

Artificial intelligence in Traditional Chinese Medicine: systematic insights from data mining, large language models, and multimodal fusion

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ABSTRACT

Traditional Chinese medicine (TCM), characterized by multi-component, multi-target, and systemic therapeutic mechanisms, provides unique advantages in managing complex diseases. However, the inherent complexity of TCM formulations, including nonlinear component interactions, elusive compatibility principles, and a lack of quantitative biomarkers, has hindered the systematic elucidation of their efficacy mechanisms and clinical translation. Artificial intelligence (AI) technologies, including machine learning and deep learning, combined with network pharmacology approaches, have emerged as transformative tools to systematically characterize and model TCM's complexity. Given that TCM and AI share a foundational emphasis on systemic interactions rather than isolated components, AI approaches can facilitate high-throughput prediction of bioactive components, rational design of synergistic formulas, and dynamic modeling of pharmacological effects. Recent interdisciplinary studies have harnessed AI to address TCM challenges including predicting bio-active constituents, optimizing herbal compatibility, and standardizing diagnostic parameters. Whereas prior reviews focused on AI applications in TCM data mining and drug development, this work comprehensively integrates active component prediction, compatibility mechanisms, and pharmacological effect modeling, and additionally discusses emerging applications of large-scale AI models in modern TCM research.

Keywords: Traditional Chinese Medicine, Artificial Intelligence, Machine Learning, Multi-omics Integration, Target Identification, Large Language Models

1. INTRODUCTION

Traditional Chinese medicine (TCM), rooted in the ancient philosophical framework of *yin-yang* balance theory, encompasses diverse practices including acupuncture, herbal medicine, and dietary therapy [1]. TCM is increasingly gaining global recognition for its efficacy in treating diseases and promoting overall well-being [2, 3]. TCM refers to medicinal substances that exert therapeutic effects through multi-component, multi-pathway, and multi-target interactions [4, 5]. Multicomponent

herbal formulations are central to TCM's therapeutic efficacy, and exert pharmacological effects through poly-pharmacological interactions across multiple biological targets and pathways [6, 7]. Numerous studies have demonstrated TCM's considerable therapeutic potential in the treatment of various diseases [8, 9]. Many TCM formulations have been validated through modern evidence-based clinical research. For example, formulas such as Tongxinluo have been found to lower the risk of adverse cardiovascular events in acute myocardial infarction, and Pien Tze Huang has shown anticancer

Review Article

effects in colorectal cancer by modulating the gut microbiota [10, 11]. In addition, monomers extracted from TCM exhibit excellent efficiency in treating diseases. For example, artemisinin and β -elemene, extracted from *Artemisia annua* and *Curcuma Wenyujin*, have shown promising antimalarial and anticancer effects, respectively [12, 13]. However, the inherent complexity of TCM presents substantial challenges in elucidating its pharmacological mechanisms and facilitating drug discovery [14]. Advanced computational methods are therefore needed to solve these problems, and artificial intelligence (AI) is becoming key to the modernization of TCM research.

AI, first proposed by John McCarthy at the Dartmouth Conference in 1956 and defined as “the science and engineering of building intelligent machines,” emphasizes the simulation of human intelligence through computational systems for representation learning and complex reasoning [15, 16]. In applications such as decoding complex patterns and enabling dynamic decision systems, AI’s advancements have not only expanded cognitive capabilities but also transformed pharmaceutical research through predictive drug modeling [17]. AI methods typically include two main classes of algorithms: machine learning (ML) and deep learning (DL) [18]. ML focuses on letting machines learn autonomously from data and has been applied in drug discovery [19–22]. ML techniques such as support vector machine (SVM) and random forest (RF) are effective in tasks such as drug screening and target prediction, but have difficulties in analysis of complex biological systems, particularly compounds with diverse structures [23]. DL, a subset of ML, has achieved substantial progress in computer vision, natural language processing, bioinformatics, and other fields, because of its ability to independently learn hierarchical data representation [24–26]. In drug research and development, DL architectures such as multilayer perceptrons, convolutional neural networks, and autoencoders can directly extract high-dimensional molecular features from raw data, thereby transcending traditional methods [27, 28]. By integrating drug

structures, omics features, and clinical trial data, DL can enhance target prediction, toxicological assessment, and treatment effect modeling [29, 30]. Given its powerful capabilities in data analysis, pattern recognition, and predictive modeling, AI has great potential to elucidate multicomponent–multitarget mechanisms and optimize herbal compatibility, thereby driving TCM modernization [31].

With advances in systems biology and the application of contemporary techniques to TCM theories, researchers have sought to understand how multiple components work together synergistically to affect various targets and to elucidate overall mechanisms of action rather than focusing solely on single active ingredients [32]. AI’s ability to process intricate data sets is well suited to the complex relationships among components, targets, and therapeutic efficacy in TCM. An overview of this evolving interdisciplinary field (Figure 1) illustrates key milestones in AI integration into TCM research, and highlights the progressive convergence of AI and TCM. Whereas recent reviews by Song et al. and Zhu et al. have described AI’s potential in herb–target prediction and formulation optimization [33, 34], this review systematically discusses the roles of AI technology in analyzing complex TCM systems, including AI-driven mechanisms for ingredient prediction, the composition principles of TCM prescriptions, target prediction, applications in multi-omics research, and quality control. Applications of large-scale AI models in modern TCM research are further described.

2. APPLICATIONS OF AI TECHNOLOGY IN TCM RESEARCH

AI technology has been applied to the detection and diagnosis of various diseases, such as neurodegenerative diseases [35], cardiovascular diseases [36], and malignant tumors [37]. Figure 2 presents an overview of the multi-level integration framework of AI technology in TCM research and application, particularly in (a) prediction

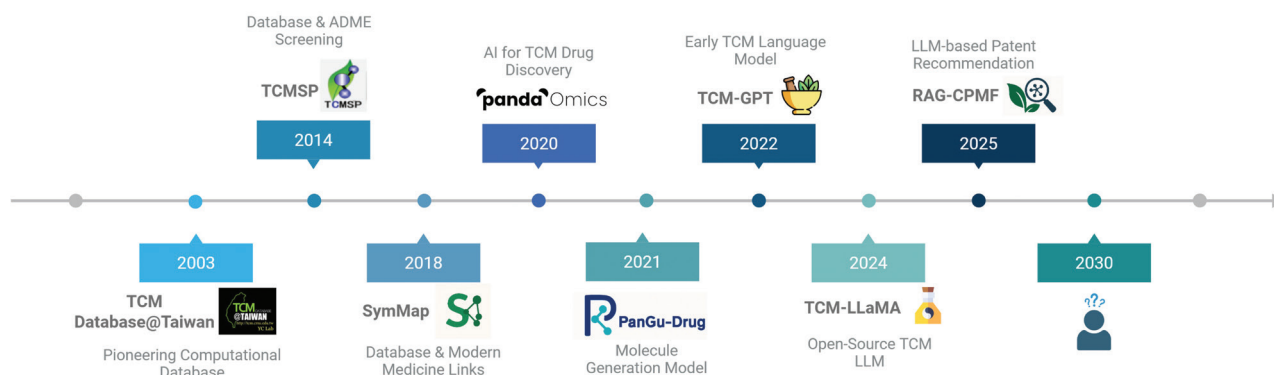


Figure 1 | Timeline of the development and application of AI in TCM (created in <https://BioRender.com>).

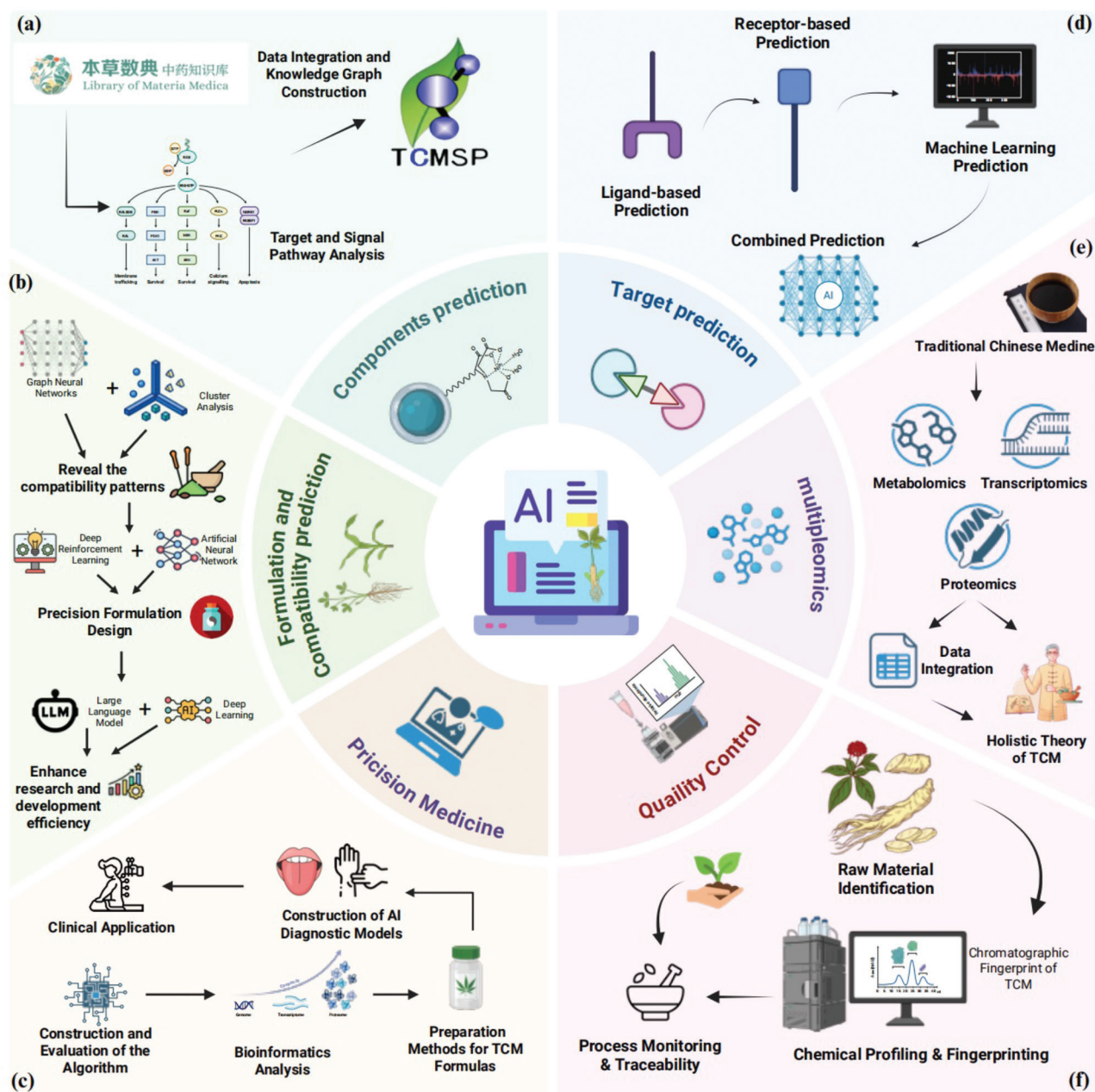


Figure 2 | Multifaceted AI-enhanced approach to TCM analysis, from component prediction to clinical integration (created in <https://BioRender.com>).

of ingredients, (b) discovery of compounding relationships, (c) validation of medicinal efficacy, (d) target prediction and identification, (e) multi-omics analysis, and (f) quality control in TCM. At the component prediction level, relevant literature, experimental data, and heterogeneous multi-source information are first integrated via specialized databases, and a three-dimensional knowledge map of drug-target-disease is subsequently constructed through a graph database to provide a structured knowledge foundation for intelligent screening

of components. In the target prediction chain, receptor structure prediction is used to preliminarily screen potential active ingredients, and the DL model is subsequently used for cross-validation and dynamic optimization of targets to ultimately achieve accurate target prediction for active ingredients. To enhance the robustness of the quality assurance framework, ML classifiers and block-chain protocols are embedded from chromatographic fingerprinting of herbal materials to end-to-end process traceability, thereby ensuring batch-to-batch ingredient

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uniformity and accurate authentication in TCM production. Moreover, in compatibility and formulation design, researchers have used graph neural networks to analyze classical prescriptions, and then, through collaborative optimization of deep reinforcement learning and artificial neural networks, re-constructed the compatibility logic of traditional prescriptions, thereby advancing research and improving the efficiency of developing new TCM prescriptions. Through systematic integration of multidimensional data, contemporary herbal formula formulation principles can be leveraged to elucidate TCM theory, thereby enabling the interpretation and refinement of traditional pharmacological paradigms. In mechanistic analysis, combining the drug-target interaction network in the knowledge map with pathway enrichment analysis and network topology calculation has revealed the multi-component, multi-target, multi-pathway nature of TCM compounds at the molecular network level. AI has been extensively applied in precision medicine. Integrating three-stage technology comprising bioinformatics analysis, DL diagnostic models, and clinical data calibration has not only enabled intelligent identification of TCM syndromes but also provided dynamic decision support for individualized prescription optimization. These advancements highlight TCM's critical transition to integrated computational-empirical frameworks, which provide a powerful technical engine for the modernization of TCM [38, 39].

2.1. AI-powered prediction of active TCM ingredients

The complexity of TCM originates from its diverse chemical components, whose polypharmacological interactions within organisms can notably modulate therapeutic outcomes [40]. Precise determination and forecasting of TCM's chemical constituents are critical to uncover pharmacological mechanisms, maintain clinical safety and consistency, and advance the standardization of TCM [41]. Traditional analytical methods have limitations in comprehensively investigating the complex relationships among numerous chemical components and potentially bioactive compounds in TCM. AI techniques, particularly ML and DL, offer new possibilities to address these challenges, and provide strong support for predicting components and component changes in various disease states through network modeling and efficient data mining; learning from large complex datasets; and identifying subtle patterns and correlations that might not be apparent through traditional statistical methods [42, 43]. With the widespread application of AI technology in TCM research, the demand for high-quality TCM data resources is increasing. To address this need, multiple databases have been developed through multi-source data integration, standardized processing, and AI-driven technologies. These databases systematically organize TCM components and their relationships into functional annotations, including targets, diseases, and signaling pathways (Table 1).

On this basis, researchers have further combined network modeling methods to explore the rich information on TCM components in the database. Chen et al. have integrated multiple algorithms, such as SVM and RF, to predict potential therapeutic TCM ingredients for Alzheimer's disease; moreover, they have successfully identified active ingredients in *Phellodendron amurense* and *Cynanchum atratum* that stably bind GSK3 β and have application potential in TCM prescription discovery [60]. Jafari et al. have constructed a bipartite network model revealing associations between the classification of TCM and the chemical properties of TCM ingredients; extracted the largest connected component of the network, comprising 7,004 nodes and 17,555 edges; and further reconstructed Natural Product Similarity Network (NPSN) and Ingredient Similarity Network (ISN) projection networks [61]. Subsequently, they identified 42 clusters in NPSN and 24 clusters in ISN, thereby reflecting the intrinsic similarity of herbs and ingredients. Using a network pharmacology approach, Wang et al. constructed a multi-layer herb-component-target protein network to investigate the synergistic mechanisms of TCM herb pairs [62]. By analyzing the top 200 high-frequency herb pairs from TCMID and comparing them with random pairs using 25 network distance models, the study showed that commonly used herb pairs exhibited significantly shorter network distances, suggesting potential synergy at the ingredient level (AUPRC = 0.87). Subsequent studies and methodological advances have further highlighted the importance of network-based strategies in elucidating synergistic mechanisms in TCM formulations [63, 64]. Recently, Liang et al. have integrated RF and SVM algorithms to mine the Traditional Chinese Medicine Systems Pharmacology (TCMSP) database [65]. Of 1,011 predicted anti-SARS-CoV-2 compounds in TCM, six were demonstrated to be effective viral entry inhibitors, thus highlighting the utility of AI in accelerating antiviral drug discovery. Guo et al. have integrated a DL-assisted mass defect filtering (MDF) method with scheduled multiple reaction monitoring (sMRM) to efficiently identify the similarities between TCM and its constituents; further classified the phytochemical constituents in Qiangwu Shengzhi Tang; and accurately quantified 37 target analytes [66]. To address challenges regarding complex TCM components and difficulties in predicting adverse drug reactions, Wei et al. have constructed a TIRPnet model based on a seven-layer deep neural network [67]. The model performed well under the optimal threshold, and the F1 value variance in five independent experiments of only 0.000085 verified the stability of the model's performance. In a prediction test of ten typical TCM ingredients, TIRPnet accurately predicted 96.4% of known adverse reactions and identified 28.9% of potential adverse reactions, thereby providing a high-throughput and stable AI tool for large-scale safety assessment of TCM ingredients. Recently, Guo et al. have constructed a DL model integrating the

Table 1 | Comparison of commonly used TCM databases and features.

Database name	Website	Core features	AI-relevant features	Data scale	Limitations	References
TCMSP	https://old.tcmsp-e.com/tcmsp.php	Provides systems pharmacology tools for TCM research, supporting pharmacokinetics, ADME properties, and drug-likeness analysis	Provides standardized pharmacokinetic and ADME data for AI-based prediction and virtual screening	Large	Limited updates; lack of recent data on new herbs and clinical applications	[44]
TCMIO	http://tcmio.xielab.net/	Specializes in immuno-oncology applications, linking herbs, formulas, and ingredients to the cancer immune microenvironment	Links herbal compounds to immune targets, supporting AI analysis in immuno-oncology	Medium	Focus solely on immuno-oncology, thus limiting broader applicability	[45]
TCMID	https://ngdc.cnrb.ac.cn/databases/commons/database/id/437	Visualizes herb-target-disease networks, integrating prescription, herb, and ingredient data	Enables network modeling of herb-compound-target-disease relationships for mechanistic prediction	Medium	Infrequent updates; need for more experimental validation	[46]
TCMIP	http://www.tcmip.cn/TCMIP/index.php/Home/Login/login.html	Provides information on the mechanisms of action of TCM compound prescriptions and prediction of component-target networks	Offers structured molecular data for graph neural network modeling of component-target interactions	Medium	Lack of modern clinical trials; inadequate predictive accuracy	[47]
HERB	http://herb.ac.cn/	Combines transcriptomics and network pharmacology to support evidence-based research	Integrates omics-level data to support AI-driven correlation analysis and knowledge graph construction	Medium	Need for further optimization of user interface and data coverage	[48]
CDCDB	https://icc.ise.bgu.ac.il/medical_ai/CDCDB/	Provides comprehensive information on drug combinations, supporting synergy prediction and retrospective evaluation	Supports AI-assisted drug combination studies by predicting synergistic or antagonistic effects	Large	Need for further optimization of user interface to increase the efficiency of data retrieval	[49]
ETCM	https://ngdc.cnrb.ac.cn/databases/commons/database/id/6146	Focuses on herbs, formulas, and ingredients with habitat and quality control data	Contains standardized chemical and quality control data for AI-based quality assessment	Large	Lack of modern clinical trial integration and deep pharmacological insights	[50]
TCMAnalyzer	http://www.rcdd.org.cn/tcmanalyzer	Provides information on various medicinal plants and the diseases regulated by these plants Focuses on integrating diverse TCM data to explore therapeutic relationships and mechanisms	Provides herb-disease-target data for AI-supported clustering and mechanism exploration	Medium	Limited updates and insufficient coverage of recent advances in TCM formulations and mechanisms	[51]
BioGRID	https://thebiogrid.org/	Provides a database of protein, genetic, and chemical interactions, supporting multiple model organisms and humans	Offers protein-gene-compound interaction data applicable to AI-assisted target discovery	Large	Limited scope of data; need for regular updates to include new research findings	[52]
TCMBank	https://tcmbank.cn/	Offers 3D structure information for drug repurposing and mechanistic analysis	Supplies 3D molecular structures for DL-based docking and binding prediction	Large	Resource-intensive data curation; dependence on automated text mining	[53]

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Table 1 | Continued

Database name	Website	Core features	AI-relevant features	Data scale	Limitations	References
YaTCM	http://cadd.pharmacy.nankai.edu.cn/yatcm/home	Provides a comprehensive toolkit for TCM research, covering 47,696 natural compounds, 6,220 herbs, 18,697 targets, and 390 pathways Supports drug discovery and mechanistic analysis through tools including substructure and similarity searches	Provides chemical and pharmacological profiles for compound similarity and property prediction	Medium	Reliance on computational predictions; need for more experimental evidence	[54]
SymMap	http://www.symmap.org/	Provides both direct and indirect pairwise relationships, including TCM-symptom, TCM-ingredient, ingredient-target, and target-disease	Enables multimodal AI models linking clinical symptoms with molecular and herbal data	Medium	Timeliness and consistency affected by manual validation processes	[55, 56]
BATMAN-TCM	http://bionet.ncpsb.org.cn/batman-tcm/#/home	Analyzes molecular mechanisms of TCM and supports pathway enrichment and visualization	Offers molecular annotations for AI-assisted pathway analysis and therapeutic inference	Medium	Limited data coverage; need for experimental validation of predictions	[57]
TCMGeneDIT	https://www.w3.org/wiki/Data/TCMGeneDIT	Integrates data on TCM, genes, diseases, drug ingredients, and literature abstracts, by using text mining techniques to automatically extract information	Contains text-mined TCM-gene-disease links for NLP-based knowledge extraction	Medium	Persistent error rate despite relatively high accuracy in associating TCM, genes, and diseases	[58]
ShennongAlpha	https://shennongalpha.westlake.edu.cn/name	Establishes a systematic classification framework for precise NMM identification, implementing chat-driven knowledge acquisition, AI-powered translation protocols, and crowdsourced refinement mechanisms	Applies conversational AI and molecular identification tools for intelligent natural product databases	Large	Inclusion of primarily Chinese natural molecules with limited global diversity Frequent data updates and unstructured formats, thus hindering timely integration and global applicability	[59]

multimodal features of molecular graph representation and Extended Connectivity Fingerprinting, and have revealed the intrinsic correlations between compound structural features and anti-*Helicobacter pylori* activity [68]. A total of 938 compounds with known activities were screened from public databases and self-built databases. Attentive fingerprinting was used to dynamically integrate atomic-level local features and long-range interactions. In the experimental validation step, the model successfully predicted four highly active berberine derivatives. This data-driven research paradigm therefore provides a new path toward efficient computation and experimental verification for TCM discovery of therapies for drug-resistant bacteria. In another example, Zou et al. have systematically analyzed the diversity of secondary metabolites in medicinal plants by combining the discrimination method of apparent equivalent diastereomers with the chemical space mapping strategy restricted by biogenesis rules [69]. On the basis of quantum chemical calculations and molecular dynamics simulations, characteristic energy difference thresholds for diastereomers were established and combined with molecular topological network analysis to achieve efficient isomer classification. Lycibarbarspermidine has been isolated and identified from *Angelica sinensis* through this method. The discovery of the new structural species verified the effectiveness of the biogenesis path prediction model, an innovative method with both theoretical depth and practical value for targeted mining of TCM. The AI-driven approach used in this study, which integrates quantum chemical calculations, molecular dynamics simulations, and molecular topological network analysis, provides a computational chemistry-based AI model for predicting and classifying novel compounds. Although the pharmacological effects of lycibarbarspermidine were not explicitly reported, the discovery of this new structural species verified the effectiveness of the biogenesis path prediction model.

2.2. AI-driven research on the composition principles of TCM prescriptions

Composition principles are central to TCM research aimed at systematically uncovering herb-herb interactions and their synergistic or antagonistic effects [63]. Variability in patient conditions and pathogenesis often renders single-herb treatments insufficient for complex clinical scenarios and highlights the importance of herbal combinations [70, 71]. Compared with the Western healthcare paradigm, TCM offers a distinctive advantage through the principle of drug combination within the Chinese medicine formula (CMF) concept. CMF refers to the combination of two or more types of Chinese medicines for specific disease symptoms, in accordance with standardized concoctions and compounding principles [72] (Figure 3A). However, identifying and optimizing numerous chemical constituents

for maximal synergy in TCM remains a major challenge [73, 74]. AI technology offers new methods to overcome this challenge through the correlation between heterogeneous data integrating heterogeneous data and applying dynamic optimization algorithms [75-77].

AI techniques provide a data-driven framework to reinterpret TCM formulation theory by modeling interactions among herbs, compounds, targets, and phenotypes. Graph convolutional networks (GCN) can capture these multi-level associations and predict formula efficacy, whereas neural and traditional supervised models can assess prescription safety and synergy through structured features [78]. Detailed network mapping of TCM components and disease genes is revealing unexpected medical applications for classic herbal formulas through module relationship analysis [79]. From the theoretical perspective of TCM, these computational networks can quantitatively represent the principle of *jun-chen-zuo-shi* ("monarch-minister-assistant-guide"). Whereas *jun* herbs usually occupy hub positions connected to core pathogenic targets, *chen* and *zuo* herbs tend to form auxiliary or regulatory subnetworks. Modeling these hierarchical relationships enables AI algorithms to systematically rediscover empirical TCM formulation principles [80]. Wang et al. have introduced a method that integrates the Ontology-Based Side-Effect Prediction Framework with artificial neural networks (ANNs) and deep learning (DL), which combines herbal ingredients in TCM prescriptions according to their attributes [81]. The herbal ingredients in TCM prescriptions were categorized according to their attributes, a database was constructed, and an ANN model was trained to predict a safety indicator for each prescription. The list of recommended prescriptions was reorganized according to safety indicator scores, and ten prescriptions with scores above 0.8 were suggested for potential COVID-19 treatment [82]. Zhou et al. have developed FordNet, an AI-powered system for TCM prescription generation that integrates multidimensional clinical data through GCN [83]. This AI-driven framework builds heterogeneous networks to map clinical-herbal interactions, then integrates real-time syndrome-state dynamics, thereby surpassing traditional modeling limits. In predicting Sini San prescriptions, FordNet achieved a precision of 0.89, outperforming SVM models by achieving 0.89 precision, 0.83 recall, and an 0.86 F1 score at the top five recommendation tier, and 92% clinical consistency in complete formula reconstruction (Figure 3B). Moreover, Liu et al. have constructed an HPE-GCN model combining GCN and TCM herbal properties to predict the efficacy of 214 classical tonic formulas [84]. The macro-precision, macro-recall, and macro-F1 of the model reached 87.70%, 84.08%, and 83.51%, respectively, and the classification accuracy of a blood supplement formula increased the test-set accuracy for blood-tonifying formulae from 80% in baseline models to 100%, thus indicating significant advantages in the prediction of TCM composition [84]. Zhao et al.

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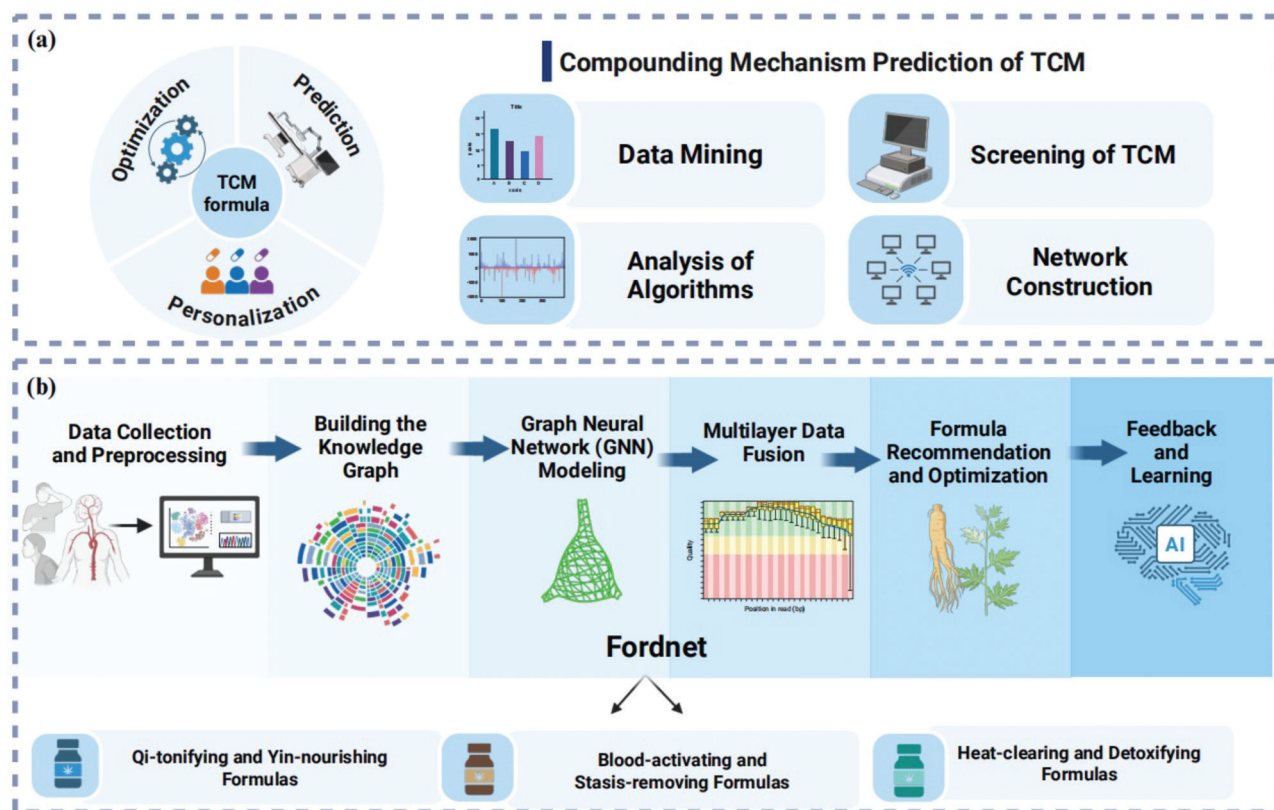


Figure 3 | AI-driven approaches in traditional Chinese medicine formulae.

(A) Workflow of AI-assisted prediction of traditional Chinese medicine formula compounding mechanisms. (B) FordNet system, based on graph convolutional network construction. A heterogeneous map based on multi-dimensional clinical data is used to simulate the complex interaction of medicinal components (created in <https://BioRender.com>).

have proposed a TCM prescription recommendation model based on multi-GCN, which can construct a symptom-state element graph and symptom-symptom-type graph [77]. Graph convolution features were extracted and combined with a multi-layer perceptron to achieve herbal medicine prediction. After testing on the *Treatise on Febrile Diseases* dataset, the precision, recall, and F1 scores of the top five indicators of multi-GCN reached 62.70%, 73.39%, and 67.52%, respectively, values 4.51%, 6.45%, and 5.31% higher than the current optimal baseline algorithm SVM, thus indicating strong recommendation accuracy. These advances suggest that the application of AI in TCM prescription research contributes to more accurate prediction as well as clearer conceptualization of herbal compatibility. By representing empirical knowledge, such as *jun-chen-zuo-shi* balance, syndrome differentiation, and herb property coordination, traditional formulation principles can be expressed in measurable terms. In practice, different algorithmic paradigms offer complementary advantages. Graph neural networks can effectively capture multilevel relationships among herbs, compounds, and targets, whereas DL architectures, such as convolutional and transformer-based

models, can extract high-dimensional representations from multi-omics and textual TCM data. Classical ML algorithms remain useful for small-sample analysis and interpretable compatibility prediction. Collectively, these approaches enable the transformation of empirical formulation knowledge into quantitative, verifiable, and generalizable models, thereby deepening mechanistic understanding and supporting the evidence-based modernization of TCM.

2.3. AI-assisted TCM target prediction

Target prediction in drug development is crucial for elucidating drug mechanisms of action and optimizing the therapeutic efficacy of candidate interventions [85-87]. In TCM research, accurate identification of the relationships between bioactive compounds and their targets is particularly important to promote precision medicine [88]. However, decoding the multiple pharmacological mechanisms of TCM faces substantial challenges arising from increasing data complexity [89]. To address this challenge, network pharmacology has become a key framework in TCM research. The concept of network pharmacology was first proposed by Hopkins in 2007 [90]. Subsequent studies further integrated

computational analysis with experimental validation, enabling the decoding of pharmacodynamic properties of TCM through high-throughput multi-omics and in vitro/in vivo systems [91, 92]. However, as biological data rapidly grow, and studies become more complex across multiple targets and dimensions, traditional network pharmacology methods struggle to handle large and diverse datasets effectively [93, 94]. In resolving the nonlinear behavior of multiple metabolites and multiple targets, the lack of computational scalability and time resolution restricts in-depth applications [95, 96]. In contrast, AI can efficiently analyze large-scale data sets and complex biological networks. By building predictive models, AI can not only reveal complex compact-target interactions but also predict treatment pathways, thus providing new opportunities and directions to solve the aforementioned problems in TCM modernization [38, 97, 98] (Figure 4A).

Under the framework of deep integration of AI and network pharmacology, the application of AI technology in target identification of TCM has markedly progressed. For example, researchers have revealed the molecular mechanism of puerarin through computational model-based network topology analysis and random network comparison, integrated with photon affinity chemical labeling and cryo-electron microscopy. The results have not only revealed the molecular pathways of the brain-gut axis in lipid metabolism but also provided a new paradigm for AI-driven target discovery and mechanistic analysis of TCM [102]. Wang et al. have proposed an herb-target interaction network (HTINet) based on heterogeneous network embedding, which constructs a symptom-herb-target heterogeneous network and uses network embedding techniques to learn low-dimensional representations of herbs and proteins and ultimately enable accurate target prediction [99]. However, integrating TCM-specific attributes and clinical treatment knowledge into HTI models remains a major challenge in improving prediction accuracy. To address this challenge, Duan et al. developed HTINet2, which incorporates TCM knowledge graph embedding, residual graph representation learning, and supervised target prediction [103]. The model constructs a large-scale knowledge graph encompassing herbal properties and clinical indications, applies deep knowledge graph embedding to learn rich representations of herbs and targets, and uses a residual-style GCN to capture complex herb-target interactions. Extensive evaluations, including performance comparisons and ablation studies, have demonstrated the notably superior predictive capability and reliability of HTINet2 versus baseline models in target prediction tasks (Figure 4B). Zhao et al. have developed the Signed Random Walk with Restart (SRWR) algorithm and applied it to simulate the propagation process of TCM action in the signal network and identify key regulated targets [104]. For example, by combining mass spectrometry component identification, target prediction, and transcriptome

analysis, SRWR screened 216 core genes notably inhibited by Erigeron Zhanxixin Injection (DZXXI) from the human signaling network. The algorithm showed strong network inference ability in the analysis of complex multi-target mechanisms of TCM. This new tool enables systematic modeling of TCM component-target-disease pathways. Similarly, Liu et al. have developed a multi-target polypharmacology prediction platform combining virtual screening with ensemble ML models. This framework has identified 20 hepatoprotective TCM ingredients against drug-induced liver injury and demonstrated AI's capacity to resolve TCM's multi-target synergies [105]. Tian et al. have proposed Multiview Heterogeneous Information Network Embedding with Hierarchical Attention Mechanisms (MHADTI), a drug-target interaction prediction model based on a multi-view heterogeneous information network and hierarchical attention mechanism [106]. This model constructs a multi-view drug-target network by integrating multi-source information such as drug structure, fingerprint information, target functional annotation, and protein structure and sequence data. Subsequently, the attention mechanism at the node, semantic, and graph levels is used to combine information from multiple sources. MHADTI is superior to the 12 current mainstream models, according to five mainstream evaluation indicators, and has shown significant predictive advantages. Multimodal fusion and hierarchical modeling embodied in MHADTI provide new methodological ideas for target identification of TCM components. Gan et al. have constructed a network medicine framework based on human protein-protein interaction groups, in which symptom-associated proteins form a modular structure in the protein network, and the topological proximity between the TCM target and the symptom module can effectively predict clinical efficacy [107]. This discovery not only explains the common mechanism of TCM syndrome differentiation and treatment at the molecular network level but also establishes an analytical paradigm that can predict the clinical efficacy of TCM, thereby opening a translational application path for drug discovery and symptom treatment prediction based on network topology.

Jin et al. have integrated AI methods such as person re-identification and random-walk network analysis to build large-scale data sets of myocardial mitochondrial dynamic phenotypes under drug action; created new tools such as MitoRelD, scRank, and scCube; and analyzed the targets of active ingredients of TCM, such as tanshinone IIA and epicatechin [100]. This method overcomes the shortcomings of traditional omics technology, such as low efficiency and insufficient resolution, and enables intelligent identification of TCM action targets on the basis of phenome and single-cell transcriptome data [101, 108] (Figure 4D). Similarly, our group has proposed the Natural Product Virtual Screening-Interaction-Phenotype (NP-VIP) strategy, which integrates virtual screening, chemical proteomics, and metabolomics

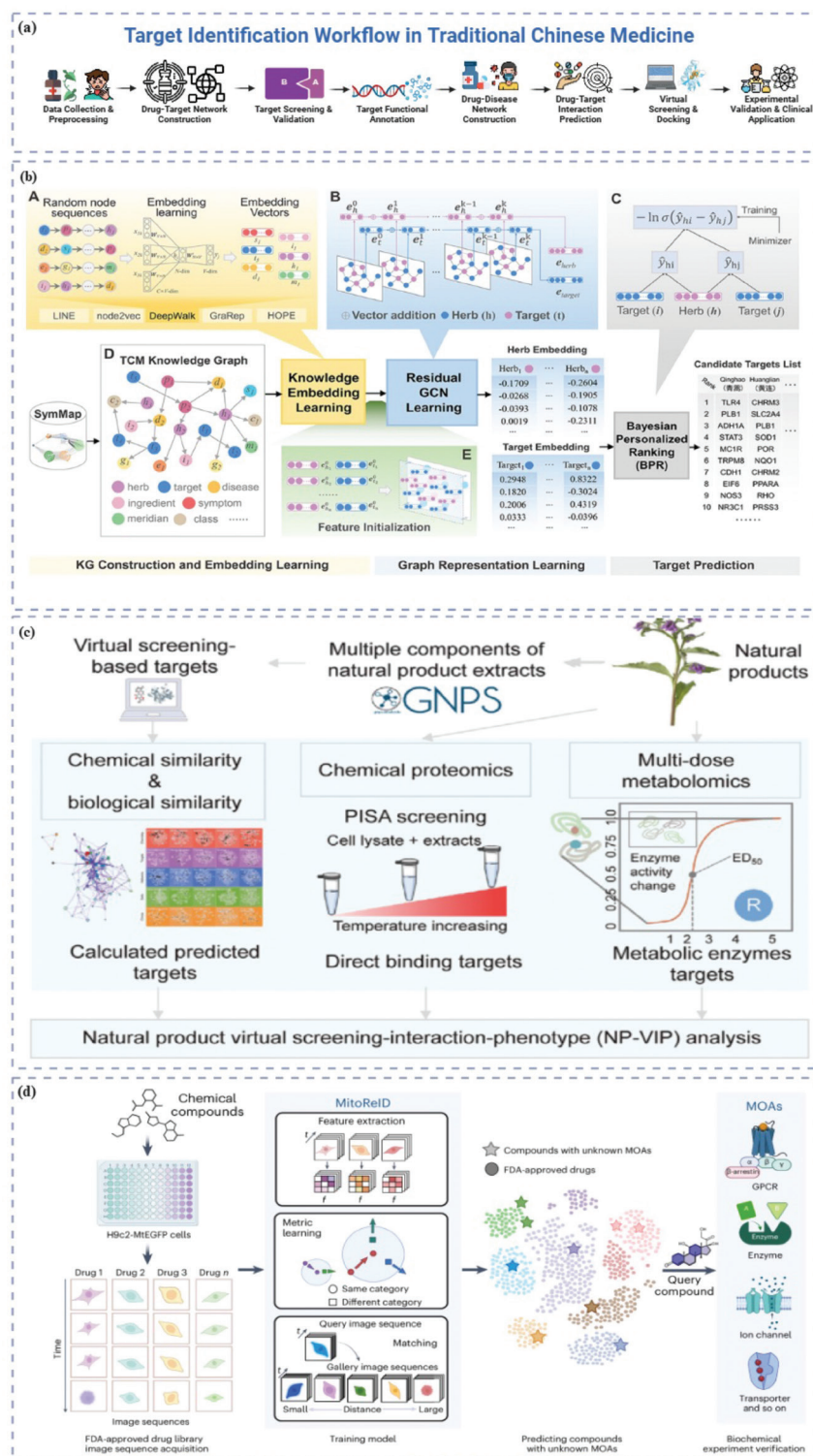


Figure 4 | AI-assisted discovery of therapeutic targets in traditional Chinese medicine.

(A) Workflow of AI-assisted target identification of traditional Chinese medicine. (B) Target prediction with the HTNet2 deep learning framework (reproduced with permission from Ref. [99]). (C) Application of the NP-VIP strategy for multi-layered target prediction and validation in ischemic stroke treatment (reproduced with permission from Ref. [100]). (D) Framework of deep-learning-based MOA prediction by profiling temporal mitochondrial phenotypes for large-scale drug discovery and repurposing (reproduced with permission from Ref. [101]; created in <https://BioRender.com>).

to systematically identify bioactive targets of TCM. In a case study of *Salvia miltiorrhiza* extract for ischemic stroke treatment, the NP-VIP strategy enabled multi-layered target prediction and validation. Specifically, on the basis of 126 structurally annotated *Salvia miltiorrhiza* extract compounds, 310, 100, and 78 potential targets were identified by virtual screening, chemical proteomics, and multi-dose metabolomics, respectively. Through integrative analysis, five high-confidence targets (PARP1, STAT3, APP, GLUL, and GAD67) were ultimately prioritized and experimentally validated. This framework not only decreases the false-positive rate associated with single-method approaches but also captures both direct compound-target interactions and downstream phenotypic responses, thereby offering a scalable paradigm for target discovery in complex TCM systems [109] (Figure 4C).

2.4. AI in multi-omics TCM research

Multi-omics approaches refer to a series of comprehensive research strategies based on high-throughput analysis and detection technologies in modern biological research systems, which are aimed at comprehensively analyzing the complexity of biological systems by integrating multi-level data, such as genomics, transcriptomics [110], metabolomics [111], and proteomics [112, 113] (Figure 5). Multi-omics approaches have been applied in studies of various diseases, such as brain diseases [114], diabetes [115], cancer [116], cardiovascular diseases, and human single-cell analysis [117, 118]. Similarly, systems-biology-driven multi-omics approaches provide powerful tools to decode the complex components and targets of TCM [119-121]. However, applying these methods to TCM research also faces challenges, such as the complexity of multi-dimensional data integration and the difficulty in identifying

AI-Integrated Multi-Omics Approach for Traditional Chinese Medicine Research

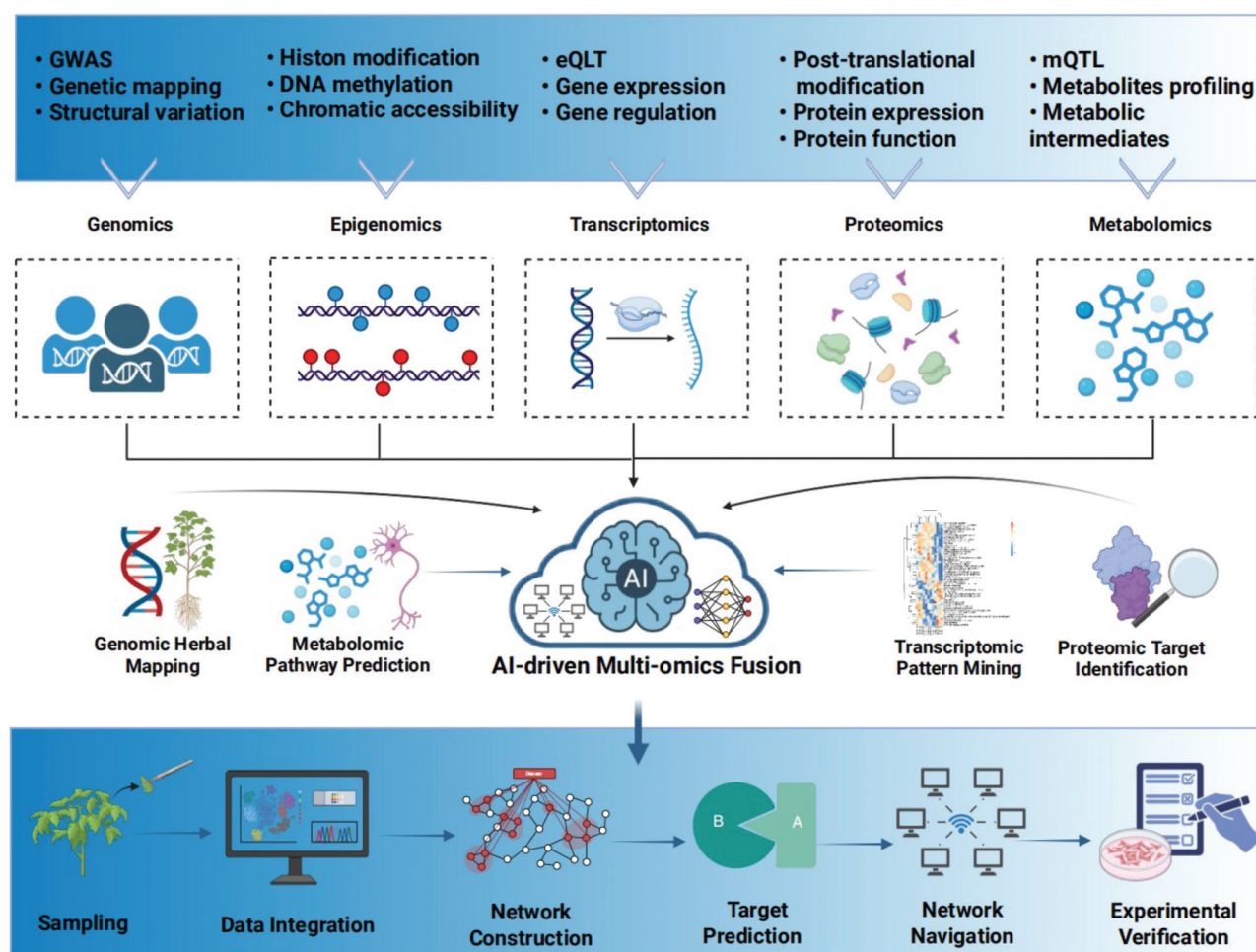


Figure 5 | AI-integrated multi-omics approach for TCM research (created in <https://BioRender.com>).

Review Article

specific treatment-associated biomarkers [122]. AI has been key in overcoming these barriers, by integrating complex multivariate data with network-based analysis methods that facilitate the integration of large and diverse data sets, thus ultimately increasing the accuracy of TCM prediction and treatment [123-125].

Many researchers have used multi-omics strategies to study the therapeutic effects of TCM [126]. Yang et al. have developed a multi-omics fusion strategy based on RNA sequencing, data-independent acquisition proteomics, and non-targeted metabolomics to analyze the characteristics of TCM syndromes characteristics of coronary heart disease phlegm and blood stasis syndrome [127]. By analyzing 90 clinical samples and leveraging AI-assisted tools, such as Cytoscape's center algorithm and ML modeling, the researchers collected 90 clinical samples, analyzed the data, and screened biomarkers with high diagnostic value. By using logistic regression combined with AI auxiliary variable screening, inhibition of the JNK/AP-1 signaling pathway and disorder of arachidonic acid metabolism were identified as the potential mechanisms underlying this syndrome type. This study demonstrates the high potential of multi-omics technology and AI-driven analysis in promoting the standardization of TCM syndrome differentiation and biological mechanistic analysis. By integrating network target analysis, clinical multi-omics experiments, and AI algorithms, Zhao et al. have systematically revealed the multi-dimensional mechanism of action of Tuomin Zhiti Decoction (TZD) in the treatment of seasonal allergic rhinitis [128]. The DrugCIPHER algorithm, which uses network propagation and logistic regression models, was used to predict the biological effect profiles of 11 herbs in TZD, and a biological network covering five functional modules, including allergic reaction, T cell immunity, and antigen presentation, was constructed. Subsequently, a single-arm clinical trial was conducted in 80 patients with seasonal allergic rhinitis to verify the efficacy and molecular mechanism of TZD combined with 16S rRNA metagenomic sequencing of gut microbiota and serum transcriptome sequencing. Moreover, Zhang et al. have conducted a multicenter, randomized, double-blind, controlled study involving 409 patients with new-onset type 2 diabetes mellitus [129]. Through AI-driven high-throughput data mining and association analysis, the study revealed that berberine regulates the bile acid signaling pathway and exerts hypoglycemic effects by inhibiting the conversion of deoxycholic acid mediated by *Ruminococcus bromii*. Zuo et al. have developed a multi-omics analysis framework integrating genomics, proteomics, and metabolomics, combined with network pharmacology and ML models, to systematically analyze the mechanisms of tonic TCM in the adjuvant treatment of gastrointestinal cancer [130]. Through multi-dimensional analysis of 72 tonic drugs in 371 types of TCM, including data on 33,765 clinical prescriptions, the combination of multi-omics and AI was confirmed to improve the efficiency of analyzing

compound synergistic mechanisms by 4.5-fold, thus providing a quantitative paradigm for the research of TCM modernization.

2.5. AI-enabled TCM quality control

With the rapid development of the TCM industry, ensuring quality, stability, and safety are fundamental. By leveraging big data analytics and ML technologies, substantial progress has been made in intelligent quality control throughout the TCM production chain. Real-time data collection and analysis from critical stages, such as medicinal material cultivation, harvesting, decoction piece processing, and preparation production, have enabled precise monitoring across the production lifecycle. These technologies increase production efficiency and also ensure that strict quality standards are followed at every step, thereby safeguarding the health and rights of consumers [131]. Similarly, AI-enabled traceability systems have increased TCM transparency and authenticity. Comprehensive databases have been compiled to document chemical profiles, pharmacological properties, and treatments, in support of resource management and supply chain sustainability [132] (Figure 6A).

A notable innovation in TCM quality assurance involves the identification of quality markers (Q-markers), which are chemical indicators closely associated with efficacy and safety [134]. Zhao et al. have developed an HPLC fingerprint method integrated with network pharmacology to predict Q-markers for *Atractylodes Rhizoma*, thereby facilitating a more precise quality control system [135]. Liu et al. have applied ML models such as RF, SVM, and partial least squares discriminant analysis (PLS-DA) to monitor various processing stages of ginger through UPLC-MS chemical profiling [136]. Both the RF and PLS-DA models achieved classification accuracy exceeding 95% and successfully distinguished five processing levels. In addition, 26 key chemical components were identified as markers, including bioactive compounds such as gingerols and shogaols. These marker compounds were selected through variable importance in projection analysis, and gingerol and shogaol derivatives were identified as critical indicators for the processing stages of ginger. ML models such as SVM and ANN have further enhanced this process by analyzing chromatographic data, and have achieved sensitivity and specificity rates exceeding 95% in detecting adulteration and contamination [137]. AI-driven big data analysis has been applied to optimized cultivation of medicinal plants such as *Salvia miltiorrhiza* and *Panax notoginseng*. Ren et al. have used algorithms including gradient boosting decision tree and RF to analyze multivariate environmental data, such as soil quality, climate, and light conditions, and to identify optimal growing regions [138]. As a result of this AI-assisted identification of optimal growing regions, the yield and active ingredient content of tanshinones and ginsenosides were increased by 22% and 18.5%, respectively. To address the problems of appearance similarity and adulteration frequently

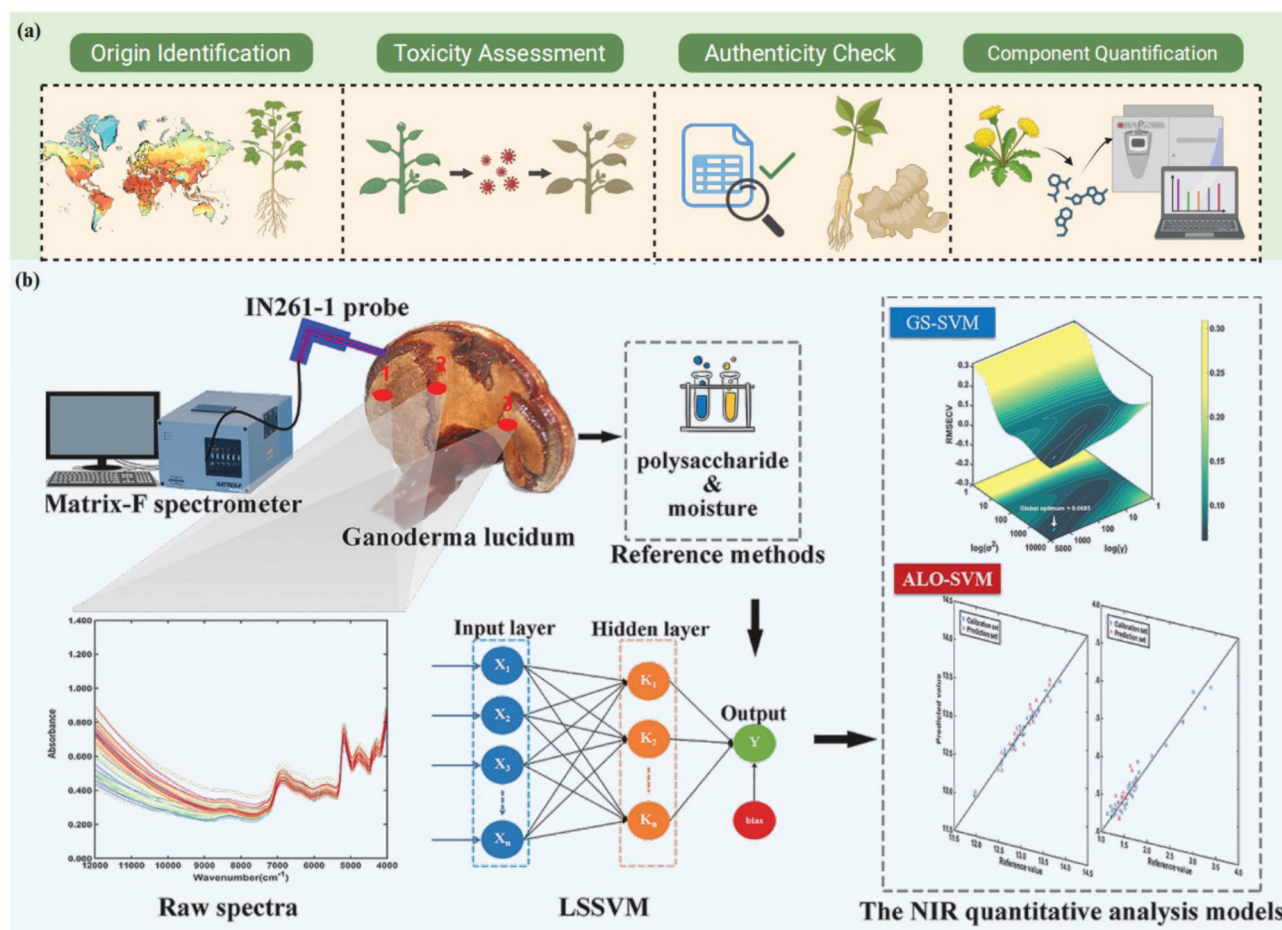


Figure 6 | AI-powered holistic approach to TCM quality control.

(A) Main contents of AI-assisted quality control of TCM. (B) Schematic diagram of acquisition of *Ganoderma lucidum* near infrared spectra (reproduced with permission from Ref. [133]; created in <https://BioRender.com>).

occurring during the distribution and trade of high-value TCM materials such as *Crocus sativus*, Husaini et al. have proposed two low-cost, user-friendly rapid identification methods [139]. An image recognition model based on a convolutional neural network was used to realize automatic forgery detection. A total of 2,250 saffron samples were collected, and a dataset of 3,794 images was constructed. ResNet18 and DenseNet121 models were used for binary classification training. The recognition accuracy of the model on the test set was 99.5%, the precision was 99.3%, and only two samples were misjudged. This method greatly outperformed traditional methods such as RF and SVM. This study verified the superior performance of ML and DL methods in the image recognition and adulteration detection of TCM, and has provided a technical path toward visual quality control [139]. By integrating the ConvNeXt architecture with the ACMix module, Miao et al. have developed an enhanced DL model for image recognition and authenticity verification of six TCM materials: *Angelica sinensis Radix*, *Citri Reticulatae Pericarpium*, *Angelica dahuricae Radix*, *Lilii*

Bulbus, *Lonicerae Japonicae Flos*, and *Glycyrrhizae Radix* [140]. Experimental results demonstrated that incorporating the ACMix module increased recognition rates to 89.3% on the training set and 83.1% on the validation set. Through systematic data augmentation, multi-scale feature fusion, and depth-optimized network design, the proposed method establishes a robust framework for automated identification of TCM materials. Intelligent decoction centers integrating AI and real-time sensor systems have been developed. Li et al. have demonstrated an AI and Internet of Things–based intelligent decoction system capable of standardizing and stabilizing therapeutic efficacy by optimizing decoction parameters [141]. Consequently, the variability in decoction concentration was decreased to within $\pm 5\%$, thereby improve batch consistency and therapeutic reliability.

Despite these advances, the effective application of AI in TCM heavily relies on high-quality datasets, standardized protocols, and interdisciplinary collaboration. Combining domain expertise with AI technologies is essential to address the inherent complexity of TCM

Review Article

and to unlock the full potential of AI in TCM for quality control, cultivation, and processing [142]. In processing, ML-based models combined with hyperspectral imaging have enhanced the standardization and quality stability of TCM [133]. In our previous study, we combined near infrared technology with an SVM algorithm to collect near infrared band (400–1,000 nm) data and established a model system suitable for non-destructive identification of Chinese herbal seeds. *Astragalus membranaceus* and frequently confused species with highly similar appearance served as an example for verification. The model's 97.22% recognition accuracy in the seed classification task greatly outperformed the traditional manual discrimination method based on morphological characteristics. Notably, the model showed more consistent performance in distinguishing commonly confused varieties, such as *Astragalus mongolicus* and *Astragalus membranaceus*. This method not only enables non-destructive, automatic processing of TCM seed identification but also provides an efficient intelligent image recognition scheme for TCM quality traceability and breeding [143] (Figure 6B).

2.6. AI-assisted personalized and precision medicine in TCM

The theoretical framework of TCM emphasizes the principle of evidence-based treatment, and requires individualized treatment plans based on each patient's symptoms and phenotypic characteristics. Consequently, accurate prediction of the changes in TCM components across various disease states is crucial for developing customized treatment strategies [55, 144] (Figure 7A). AI techniques can be used to mine clinical phenotypes, infer similarities among clinical symptoms, and elucidate relationships between evidence and phenotypes [145, 146].

By integrating disease phenotypes with symptom characteristics, researchers can analyze related gene predictions or histological data, subsequently construct similarity metrics, and conduct correlation analyses based on biomolecular networks [147]. For example, by analyzing the biological basis of spleen deficiency and its relationship with digestive diseases, and exploring the biological basis of coronary heart disease and establishing diagnostic markers, differentiated treatment strategies for various manifestations of the same disease can be achieved, thus exemplifying the concept of different treatments for the same disease [148]. Building on this foundation, Ruan et al. have proposed a novel deep autoencoder model called Automatic Medicinal Network Embedding (AMNE) for automatic detection of specific symptoms in TCM formulas, which learns and represents the complex structures and attributes of TCM formulas through network embedding technology, and achieves automatic detection and recognition of specific symptoms [149]. Additionally, Yao et al. have proposed a Prescription Topic Model (PTM) based on TCM theory, which portrays and integrates the TCM domain knowledge with the prescription generation process,

such as the “ruler, minister, adjuvant, and enabler” roles of drugs. The PTM, when applied to 33,765 prescriptions, outperformed previous models in terms of drug recommendation and symptom prediction perplexity, and showed superior generalization performance and prescription pattern discovery [150]. Furthermore, Yang et al. have proposed the multi-layer information fusion model Knowledge Driven Herb Recommendation (KDHR), which constructs a TCM knowledge graph and incorporates TCM properties as auxiliary information to obtain information-rich symptom and TCM feature representations with reduced noise, compared with models without such knowledge-graph guidance [75]. The KDHR model enabled in-depth understanding of the complex patterns between symptoms and herbal medicines in prescriptions, in an analysis of data from 33,765 prescriptions. Moreover, the network medicine framework proposed by Gan et al. creates a network medicine model for analysis and prediction by mapping the human protein-protein interaction networks to brain-associated proteins and herbal targets, and analyzing the topology of these networks, thus revealing the interactions between herbal components and disease-associated proteins, and predicting the therapeutic effects of herbal medicines for specific symptoms [107]. Zhang et al. have constructed and released the platform Using Network target for Intelligent and Quantitative analysis on drug actions (UNIQ), which combines the key technologies of TCM and AI [151]. The authors established a multi-level phenotype-cell-molecular-drug network for TCM and Western medicine; comprehensively analyzed the scientific principles of TCM; and developed a multimodal and multi-omics AI algorithm for TCM and Western medicine (AI-TWM) based on the platform and big data (Figure 7B). The rules of diagnosis and treatment associated with gastritis cancer transformation were analyzed, and a very early intelligent identification system of gastric cancer was constructed, thereby providing an important basis for risk warning, prevention, and treatment [38]. Recent studies have demonstrated that DL can improve the precision and reliability of visual diagnostics in TCM. For instance, convolutional neural network-based tongue image recognition systems have achieved accurate syndrome differentiation across diverse patient cohorts [152]. Similarly, AI-driven spectral and imaging analysis has enhanced the discrimination and standardization of herbal materials [153, 154], thereby bridging traditional empirical assessments with data-driven quantification. These advances highlight the transition from subjective evaluation toward intelligent, reproducible, and mechanistically interpretable quality control frameworks in TCM modernization.

2.7. Application of large language AI models in modern TCM research

The theoretical system of TCM, which is characterized by its holistic approach and syndrome-differentiation-

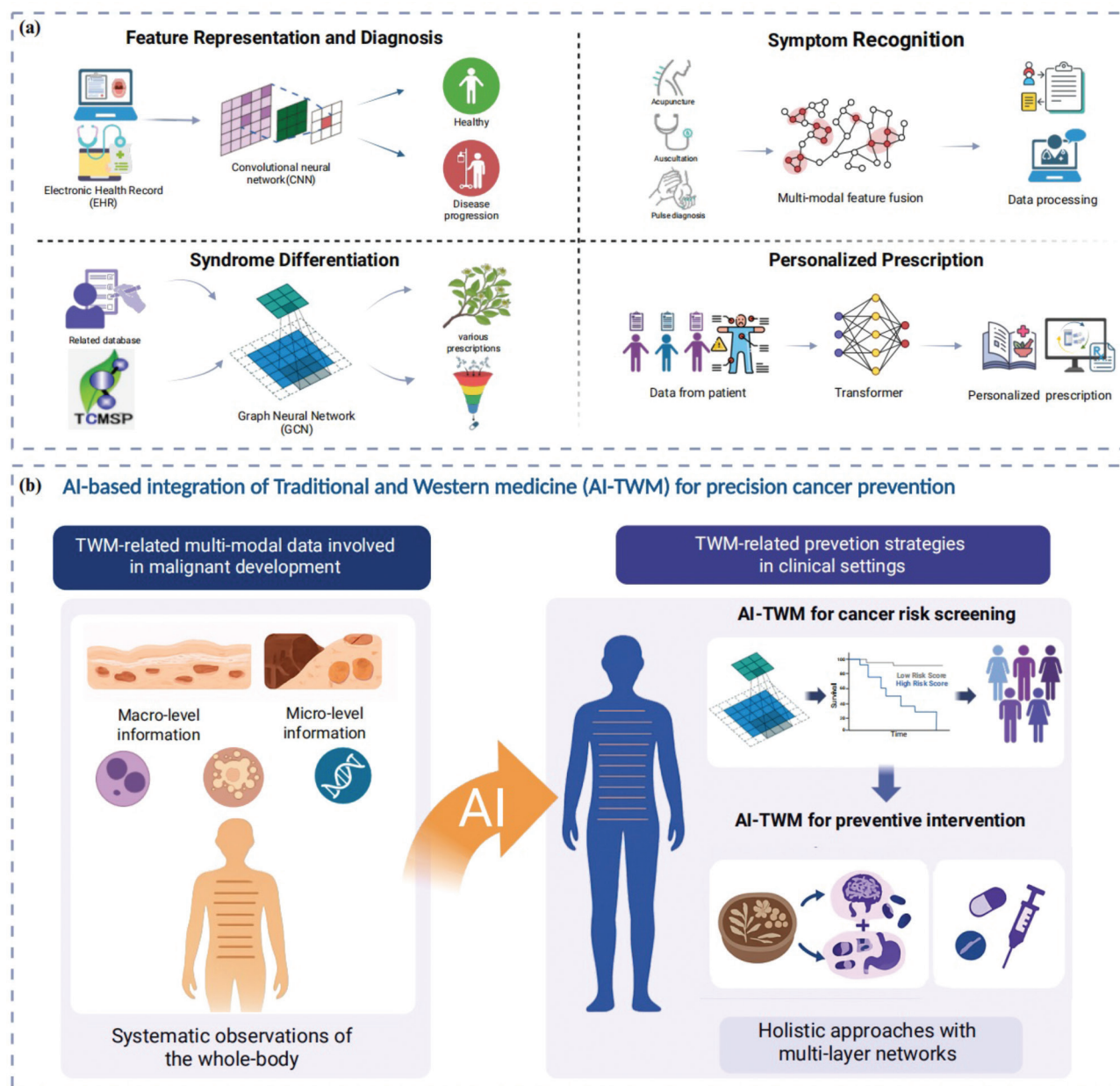


Figure 7 | AI-assisted personalized and precision medicine in TCM.

(A) Application of AI methods in TCM diagnosis and treatment processes. (B) A new paradigm of cancer prevention and treatment with AI-based Traditional Chinese Medicine and Western Medicine (AI-TWM) (created in <https://BioRender.com>).

based treatment, presents unique challenges for model evaluation, because of the highly individualized nature of diagnostic processes, need for enhanced theoretical understanding, and clinical reasoning capabilities in AI systems [155]. The rapid advancement of AI technologies has accelerated transformative progress in TCM research and established a dialogue between traditional medical wisdom and modern scientific paradigms through synergistic integration of multimodal data fusion and deep neural network architectures. In the modernization of

TCM, the scarcity of data resources and the high complexity of domain knowledge pose unique challenges to development. To overcome the limitations of small samples, researchers have integrated large language models (LLMs) into TCM knowledge systems. LLMs, built upon natural language processing foundations and DL techniques, aim to simulate TCM experts' cognitive processes by assimilating classical texts, clinical records, and therapeutic data [156] (Figure 8A). These models use recurrent neural networks, transformer architectures, and

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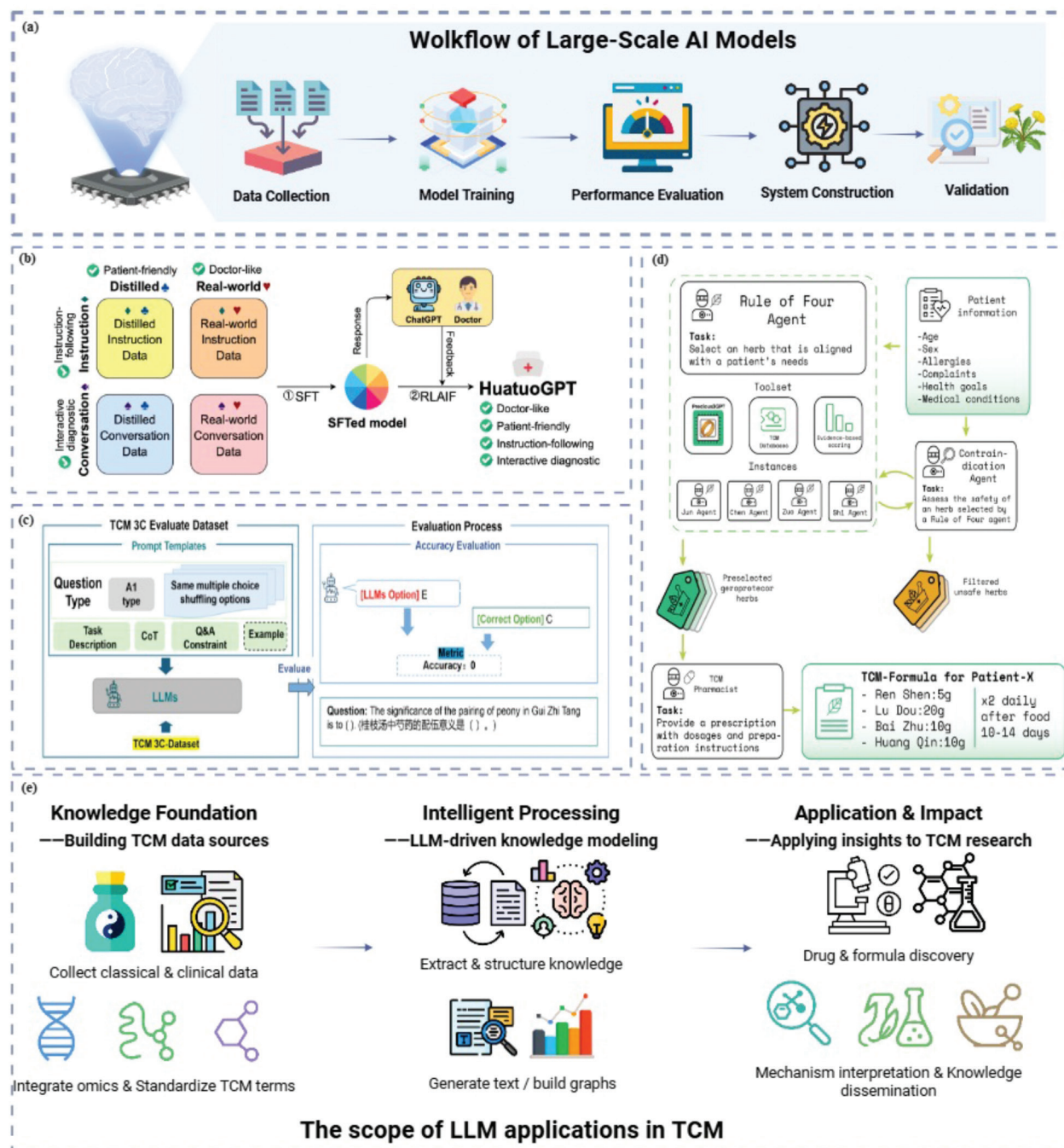


Figure 8 | Application of large language AI models in modern TCM research.

(A) Workflow of AI large language models in traditional Chinese medicine research. (B) Performance of HuatuoGPT in a medical consultation task (reproduced with permission from Ref. [157]). (C) DeepSeek's performance on TCM-specific benchmarks (reproduced with permission from Ref. [158]). (D) Workflow for identifying cross-species TCM geroprotectors with Precious3GPT (reproduced with permission from Ref. [159]). (e) Scope of LLM applications in TCM, in three stages: building TCM data sources, LLM-driven knowledge processing, and applying outputs to drug discovery and mechanistic studies (created in <https://BioRender.com>).

long short-term memory networks [157], augmented with reinforcement learning mechanisms, to develop medical reasoning capabilities for clinical decision support and patient-physician interaction systems [160].

To ensure reliability, LLM applications in TCM emphasize standardized and ethically curated datasets, along with task-specific benchmarks such as prescription recommendation, syndrome classification, and multimodal

diagnosis. Measures to mitigate risks, including hallucination and algorithmic bias, include grounding outputs to authoritative sources, dataset balancing, and human-in-the-loop validation. Cross-institutional testing and prospective monitoring enhance model generalizability and clinical safety. These practices establish a robust foundation for applying LLMs in complex, individualized TCM contexts [161]. Building on these foundations, various AI modalities are leveraged according to data type and task. NLP models excel in analyzing textual data from classical literature, clinical notes, and electronic medical records, thus supporting entity recognition, relation extraction, and automated prescription suggestions. Computer vision models can complement NLP by analyzing diagnostic images, including tongue and facial morphology, for syndrome differentiation. Integrating these modalities enables a comprehensive AI framework that mirrors the multidimensional reasoning central to TCM practice [162].

Current applications of LLM technology in TCM have demonstrated accelerated development [163, 164]. Notably, ChatGPT has gained substantial traction in modern medical data analysis. Zhang et al. have proposed HuatuoGPT, an LLM designed for medical consultation, by combining distilled data from ChatGPT with real-world data from physicians during supervised fine-tuning [165]. Experimental results have indicated that HuatuoGPT outperforms ChatGPT in medical consultation tasks, including GPT-4 evaluations, human assessments, and medical benchmark datasets (Figure 8B). The TCMChat model proposed by Dai et al. is a large model in the field of TCM optimized on the basis of Baichuan2-7B-Chat [166]. Its professional ability is strengthened through pre-training and supervised fine-tuning. This TCM model provides open-source code and an online dialogue tool. It achieves an end-to-end task chain covering case diagnosis, herbal medicine recommendation, and molecular screening. It has achieved an accuracy more than 30% greater than that of existing TCM models. In the performance comparison, the accuracy in answering herbal medicine-related multiple-choice questions was 71.6%, and the accuracy of prescription was 76.8%, thus representing significant improvements over similar TCM models, such as HuatuoGPT achieved only 7.7% accuracy in this performance comparison, which represents a significant gap when compared to other TCM models. Yang et al. have proposed the TCM-GPT model, which focuses on pre-training and fine-tuning by using the TCM corpus, combined with Low-Rank Adaptation (LoRA) technology, to efficiently manage large-scale models, and enhance the understanding and application of models in TCM [167]. TCM-GPT performed notably better than other models in TCM examination and diagnosis tasks. However, the main limitation of this model is that it relies on text-based information and cannot integrate non-textual data such as medical images. Zhang et al. have proposed the Qibo model dedicated to the application of language models in the field of

TCM [168]. Through continuous pre-training on the TCM corpus combined with supervised fine-tuning, Qibo can effectively perform specific TCM tasks, such as symptom identification, diagnosis, and prescription recommendation. Through deep mining of the TCM corpus, the accuracy of Qibo was improved by 22% in complex TCM question answering tasks.

Recent advancements in multimodal diagnostic systems have achieved paradigm-shifting innovations [169, 170]. TCM diagnosis fundamentally relies on pattern recognition of seemingly unrelated symptoms, guided by theoretical constructs including *yin-yang* balance, five-phase correspondence, and *zang-fu* organ system functionality [158, 171, 172]. Models lacking adequate understanding of these conceptual frameworks face particular challenges in syndrome differentiation tasks requiring holistic pattern recognition rather than linear diagnostic reasoning [159, 173]. Researchers have used DeepSeek in specialized studies, because of its advanced TCM knowledge representation, including recent investigations of medical applications of tai chi and qigong, thus highlighting its ability to integrate complex traditional practices within modern research frameworks [174]. DeepSeek has simulated clinical interactions by integrating generative models with reinforcement learning, thereby achieving a 30% decrease in diagnostic errors through analysis of millions of tongue/facial images capturing subtle morphological variations. Huang et al. have reported DeepSeek's superior performance across critical TCM benchmarks, including 88.59% accuracy in TCM-Exam, 71.81% in TCM-LitQA, and 78.52% in TCM-MRCD [158] (Figure 8C). These performance differentials fundamentally reflect epistemological alignment with TCM's unique conceptual framework. DeepSeek has achieved a 50-percentage-point improvement over general models in interpreting classical texts, thus demonstrating the successful computational internalization of TCM's distinctive cognitive patterns. This approach effectively bridges modern computational methods with TCM's theoretical framework [175]. Galkin et al. have integrated the generative AI model Precious3GPT and BATMAN-TCM2 database to construct an AI-driven framework for systematic screening of anti-aging TCM ingredients [176]. This approach has used P3GPT to simulate age-related RNA expression differences between humans and mice in liver, lung, and muscle tissues. This method led to the identification of a tissue-specific aging signature containing 100 up-regulated genes, as well as 13 conserved aging genes, including LBP, ACSM1, and NNMT. On the basis of these findings, the research group designed ISM-Formulaf1 and simplified ISM-Formulaf2, and developed a multi-agent system based on the "monarch and minister" principle to achieve personalized prescription, thus providing an extensible methodological paradigm for AI-driven modernization of TCM (Figure 8D). A summary of the broader scope of LLM applications in TCM (Figure 8E) outlines how LLMs integrate multi-source

Review Article

TCM data; perform knowledge extraction and modeling; and apply the results to drug discovery, formula development, and mechanistic studies.

3. OUTLOOK

The convergence of AI algorithms and multi-omics technologies has created unprecedented opportunities for TCM. TCM's holistic philosophy increasingly aligns with modern medical paradigms that prioritize comprehensive disease analysis through systemic approaches [177, 178]. This review synthesized AI-driven advancements across critical TCM modernization domains, including predictive modeling of bioactive components, deciphering herbal formula compatibility mechanisms, target identification, multi-omics integration, quality standardization, and novel applications of large AI models in contemporary TCM research. By leveraging big data analytics, AI systems have demonstrated capabilities in forecasting pharmacological responses and refining therapeutic regimens, and optimizing clinical outcomes while maintaining safety profiles. The technology further enhances clinical workflows by enabling rapid interpretation of patient-specific disease patterns, thereby supporting data-informed personalized interventions. Emerging network topology analyses can reveal disease-syndrome correlations through structural similarities between pathological phenotypes and TCM diagnostic patterns. As AI integration intensifies in TCM practice, these technological innovations are paving the way to systematic modernization and global acceptance of this ancient medical tradition [83].

Despite its transformative potential, the incorporation of AI into TCM research continues to face multiple unresolved challenges. One critical issue is the heterogeneity and limited standardization of existing pharmacological and clinical datasets, which hinder model reproducibility and the generalizability of findings [38]. The interpretability of computational predictions also remains a major obstacle, because current algorithms often function as “black boxes,” which provide limited mechanistic insights that align with traditional theoretical frameworks. Moreover, ethical and regulatory concerns, such as patient data privacy, informed consent in clinical data use, and algorithmic bias in decision-making, require more rigorous oversight. Future work should also address the inherent limitations of AI applications in TCM, including bias, interpretability, and generalizability. Data imbalance and inconsistent labeling across pharmacological and clinical sources can introduce bias, and the opacity of DL models constrains mechanistic interpretability within TCM theory. Developing more transparent, interpretable, and cross-validated models will therefore be essential to ensure scientific credibility and clinical relevance.

Another key priority is the creation of shared, standardized datasets integrating herbal, omics, and clinical data to increase reproducibility and enable robust

model training. An equally important goal is achieving syndrome classification consistency, because heterogeneous diagnostic criteria limit model transferability and the comparability of AI-driven findings. Establishing clear evidence standards for AI use in clinical TCM through multicenter validation and unified performance metrics will be crucial for bridging computational predictions with clinical outcomes [179, 180].

Future progress will rely on developing unified data standards for herbal, clinical, and omics information, as well as transparent and interpretable modeling approaches capable of integrating both empirical knowledge and biomedical mechanisms. Establishing interdisciplinary frameworks that bridge computational science with traditional diagnostic principles will be essential for achieving reliable and ethically sound applications. These efforts will ultimately advance the evidence-based modernization of TCM.

AUTHORS CONTRIBUTIONS

T.F.-X. conceived the article. L.Y. and X.Y.-X. wrote the manuscript. S.S.-P., L.-N., S.-Z., Y.-C., and X.S.-L. edited and proofread the manuscript. T.F.-X., J.H.-Z., and Y.-Z. assisted in writing and reviewing the manuscript. All authors have read, discussed, and approved the article.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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