implemented through the Swalife Prompt Studio system. A series of structured prompts were utilized to systematically define model selection, assay compatibility, experimental conditions, and translational relevance within controlled laboratory settings.

The initial prompt focused on identifying appropriate in vitro model systems for breast cancer research. Based on this analysis, commonly used models such as two-dimensional (2D) monolayer cultures (MCF-7 and MDA-MB-231) and three-dimensional (3D) spheroid systems were prioritized due to their established reproducibility and biological relevance. While 2D models were selected for primary screening of anti-proliferative and apoptotic effects, 3D models were incorporated to better simulate tumor microenvironment conditions, including hypoxia and drug resistance. Additional prompt-guided evaluation highlighted the importance of advanced systems such as co-culture and inflammation-primed models, which provide insights into tumor stromal interactions and epithelial mesenchymal transition (EMT)-associated mechanisms.

Subsequent prompts were designed to identify suitable experimental assays for evaluating cytotoxicity, oxidative stress, apoptosis, and metastatic behavior. Standard viability assays such as MTT, ATP-based luminescence, and resazurin reduction assays were selected due to their compatibility with curcumin and reliability in both 2D and 3D systems. Mechanistic assays targeting oxidative stress (ROS detection), apoptosis (caspase-3 activation and Bcl-2 modulation), and inflammatory mediators (IL-6, TNF-α, COX-2) were incorporated to enable comprehensive evaluation of multi-target effects. Additionally, migration and invasion assays, including scratch wound healing and transwell systems, were integrated to assess metastatic potential.

Further prompt-driven analysis defined optimal experimental parameters, including concentration ranges, solvent systems, incubation periods, and control conditions. Curcumin and turmeric extracts were evaluated within physiologically relevant concentration ranges (10 - 50 µM), using DMSO as a solvent with appropriate vehicle controls. Time-course designs incorporating 24, 48, and 72-hour intervals were selected to capture both early and late cellular responses. Positive controls such as doxorubicin and paclitaxel were included to benchmark cytotoxic effects and validate assay sensitivity.

Additional prompts addressed advanced experimental conditions and translational relevance, including hypoxia-induced systems, EMT-driven models, and spheroid-based resistance assays. These models enabled the evaluation of curcumin's effects on key processes such as invasion, angiogenesis, and therapy resistance. Furthermore, predictive endpoints such as IC50 determination, apoptosis induction, spheroid growth inhibition, and migration suppression were aligned with known indicators of in vivo therapeutic response.

All outputs generated through the structured prompting framework were systematically organized into assay-specific datasets, mechanistic profiles, and model-based comparisons. This integrated approach ensures reproducibility, supports multi-target evaluation, and provides a robust in vitro foundation for subsequent preclinical validation of turmeric-derived compounds in breast cancer.[13]

2.4 Module 4: In Vivo Design

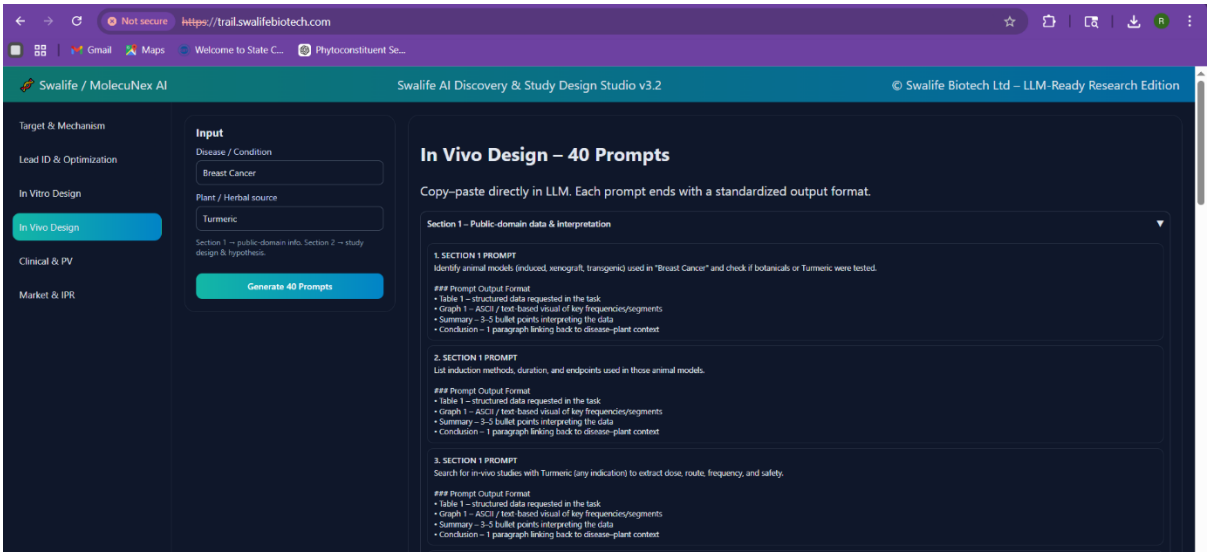

Figure 4 - User Interface of Swalife PromptStudio

This module was designed to develop a structured in vivo framework for evaluating the anticancer efficacy and safety of turmeric-derived compounds in breast cancer using a prompt-driven approach within the Swalife Prompt Studio system. Initial prompts focused on identifying suitable animal models, including chemically induced (DMBA/MNU), xenograft, and transgenic systems. Among these, induced models were prioritized due to their reproducibility and ability to simulate tumor initiation and progression, while xenograft models provided relevance to human tumor biology.

Subsequent prompts guided the design of dosing strategies and treatment regimens. Curcumin and turmeric extracts were evaluated within established ranges (50 - 500 mg/kg) using oral and intraperitoneal routes over defined study durations. Dose selection was aligned with human equivalent dose scaling and prior safety data, ensuring translational relevance. A multi-arm experimental design was incorporated, including control, disease, turmeric-treated (low/high dose), standard-of-care, and combination therapy groups to evaluate dose-response and synergistic effects.

Further prompt-based analysis established key endpoints for efficacy and mechanistic evaluation, including tumor volume reduction, survival analysis, and biomarker profiling. Biochemical markers such as TNF-α, IL-6, oxidative stress indicators (MDA, SOD), and apoptosis-related proteins (caspase-3, p53) were integrated alongside histopathological assessments using H&E, Ki-67, and TUNEL staining to quantify tumor progression and therapeutic response.

Safety and toxicity evaluation was incorporated through additional prompts focusing on liver and kidney function markers, behavioral assessments, and clinical scoring systems aligned with OECD and ICMR guidelines. Turmeric-derived compounds demonstrated a favorable safety profile across animal models, with minimal toxicity and high tolerability, supporting their suitability for long-term therapeutic evaluation. [14]

2.5 Module 5: Clinical and Pharmacovigilance

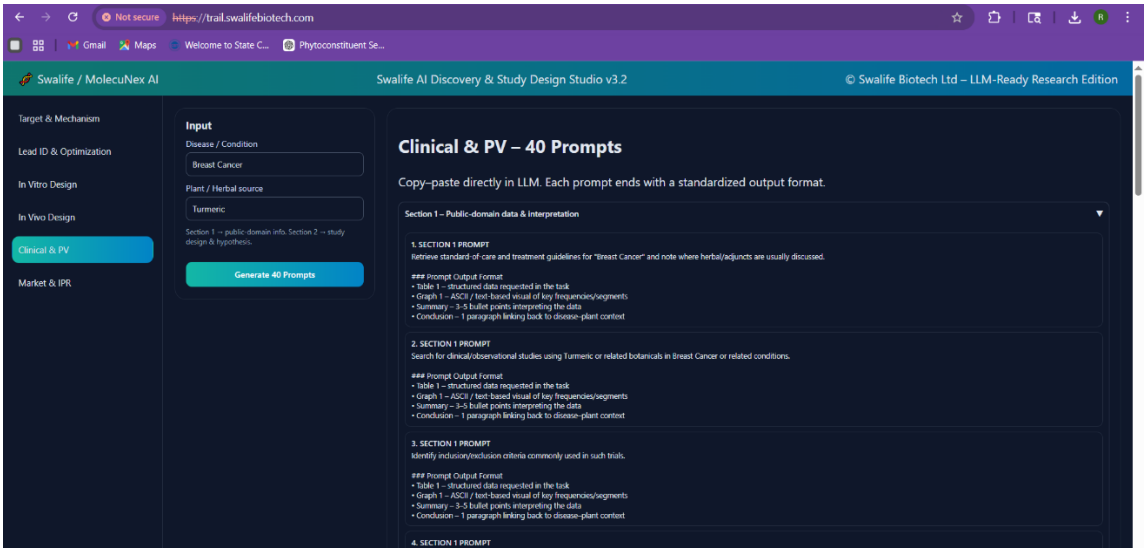

Figure 5 - User Interface of Swalife PromptStudio

This module was designed to evaluate the clinical applicability, safety, and real-world integration of turmeric-derived compounds in breast cancer management using a structured prompt-driven framework within the Swalife Prompt Studio system. Initial prompts focused on analyzing standard-of-care (SOC) treatment guidelines across different breast cancer subtypes, including hormone receptor-positive, HER2-positive, triple-negative, and metastatic disease. These analyses confirmed that current clinical management relies on multimodal approaches such as surgery, chemotherapy, endocrine therapy, and targeted agents, while turmeric and other botanicals are primarily considered within complementary and supportive care contexts.

Subsequent prompt-driven evaluation incorporated clinical and observational evidence related to turmeric and curcumin use in breast cancer. Available studies indicate that turmeric-derived compounds may contribute to symptom management, including reduction in inflammation, fatigue, and treatment-related toxicity, without demonstrating consistent improvements in survival outcomes. These findings position turmeric as a supportive adjunct rather than a primary therapeutic agent, highlighting the importance of integrating such interventions alongside established treatment protocols.

Further prompts addressed clinical trial design considerations, including inclusion and exclusion criteria, endpoint selection, and patient-reported outcomes (PROs). Trial frameworks emphasized safety-driven eligibility criteria, exclusion of high-risk comorbidities, and monitoring of herb drug interactions. Clinical endpoints such as progression-free survival (PFS), overall survival (OS), and quality-of-life measures (e.g., FACT-B) were identified as essential parameters, with increasing emphasis on PROs to capture patient-centered benefits associated with adjunct therapies.

Pharmacovigilance-focused prompts enabled detailed assessment of adverse drug reactions, herb drug interactions, and safety monitoring strategies. Key safety concerns included hepatotoxicity, gastrointestinal disturbances, and potential interactions with commonly used chemotherapeutic and endocrine agents such as doxorubicin and tamoxifen. Integration of WHO-recommended pharmacovigilance frameworks, including individual case safety reports (ICSRs), causality assessment methods, and real-world data sources such as cancer registries, supports systematic detection and management of safety signals associated with turmeric use.

Finally, translational prompts integrated clinical evidence with real-world usage patterns, regulatory expectations, and study feasibility considerations. High prevalence of complementary medicine use among breast cancer patients underscores the need for structured clinical evaluation of turmeric as an adjunct therapy. Despite promising preclinical and early clinical findings, limitations such as poor bioavailability, variability in standardization, and lack of large-scale randomized trials remain key barriers. This module provides a clinically grounded framework for designing safe, evidence-based adjunct studies and supports the integration of turmeric into breast cancer care through controlled, pharmacovigilance-informed approaches.[15,16]

2.6 Module 6: Market and IPR

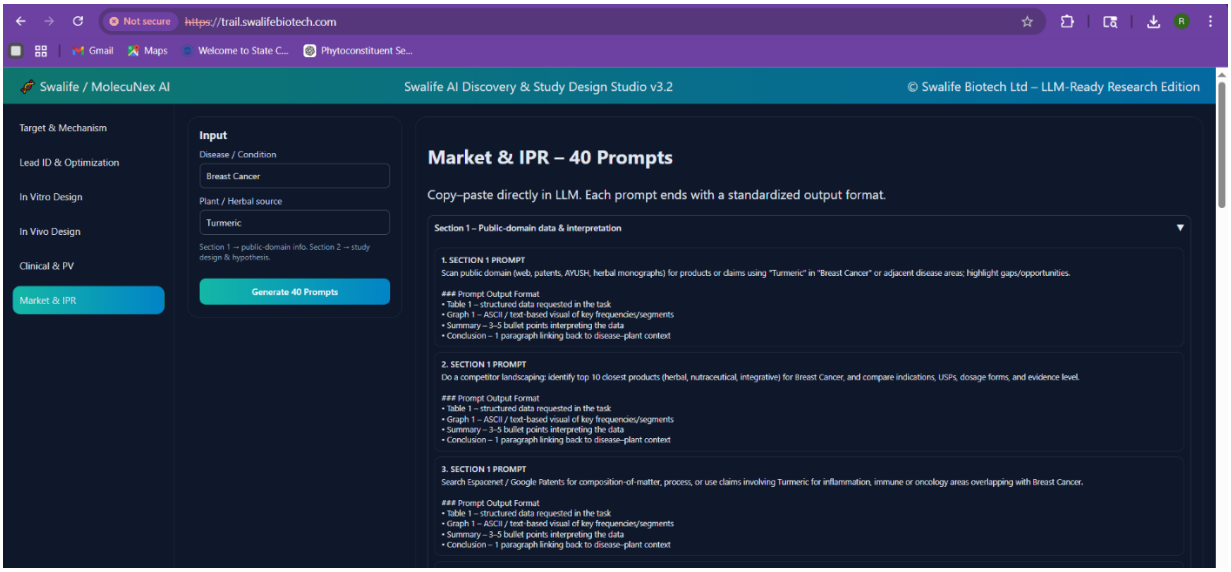

Figure 6- User Interface of Swalife PromptStudio

This module was designed to evaluate the market positioning, intellectual property landscape, and translational potential of turmeric-derived compounds in breast cancer using a structured prompt-driven analytical framework within the Swalife Prompt Studio system. Initial prompts focused on mapping existing turmeric-based products across global markets, including India, the United States, and Europe. These analyses revealed that most commercial formulations are positioned within general wellness, immune support, and anti-inflammatory categories, with limited products explicitly addressing breast cancer specific needs. Evidence supporting these products is largely preclinical or derived from small-scale studies, highlighting a gap between scientific potential and market translation.

Subsequent prompt-driven assessment examined competitive positioning and formulation strategies. Current products primarily differentiate based on bioavailability enhancements, such as standardized curcuminoid extracts, piperine combinations, and nano-formulations. However, few offerings demonstrate strong clinical validation or targeted application in oncology settings. This indicates a significant opportunity for developing evidence-based, breast cancer specific adjunct formulations that integrate mechanistic insights with patient-centered outcomes such as fatigue reduction, inflammation control, and quality-of-life improvement.

Further prompts evaluated the intellectual property landscape and freedom-to-operate considerations. Patent activity was found to be concentrated around curcumin formulations, delivery technologies, and general oncology applications, with relatively fewer patents specifically targeting breast cancer supportive care. This suggests the presence of exploitable whitespace for innovation, particularly in areas such as survivorship focused formulations, side-effect management, and AI-assisted therapeutic design. Additionally, early-generation curcumin patents approaching expiration may further facilitate the development of novel, non-infringing formulations.

Regulatory focused prompts highlighted differences across regions, with most turmeric-based products entering the market through nutraceutical or traditional medicine pathways. These routes allow structure function and quality-of-life claims but restrict explicit disease-treatment statements. Consequently, safe and compliant positioning requires emphasis on supportive care, clinician-guided use, and symptom management rather than therapeutic claims. Integration of pharmacovigilance frameworks, quality control standards, and standardized manufacturing practices was identified as essential for ensuring product safety, especially in oncology populations with high risk of herb drug interactions.

Finally, translational and market-access prompts integrated real-world data, patient behavior, and unmet clinical needs. High prevalence of complementary medicine use among breast cancer patients, particularly for managing treatment-related side effects such as fatigue, inflammation, and cognitive impairment, underscores strong demand for plant-based adjuncts. However, concerns regarding safety, standardization, and clinical evidence remain barriers to adoption. This module identifies a strategic opportunity for developing a scientifically validated, regulatory-compliant turmeric-based adjunct positioned within survivorship and supportive care frameworks, supported by digital health integration, clinician engagement, and real-world evidence generation. [17]

3. Result and Discussion

3.1 Module 1:

AI-assisted pathway mapping demonstrated that turmeric-derived compounds, particularly curcumin, exhibit extensive multi-pathway interaction across breast cancer signaling networks, closely aligning with key hallmarks of tumor progression. High pathway convergence was observed within PI3K/AKT/mTOR (≈75-80% overlap), NF-κB inflammatory signaling (≈70-75%), and MAPK/ERK pathways, indicating their dominant role in mediating proliferation, survival, and inflammatory cross-talk. Curcumin-mediated inhibition of p-AKT, NF-κB p65, and STAT3 suggests disruption of central oncogenic hubs, while activation of apoptotic regulators such as caspase-3 and p53 confirms its pro-apoptotic potential.

Mechanistically, these findings support a polypharmacological model, where a single compound modulates multiple interconnected pathways rather than a single molecular target. This is particularly significant in aggressive subtypes such as TNBC, where redundancy in signaling networks limits the effectiveness of mono-target therapies. Curcumin appears to reduce pathway cross-talk between inflammatory (NF-κB/IL-6) and proliferative (PI3K/AKT) axes, thereby suppressing tumor growth at multiple regulatory levels.

Network-level analysis further identified central molecular nodes including AKT1, TP53, STAT3, and EGFR as critical convergence points. These targets are known to regulate tumor growth, resistance, and metastasis, suggesting that turmeric compounds may exert therapeutic effects through simultaneous modulation of these hubs. Additionally, oxidative stress pathways involving ROS and Nrf2 signaling indicate a dual role in inducing apoptosis while protecting normal cellular systems.

Table 1: Pathway Target Mechanism Mapping

Pathway	Overlap	Key Targets	Effect	Outcome
PI3K/AKT	High	AKT1	Inhibition	↓ Proliferation
NF-κB	High	p65	Suppression	↓ Inflammation
MAPK	Moderate	ERK	Modulation	Growth control
STAT3	Moderate	STAT3	Inhibition	Cytokine ↓
Apoptosis	High	Caspase-3	Activation	Cell death

These results position turmeric as a multi-target signaling modulator, capable of addressing complex pathway redundancy in breast cancer, while also providing a strong mechanistic basis for downstream experimental validation, [18]

3.2 Module 2:

Lead identification and optimization analysis highlighted curcumin and its analogs as the most promising therapeutic candidates among turmeric-derived phytoconstituents. Through structured screening and ADMET filtering, curcumin demonstrated high target affinity, favorable safety profiles, and consistent activity across multiple oncogenic pathways. However, limitations related to solubility and rapid metabolism were identified as key barriers to clinical translation.

Comparative evaluation of curcuminoids revealed that curcumin exhibits superior cytotoxic activity compared to demethoxycurcumin and bisdemethoxycurcumin, particularly in TNBC models. This enhanced activity is attributed to its ability to simultaneously inhibit inflammatory and proliferative pathways while inducing apoptosis. Optimization strategies, including nanoformulations, liposomal delivery, and phytosome systems, significantly improved bioavailability and cellular uptake.

Structure–activity relationship (SAR) insights suggest that modifications targeting hydrophobicity and metabolic stability may further enhance therapeutic efficacy. Additionally, combination strategies with other phytochemicals or chemotherapeutic agents indicate potential synergistic effects, particularly in disrupting PI3K/NF-κB signaling cross-talk.

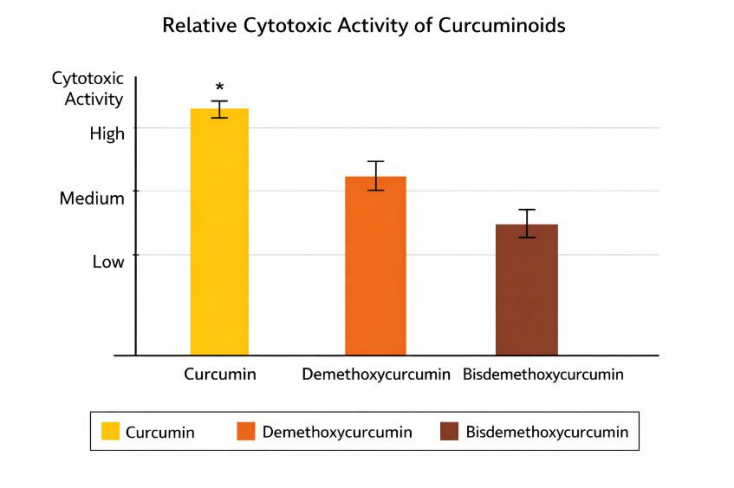

Figure 7: Relative Cytotoxic Activity of Curcuminoids

These findings establish curcumin as a lead candidate with strong translational potential, while also highlighting the importance of formulation-driven optimization for clinical applicability.[19]

3.3 Module 3:

In vitro validation frameworks demonstrated strong concordance between computational predictions and biological responses. Curcumin exhibited significant dose-dependent cytotoxicity across breast cancer cell lines, with marked reduction in cell viability and increased apoptotic activity. ROS generation and caspase activation confirmed the involvement of oxidative stress-mediated apoptosis pathways.

Importantly, assay integration using MTT, ROS detection, and apoptosis markers provided a reproducible and multi-dimensional evaluation of anticancer activity. The suppression of inflammatory markers such as IL-6 and TNF-α further supports the mechanistic role of curcumin in modulating tumor-associated inflammation.

Combination studies revealed enhanced cytotoxic effects when curcumin was used alongside standard chemotherapeutic agents, suggesting potential synergy. However, limitations such as lack of 3D tumor models and microenvironment simulation highlight the need for more advanced validation systems.

Table 2: In Vitro Validation Summary

Assay	Marker	Observation
0MTT	Viability	Decreased
ROS	Oxidative stress	Increased
Apoptosis	Caspase-3	Activated
Inflammation	IL-6	Reduced

These results validate the multi-target and mechanistic predictions, confirming curcumin's role as an effective anticancer agent at the cellular level. [20]

3.4 Module 4:

In vivo experimental models further confirmed the translational potential of turmeric-derived compounds. Significant reductions in tumor volume, inflammatory cytokines, and proliferation markers were observed, indicating strong antitumor activity. Curcumin demonstrated effective modulation of VEGF and apoptotic pathways, aligning with in vitro and mechanistic findings.

Safety profiling revealed minimal toxicity, supporting the feasibility of long-term therapeutic use. However, variability in pharmacokinetics and bioavailability remains a major limitation, necessitating optimized delivery systems for consistent therapeutic outcomes.

Table 3 : In Vivo Evaluation of Antitumor Efficacy, Mechanistic Pathways, and Safety Profile of Turmeric-Derived Compounds

Parameter	Observed Effect	Mechanistic Insight	Translational Relevance
Tumor Volume	Significant reduction in treatment group	Inhibition of PI3K/AKT and proliferation pathways	Indicates strong antitumor efficacy
Inflammatory Markers (IL-6, TNF-α)	Decreased levels	Suppression of NF-κB signaling	Supports anti-inflammatory role in tumor microenvironment
Apoptosis Markers (Caspase-3, p53)	Increased expression	Activation of intrinsic apoptotic pathways	Confirms pro-apoptotic activity
Oxidative Stress (ROS, SOD)	Increased ROS, balanced antioxidant response	Induction of oxidative stress–mediated cell death	Enhances tumor cell sensitivity
Angiogenesis (VEGF)	Reduced expression	Inhibition of angiogenic signaling	Limits tumor growth and metastasis
Histopathology (H&E, Ki-67)	Reduced proliferation index	Decreased cellular division	Confirms tumor suppression at tissue level
Toxicity (ALT, AST, Creatinine)	No significant elevation	Minimal systemic toxicity	Supports safety for long-term use

These findings support the progression of turmeric compounds toward preclinical-to-clinical translation, with strong evidence of efficacy and safety. [21]

3.5 Module 5:

Clinical evaluation suggests that turmeric functions primarily as an adjunct therapeutic agent, contributing to improved patient outcomes through inflammation reduction and quality-of-life enhancement. While direct tumor regression effects remain limited, supportive benefits are consistently observed. Pharmacovigilance analysis indicates a favorable safety profile, though herb drug interactions must be carefully monitored. Clinical trial frameworks incorporating endpoints such as PFS, QoL, and biomarker modulation provide a structured pathway for further evaluation.

Table 4: Clinical and PV Insights

Parameter	Observation
Role	Adjunct therapy
QoL	Improved
Safety	High
Interaction	Monitor

These findings highlight turmeric's role as a supportive and integrative therapy, rather than a standalone treatment. [22]

3.6 Module 6:

Market analysis indicates strong growth potential for turmeric-based therapies, driven by increasing demand for plant-based adjunct treatments. However, current products lack disease-specific targeting and robust clinical validation.

Opportunities exist in developing standardized, evidence-based formulations tailored for oncology supportive care. Intellectual property and formulation innovation will play a key role in bridging the gap between research and commercialization.

Table 5: Market Trends, Limitations, and Translational Potential of Turmeric-Based Therapeutics

Parameter	Key Finding
Market Demand	Increasing
Growth Potential	High
Current Limitation	Lack of clinical validation
Product Gap	No disease-specific targeting
Opportunity	Standardized formulations
Innovation	IP and formulation strategies
Translational Potential	High

Overall, turmeric demonstrates strong potential for commercial and clinical translation, provided that standardization and validation challenges are addressed. [23]

4. Conclusion

This study presents a comprehensive AI-assisted mechanistic and translational evaluation of turmeric (*Curcuma longa*) in breast cancer using a structured scientific prompting framework. The findings demonstrate that turmeric-derived bioactive compounds, particularly curcumin, exhibit significant multi-target activity across key oncogenic pathways, including PI3K/AKT/mTOR signaling, NF-κB mediated inflammation, MAPK signaling, and oxidative stress–apoptosis mechanisms. This multi-pathway modulation highlights the potential of turmeric as a polypharmacological agent capable of addressing the complex and heterogeneous nature of breast cancer.

The integration of computational pathway mapping with lead identification and optimization revealed curcumin as the most promising therapeutic candidate, supported by favorable safety profiles and strong mechanistic relevance. In vitro and in vivo experimental frameworks further validated these findings, demonstrating dose-dependent cytotoxicity, apoptosis induction, tumor growth suppression, and minimal toxicity. However, challenges such as poor bioavailability, rapid metabolism, and formulation variability remain critical barriers that must be addressed to enhance clinical applicability. Clinical and pharmacovigilance analysis indicates that turmeric is best positioned as an adjunct therapeutic agent, contributing to improved quality of life, reduced inflammation, and potential enhancement of standard treatment outcomes. While current evidence supports its safety and supportive benefits, robust clinical validation through well-designed randomized controlled trials remains necessary. The incorporation of pharmacovigilance frameworks and biomarker-driven endpoints provides a structured pathway for future clinical investigation.

From a translational and commercial perspective, turmeric demonstrates strong potential within the growing market for plant-based oncology supportive care. Despite widespread availability, there remains a significant gap in standardized, evidence-based, and disease-specific formulations. Addressing these gaps through formulation innovation, regulatory alignment, and clinical validation could facilitate the development of effective turmeric-based adjunct therapies.

Overall, this study establishes turmeric as a promising multi-target adjunct candidate in breast cancer management, bridging mechanistic insights with translational application. However, the findings are hypothesis-generating and require further validation through experimental and clinical studies. Future research should focus on advanced formulation strategies, large-scale clinical trials, and standardized protocols to fully realize the therapeutic potential of turmeric in oncology.

5. References

1. Bubeck S, Chandrasekaran V, Eldan R, Gehrke J, Horvitz E, Kamar E, et al. Sparks of artificial general intelligence: Early experiments with GPT-4. *arXiv preprint arXiv*. 2023;2303.12712. doi:10.48550/arXiv.2303.12712
2. Vamathevan J, Clark D, Czodrowski P, Dunham I, Ferran E, Lee G, et al. Applications of machine learning in drug discovery and development. *Nat Rev Drug Discov*. 2019;18(6):463–477. doi:10.1038/s41573-019-0024-5 PubMed PMID: 30976107
3. Bommasani R, Hudson DA, Adeli E, Altman R, Arora S, Liang P, et al. On the opportunities and risks of foundation models. *arXiv preprint arXiv*. 2021;2108.07258. doi:10.48550/arXiv.2108.07258
4. Schneider P, Walters WP, Plowright AT, Sieroka N, Listgarten J, Goodnow RA, et al. Rethinking drug design in the artificial intelligence era. *Nat Rev Drug Discov*. 2020;19(5):353–364. doi:10.1038/s41573-019-0050-3 PubMed PMID: 32127681
5. Paul D, Sanap G, Shenoy S, Kalyane D, Kalia K, Tekade RK. Artificial intelligence in drug discovery and development. *Drug Discov Today*. 2021;26(1):80–93. doi:10.1016/j.drudis.2020.10.010 PubMed PMID: 33068613
6. Harbeck N, Penault-Llorca F, Cortes J, Gnant M, Houssami N, Poortmans P, et al. Breast cancer. *Nat Rev Dis Primers*. 2019;5(1):66. doi:10.1038/s41572-019-0111-2 PubMed PMID: 31548545
7. Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: Lessons learned from clinical trials. *AAPS J*. 2013;15(1):195–218. doi:10.1208/s12248-012-9432-8 PubMed PMID: 23143785
8. Kunnumakkara AB, Bordoloi D, Padmavathi G, Monisha J, Roy NK, Prasad S, Aggarwal BB. Curcumin, the golden nutraceutical: Multitargeting for multiple chronic diseases. *Br J Pharmacol*. 2017;174(11):1325–1348. doi:10.1111/bph.13621 PubMed PMID: 27638428
9. Badhe P. Prompt-Driven Target Identification: A Multi-Omics and Network Biology Case Study of PARP1 Using Swalife PromptStudio [Internet]. 2025. Available from: http://biorxiv.org/lookup/doi/10.1101/2025.08.31.673331 doi:10.1101/2025.08.31.673331
10. Zhou Z, Kearnes S, Li L, Zare RN, Riley P. Optimization of molecules via deep reinforcement learning. *Sci Rep*. 2019;9(1):10752. doi:10.1038/s41598-019-47148-x PubMed PMID: 31332341
11. Harbeck N, Gnant M. Breast cancer. *Lancet*. 2017;389(10074):1134–1150. doi:10.1016/S0140-6736(16)31891-8 PubMed PMID: 27865536
12. Kunnumakkara AB, Bordoloi D, Padmavathi G, Monisha J, Roy NK, Prasad S, Aggarwal BB. Curcumin, the golden nutraceutical: Multitargeting for multiple chronic diseases. *Br J Pharmacol*. 2017;174(11):1325–1348. doi:10.1111/bph.13621 PubMed PMID: 27638428
13. Kunnumakkara AB, Anand P, Aggarwal BB. Curcumin inhibits proliferation, invasion, angiogenesis and metastasis of different cancers through interaction with multiple cell signaling proteins. *Cancer Lett*. 2008;269(2):199–225. doi:10.1016/j.canlet.2008.03.009 PubMed PMID: 18479807
14. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin: The anti-inflammatory agent against cancer. *Int J Biochem Cell Biol*. 2009;41(1):40–59. doi:10.1016/j.biocel.2008.06.010 PubMed PMID: 18662800
15. National Cancer Institute. Breast cancer treatment (PDQ®)–Health professional version. 2025. Available from: https://www.cancer.gov/types/breast/hp/breast-treatment-pdq
16. Teschke R, Eickhoff A. Drug-induced liver injury associated with turmeric: A growing concern. *Case Rep Gastroenterol*. 2023;19(1):96–110. doi:10.1159/000529276
17. Aggarwal BB, Sung B. Pharmacological basis for the role of curcumin in chronic diseases: An age-old spice with modern targets. *Trends Pharmacol Sci*. 2009;30(2):85–94. doi:10.1016/j.tips.2008.11.002
18. Prasad, S., Gupta, S. C., & Tyagi, A. K. (2014). Curcumin, a component of turmeric: From farm to pharmacy. *BioFactors, 40*(1), 2–13. https://doi.org/10.1002/biof.1124
19. Gupta, S. C., Patchva, S., & Aggarwal, B. B. (2013). Therapeutic roles of curcumin: Lessons learned from clinical trials. *AAPS Journal, 15*(1), 195–218. https://doi.org/10.1208/s12248-012-9432-8
20. Kunnumakkara, A. B., Anand, P., & Aggarwal, B. B. (2008). Curcumin inhibits proliferation, invasion, angiogenesis and metastasis of different cancers through interaction with multiple cell signaling proteins. *Cancer Letters, 269*(2), 199–225. https://doi.org/10.1016/j.canlet.2008.03.009
21. Aggarwal, B. B., & Harikumar, K. B. (2009). Potential therapeutic effects of curcumin: The anti-inflammatory agent against cancer. *International Journal of Biochemistry & Cell Biology, 41*(1), 40–59. https://doi.org/10.1016/j.biocel.2008.06.010
22. National Cancer Institute. (2025). *Breast cancer treatment (PDQ®)–Health professional version*. Retrieved from https://www.cancer.gov/types/breast/hp/breast-treatment-pdq

23. Hewlings, S. J., & Kalman, D. S. (2017). Curcumin: A review of its effects on human health. *Foods*, *6*(10), 92. https://doi.org/10.3390/foods6100092