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MEDICINAL PLANTS FOR LIVER DISORDERS IN EASTERN MEDICINE: PHARMACOGNOSTIC AND PHARMACOLOGICAL PERSPECTIVES

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Abstract

Medicinal plants and naturally derived compounds have played an important role in the historical development of therapeutics and continue to represent a valuable source of bioactive molecules for modern pharmacology and medicinal chemistry. The scientific heritage of Abu Bakr al-Razi, Abu Ali ibn Sina (Avicenna), and Abu Rayhan al-Biruni contains extensive information on medicinal substances historically used in disorders associated with the liver and digestive system. The aim of this narrative review was to reassess selected liver-related therapeutic concepts described in their works from the contemporary perspectives of pharmacognosy, pharmacology, medicinal and pharmaceutical chemistry, toxicology, and biochemistry. Historical medical and pharmaceutical sources were considered together with contemporary scientific publications addressing hepatoprotective medicinal plants, phytochemical constituents, molecular mechanisms of hepatic injury, herbal safety, and pharmaceutical standardization. Modern analysis of Avicenna's *Canon of Medicine* has identified 163 plant species belonging to 73 botanical families that were historically associated with liver and spleen disorders, together with approximately 30 non-herbal remedies. Al-Biruni's *Kitab al-Saydana fi al-Tibb* contributed to the systematic identification, description, origin, quality assessment, and substitution of medicinal substances, whereas al-Razi emphasized clinical observation and therapeutic experience. Contemporary evidence indicates that plant-derived flavonoids, phenolic compounds, alkaloids, terpenoids, glycosides, saponins, and related metabolites may modulate oxidative stress, inflammatory signaling, lipid metabolism, mitochondrial dysfunction, cell death, and fibrogenic pathways involved in liver injury. However, most evidence remains preclinical, and historical use cannot be regarded as proof of modern clinical efficacy or safety. The scientific translation of historical materia medica therefore requires botanical authentication, phytochemical profiling, pharmacological and biochemical validation, toxicological assessment, pharmaceutical standardization, pharmacokinetic evaluation, and well-designed clinical studies.

Keywords: Avicenna; al-Razi; al-Biruni; medicinal plants; pharmacognosy; natural products; hepatoprotection; pharmacology; medicinal chemistry; toxicology; liver disease.

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Introduction

The liver is one of the principal metabolic organs of the human body and participates in carbohydrate, lipid, and protein metabolism, bile production, nutrient storage, detoxification, and the biotransformation of endogenous and exogenous substances. Disturbances in hepatic function may therefore have systemic consequences. Oxidative stress, chronic inflammation, mitochondrial dysfunction, altered lipid metabolism, endoplasmic reticulum stress, cell death, and fibrogenic signaling are among the mechanisms involved in the development and progression of liver injury [1–4].

Natural products continue to attract considerable scientific attention because medicinal plants contain structurally diverse secondary metabolites, including flavonoids, phenolic acids, terpenoids, alkaloids, saponins, glycosides, sterols, and other biologically active compounds. Many of these substances have demonstrated antioxidant, anti-inflammatory, metabolic, cytoprotective, or antifibrotic activity in experimental systems [1,2,5]. Natural compounds may therefore serve not only as direct therapeutic candidates but also as chemical lead structures for the development of new pharmaceutical agents.

The use of natural substances for disorders associated with the liver long predates modern pharmacology. Greek, Persian, Indian, Central Asian, and Islamic medical traditions accumulated extensive empirical knowledge concerning diet, medicinal plants, mineral substances, natural preparations, and clinical conditions interpreted as disorders of hepatic and digestive function.

Among the major representatives of medieval Eastern medicine were Abu Bakr al-Razi, Abu Ali ibn Sina, widely known as Avicenna, and Abu Rayhan al-Biruni. Their works reflect three complementary dimensions of the development of medicine and pharmacy. Al-Razi gave substantial importance to observation of the patient and the response to treatment. Avicenna integrated theoretical concepts, clinical observations, dietetics, simple medicinal substances, compound preparations, and therapeutic principles into a systematic medical framework. Al-Biruni contributed particularly to the classification, identification, terminology, origin, properties, quality, and substitution of medicinal substances. The importance of these historical sources should, however, be interpreted cautiously. Medieval concepts of physiology and disease cannot be directly equated with contemporary biomedical definitions. A historical description of a medicinal plant as useful for a liver-related disorder does not prove its pharmacological efficacy, define its active constituent, establish a clinically appropriate dose, or confirm its safety. The modern scientific value of historical materia medica lies primarily in its potential to provide research hypotheses and candidate natural products for further pharmacognostic, biochemical, pharmacological, toxicological, and pharmaceutical investigation. The aim of the present review was to reassess selected liver-related medicinal concepts described in the scientific heritage of al-Razi, Avicenna, and al-Biruni and to evaluate their relevance to contemporary pharmacognosy, pharmacology, medicinal chemistry, pharmaceutical chemistry, toxicology, biochemistry, and natural-product drug discovery.

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Materials and Methods

The present study was designed as a narrative historical-pharmacological review. It integrated information derived from historical medical and pharmaceutical traditions associated with al-Razi, Avicenna, and al-Biruni with contemporary scientific evidence concerning medicinal plants and natural compounds studied in relation to liver disorders.

The historical component focused primarily on descriptions of medicinal substances, therapeutic approaches, dietetic recommendations, clinical observation, and pharmaceutical classification associated with *Al-Hawi fi al-Tibb*, Avicenna's *Al-Qanun fi al-Tibb* (*The Canon of Medicine*), and al-Biruni's *Kitab al-Saydana fi al-Tibb*.

Contemporary publications included in the reference list were analyzed to assess the relationship between historical knowledge and current pharmaceutical science. Particular attention was paid to studies and reviews addressing hepatoprotective medicinal plants, natural compounds, phytochemical classes, mechanisms of hepatic injury, pharmacognostic identification, analytical quality control, metabolic liver disease, silymarin, herbal toxicity, and herb-induced liver injury.

The extracted information was analyzed according to several interconnected domains: historical therapeutic observation, botanical identification, pharmacognostic characterization, phytochemical composition, potential medicinal-chemistry relevance, biochemical and pharmacological mechanisms, toxicological safety, and pharmaceutical quality control.

Historical therapeutic reports were not interpreted as evidence of modern clinical efficacy. Instead, they were considered as sources of potential candidates for scientific investigation. A translational framework was applied in which historical documentation represents the initial stage, followed by botanical authentication, pharmacognostic evaluation, phytochemical characterization, biological screening, pharmacological assessment, toxicological testing, pharmaceutical standardization, pharmacokinetic investigation, and eventual clinical validation.

Because the study was a narrative review based on published material and historical sources, no human participants, experimental animals, biological samples, or interventional procedures were involved.

Results

The analysis demonstrated that the scientific heritage of al-Razi, Avicenna, and al-Biruni contains substantial information relevant to the historical development of therapeutics and materia medica.

Al-Razi's contribution was strongly associated with clinical observation and therapeutic experience. His *Al-Hawi fi al-Tibb* integrated the views of earlier medical authorities with observations derived from medical practice. Particular attention was given to the patient's general condition, symptom development, disease course, and therapeutic response. From a modern perspective, this approach can be interpreted as an early form of empirical therapeutic reasoning. Although it differs fundamentally from controlled

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pharmacological studies, it reflects an attempt to relate treatment decisions to observable clinical outcomes.

Natural medicinal substances and dietary approaches were included among the therapeutic strategies used for disorders historically associated with the liver. However, the terminology and disease classifications of al-Razi's period do not correspond directly to modern concepts such as viral hepatitis, metabolic dysfunction-associated steatotic liver disease, cirrhosis, cholestatic disorders, or drug-induced liver injury. Therefore, the value of al-Razi's contribution is primarily historical and methodological rather than evidence for specific contemporary treatment strategies.

Avicenna's *Canon of Medicine* represents one of the most comprehensive medical and pharmaceutical works of the medieval period. It combined theoretical medicine, clinical observation, dietetics, individual medicinal substances, compound preparations, and disease-specific therapeutic recommendations.

Historical research has shown that Avicenna considered the liver an important organ within his physiological system and described disorders attributed to it according to several clinical characteristics [6]. From the perspective of modern pharmacognosy, the large number of natural products documented in the *Canon* is particularly significant.

A modern analysis by Ghobadi Pour and colleagues identified 163 plant species belonging to 73 botanical families that were historically associated with disorders of the liver and spleen. In addition, approximately 30 non-herbal remedies were identified [7]. This finding indicates that medieval Eastern medicine possessed a broad materia medica and that plant-derived treatments constituted an important component of therapeutic practice.

The historical diversity of medicinal plants described by Avicenna may be valuable for modern natural-product research. However, historical use alone does not establish contemporary pharmacological efficacy, therapeutic dose, active molecular constituent, pharmacokinetic behavior, or toxicological safety. The identified species should therefore be considered potential candidates for pharmacognostic and phytochemical prioritization rather than established medicines.

Al-Biruni made an important contribution to medieval pharmaceutical science through *Kitab al-Saydana fi al-Tibb*. His approach involved the systematic consideration of medicinal substances according to their names, origins, characteristics, qualities, and possible substitutes.

One of the important features of his work was the comparison of pharmaceutical terminology used across different linguistic and cultural traditions. This had practical significance because a medicinal material could be known by different names in Arabic, Persian, Greek, Indian, and other traditions. The same problem remains relevant to modern pharmacognosy. Closely related plant species may differ considerably in their phytochemical composition, while the geographical origin, plant part, harvesting period, processing method, storage conditions, and extraction procedure can substantially affect the chemical profile of a herbal preparation. Contemporary quality control therefore requires reliable taxonomic authentication, identification of the medicinal plant part,

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evaluation of purity, quantitative analysis of selected marker compounds, chemical fingerprinting, detection of adulteration, and assessment of batch-to-batch consistency [8]. In this context, al-Biruni's attention to the identity, origin, and quality of medicinal materials represents an important historical precursor of contemporary pharmacognostic principles.

The reviewed contemporary literature also demonstrates that medicinal plants contain several chemical classes potentially relevant to hepatoprotection. These include flavonoids, phenolic compounds, alkaloids, terpenoids, saponins, glycosides, anthocyanins, sterols, and related natural products [1,2,9]. From the medicinal-chemistry perspective, crude plant extracts should not be treated as single or chemically uniform substances. Modern research requires extraction, fractionation, chromatographic separation, chemical identification, and structural characterization of active or potentially active constituents. High-performance liquid chromatography, liquid chromatography coupled with mass spectrometry, gas chromatography–mass spectrometry, nuclear magnetic resonance spectroscopy, and related analytical technologies enable detailed investigation of natural-product composition. Once a pharmacologically relevant compound has been identified, structure–activity relationships can be investigated. Chemical optimization may then be used to improve potency, selectivity, solubility, stability, bioavailability, or safety. Thus, natural substances described in historical materia medica may potentially serve as chemical starting points in contemporary medicinal-chemistry programs. The reviewed evidence further indicates that liver injury is biologically heterogeneous. Important mechanisms include excessive formation of reactive oxygen species, oxidative stress, lipid peroxidation, mitochondrial dysfunction, inflammatory signaling, endoplasmic reticulum stress, apoptosis, ferroptosis, disturbances of lipid metabolism, and activation of fibrogenic pathways [3,4,11].

Several classes of natural compounds have demonstrated the ability to modify some of these mechanisms under experimental conditions [1–4,9]. Flavonoids are among the most extensively investigated phytochemical groups. Their reported experimental effects include modulation of oxidative stress, inflammatory signaling, lipid metabolism, fibrosis-related pathways, and cellular survival mechanisms [9].

Natural compounds have also been investigated for their potential effects on endoplasmic reticulum stress in metabolic liver disease [3] and on ferroptosis-associated pathways in hepatic injury [11]. Nevertheless, demonstration of a molecular or biochemical effect does not automatically establish clinical hepatoprotection. Pharmacological activity should be reproducible, concentration-dependent, mechanistically plausible, and achievable at biologically relevant exposure levels. The distinction between experimental effects and clinical efficacy is particularly well illustrated by silymarin. Silymarin is a complex of flavonolignans obtained from *Silybum marianum* and is one of the most extensively investigated plant-derived preparations in chronic liver disease. Reported mechanisms include antioxidant, anti-inflammatory, antifibrotic, membrane-stabilizing, and cytoprotective effects [13]. Meta-analyses have described reductions in aminotransferase concentrations in some patients with fatty liver disease treated with silymarin [14,15]. However, variability in study design, bioavailability, dose, preparation characteristics, and clinical outcomes limits definitive conclusions regarding its therapeutic

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magnitude. These findings demonstrate that biochemical improvement, experimental pharmacological activity, and clinically meaningful therapeutic benefit represent different levels of evidence and should not be considered interchangeable. Natural compounds have also received substantial attention in metabolic liver disorders. Experimental studies suggest that selected phytochemicals may influence hepatic lipid synthesis, fatty-acid oxidation, insulin-related signaling, oxidative stress, inflammatory pathways, and endoplasmic reticulum stress [3,16,17]. Natural compounds acting on peroxisome proliferator-activated receptor pathways have also been studied as potential modulators of metabolic liver injury [18]. These findings are relevant to natural-product drug discovery because they identify potential molecular targets and biologically active chemical structures. At the same time, the review revealed an important toxicological limitation. Natural origin does not guarantee safety. Herbal preparations may cause adverse effects because of intrinsic toxic constituents, excessive dose, reactive metabolites, contamination, adulteration, incorrect species identification, interactions with conventional medicines, or individual susceptibility. Herb-induced liver injury is a recognized clinical problem [19]. This is especially important when evaluating natural products proposed as hepatoprotective agents, because a plant historically considered beneficial for hepatic disorders may itself contain substances capable of causing hepatic injury.

Accordingly, potential candidates require evaluation of acute toxicity, repeated-dose toxicity, cytotoxicity, hepatotoxicity, genotoxicity where relevant, interactions with hepatic metabolic enzymes, herb–drug interactions, and the formation of potentially toxic metabolites. Another major finding concerns pharmaceutical standardization. The phytochemical composition of herbal products may vary according to plant genetics, geography, climate, soil conditions, harvesting season, plant part, storage, processing, extraction solvent, extraction temperature, duration, and formulation. Therefore, two preparations marketed or described under the same botanical name may not necessarily possess equivalent chemical or pharmacological properties. Modern evaluation requires chromatographic and spectroscopic fingerprints, quantitative marker analysis, chemical pattern recognition, multivariate analysis, and, where appropriate, genetic authentication [8]. These findings indicate that the transformation of historical medicinal knowledge into reproducible pharmaceutical research requires a sequence that moves from the historical description of a remedy to accurate identification and chemical standardization before any therapeutic conclusion can be considered scientifically valid.

Discussion

The results of the present review demonstrate that the pharmaceutical heritage of Eastern medicine can be meaningfully interpreted within the conceptual frameworks of modern pharmacognosy, pharmacology, medicinal chemistry, toxicology, and biochemistry, provided that historical observations are not confused with contemporary clinical evidence.

The works of al-Razi, Avicenna, and al-Biruni developed in a scientific environment substantially different from modern biomedical research. Nevertheless, several principles reflected in their work remain conceptually relevant.

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Al-Razi's emphasis on direct observation and treatment response reflects an early attempt to link therapeutic intervention with clinical outcome. Avicenna's systematic integration of medicinal substances with clinical and dietary concepts demonstrates a broad approach to materia medica. Al-Biruni's emphasis on the correct identification, origin, quality, and terminology of medicinal substances parallels several principles that are central to modern pharmacognosy and pharmaceutical quality control.

Among these contributions, Avicenna's extensive plant-based materia medica offers particularly important opportunities for natural-product research. The identification of 163 plant species historically associated with liver and spleen disorders does not mean that these plants are clinically effective hepatoprotective agents. However, it provides a historically derived pool of candidate species that may be prioritized for modern investigation [7].

The scientific evaluation of such candidates should begin with taxonomic and botanical authentication. Historical plant names may be ambiguous, and one traditional term may have referred to different species across different geographical regions or historical periods. Incorrect identification may produce misleading pharmacological results or even substantial toxicological risks.

Once the botanical identity has been established, the medicinal plant part and historical preparation method should also be investigated. Roots, leaves, flowers, seeds, bark, and fruits may contain substantially different phytochemical profiles. Similarly, decoctions, infusions, oils, powders, and solvent extracts may differ considerably in the concentration and composition of active constituents. These issues demonstrate why pharmacognostic standardization represents a critical bridge between historical knowledge and experimental pharmacology. The modern investigation of phytochemicals further requires a transition from crude medicinal material toward chemically characterized preparations. A crude extract may contain dozens or hundreds of constituents, and its apparent biological activity may result from a single dominant compound, multiple synergistic molecules, antagonistic interactions, or nonspecific toxicity. Bioactivity-guided fractionation and modern analytical chemistry can help identify the constituents responsible for reproducible pharmacological effects. Medicinal chemistry may then investigate structure–activity relationships and determine whether chemical modification can improve the pharmaceutical properties of promising natural molecules. At the biochemical level, the multi-target nature of many natural products is particularly relevant to liver disease, where oxidative stress, inflammation, metabolic dysregulation, mitochondrial dysfunction, cell death, and fibrosis interact in complex pathways. However, the ability of a natural compound to influence one or several molecular pathways should not automatically be interpreted as therapeutic efficacy. A compound may show activity in vitro at concentrations that cannot be achieved safely in humans. Poor oral absorption, rapid metabolism, insufficient tissue distribution, or toxicity may prevent translation into clinical benefit. The silymarin literature clearly demonstrates this problem. Its flavonolignans have been associated with several potentially beneficial mechanisms, and clinical studies have reported some biochemical improvements [13–15]. Nevertheless, variability in formulations, bioavailability, outcome measures, and study design prevents a

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simplistic conclusion that all silymarin preparations provide predictable clinical benefit. The same methodological caution should be applied when evaluating historical remedies. Toxicological assessment is another central issue. Traditional use is sometimes interpreted as indirect evidence of safety, but contemporary toxicology demonstrates that natural products may produce clinically significant adverse effects. Herb-induced liver injury is particularly relevant because the liver is the principal organ responsible for the metabolism of many xenobiotics [19]. A substance proposed as a hepatoprotective remedy must therefore be investigated not only for potential benefit but also for direct and metabolite-mediated hepatotoxicity. Potential herb–drug interactions are equally important. Natural products may influence cytochrome P450 enzymes, transporters, or other pathways involved in the metabolism of conventional medicines. Such interactions can alter drug concentrations and increase the risk of treatment failure or toxicity.

These considerations support a stepwise framework for transforming historical pharmaceutical knowledge into modern scientific evidence:

historical documentation → botanical authentication → pharmacognostic characterization → phytochemical profiling → bioactivity-guided fractionation → identification of active constituents → mechanistic biochemical and pharmacological investigation → toxicological evaluation → pharmacokinetic assessment → pharmaceutical standardization → clinical validation.

This framework avoids two methodological extremes. The first is the uncritical acceptance of historical therapies as clinically validated treatments. The second is the rejection of traditional knowledge without scientific investigation.

A scientifically balanced approach recognizes historical materia medica as a valuable repository of empirical observations while requiring modern experimental and clinical evidence before therapeutic claims can be made. The present review also has several limitations. First, it is a narrative rather than a systematic review or meta-analysis. Second, medieval concepts of disease do not directly correspond to current diagnostic categories. Third, identification of some historical botanical materials may remain uncertain because of changes in terminology and geographical variation. Fourth, historical dosage and preparation methods cannot always be reconstructed accurately. Fifth, much of the contemporary evidence concerning natural hepatoprotective substances remains preclinical. Finally, experimental activity may not translate into clinical efficacy because of poor bioavailability, insufficient exposure, toxicity, or differences between experimental models and human disease.

Despite these limitations, the combined historical and contemporary evidence suggests that Eastern medical heritage can provide a productive starting point for interdisciplinary research in pharmacognosy and natural-product drug discovery.

Conclusion

The medical and pharmaceutical works of al-Razi, Avicenna, and al-Biruni represent an important stage in the historical development of therapeutics, materia medica, pharmacy, and the systematic study of natural substances.

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Al-Razi contributed to an observation-based therapeutic tradition in which the patient's condition and response to treatment were important components of medical reasoning. Avicenna integrated clinical knowledge, dietetics, simple medicines, and compound preparations into a broad medical system and documented a substantial number of natural remedies historically associated with liver and spleen disorders. Al-Biruni contributed significantly to the identification, terminology, origin, characterization, and quality assessment of medicinal substances. From a contemporary scientific perspective, the primary value of this heritage lies not in the direct transfer of historical treatments into modern clinical practice, but in the identification of potential medicinal plants, phytochemicals, and natural-product research hypotheses.

Modern evaluation of these substances requires reliable botanical authentication, pharmacognostic characterization, phytochemical profiling, medicinal-chemistry analysis, biochemical and pharmacological validation, toxicological assessment, pharmacokinetic evaluation, pharmaceutical standardization, and well-designed clinical studies.

Historical use should therefore be interpreted as a starting point rather than as proof of efficacy or safety.

The scientifically appropriate integration of Eastern medical heritage with modern pharmaceutical science consists of transforming historically accumulated observations into rigorously testable hypotheses. Such an approach may preserve the intellectual value of traditional medical knowledge while contributing to the contemporary search for new natural compounds, pharmacological targets, and potentially useful hepatoprotective agents.

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