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Posted Date: 10 April 2026

doi: 10.20944/preprints202604.0731.v1

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Article

Ethnopharmacological Analysis of an Azerbaijani Booklet: A Critical Appraisal of Four Therapeutic Practice

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Abstract

Objective: This study aims to conduct a comprehensive pharmacological analysis of a medical booklet identified in a personal library in Ganja, Azerbaijan. The text is written in Azerbaijani Cyrillic script, implying a mid-20th-century (Soviet-period) origin. The study specifically isolates, translates, and evaluates four distinct therapeutic claims found within the text: a *Peganum harmala* and grape molasses practice for psychiatric disorders; a *Lawsonia inermis* and sugar decoction for gangrene; a *Lens culinaris* regimen for pain; and a *Ficus carica* latex application for epistaxis. **Material and Methods:** The study employs a trans-disciplinary approach combining philological analysis of the source text with modern pharmacognosy, toxicology, and clinical simulation. The booklet's citations—including The Canon, Ghayat al-Bayan, and Nüsrət Əfəndi—were analyzed to establish the intellectual lineage of the text. The four identified practices were deconstructed into their phytochemical constituents. Efficacy and safety profiles were modeled based on current database analyses of active metabolites (e.g., harmine, lawsone, ficin, polyphenols) and their bioavailability when processed according to the specific instructions. **Results:** The analysis reveals that the rue and doshab practice for mental illness utilizes an acid-base extraction method to maximize the bioavailability of beta-carboline alkaloids, functioning as a potent monoamine oxidase inhibitor. The fig stick method for epistaxis operates via enzymatic coagulation (factor X activation by ficin) and chemical cautery. The lentil practice for finger pain targets inflammatory pathways via polyphenolic inhibition of COX-2. Conversely, the henna-sugar practice for gangrene appears scientifically contraindicated and may carry a risk of oxidative hemolysis. **Conclusion:** The booklet represents a sophisticated synthesis of humoral (Galenic) and iatrochemical (Paracelsian) medicine. While certain practices demonstrate a rational pharmacological basis prefiguring modern drug delivery systems, others pose risks. This analysis underscores the necessity of rigorous toxicological screening before reviving traditional ethnomedical practices.

Keywords: Azerbaijan; traditional medicine; phytotherapy; *Peganum harmala*; *Lens culinaris*; *Ficus carica*

Introduction

The history of medicine in the South Caucasus is a tapestry woven from the threads of various medical traditions, serving as a geographical and intellectual bridge between the Persian, Ottoman, and Russian spheres of influence.[1] A traditional medical booklet preserved in a private collection in Gəncə (Ganja), Azerbaijan, written in Azerbaijani Cyrillic script, records a set of vernacular therapeutic practices transmitted through local medical knowledge. Ganja, historically a center of trade and culture, served as a conduit for the transmission of medical knowledge.[2]

The booklet in question is not merely a compilation of folk remedies; rather, the bibliography cited within its pages— Гаҟун (The Canon), Тəзкирə (Təzkirə), Кензү'с-Синһəтүл-Əбданијјə (Treasure of Body Health), Фирдəвс (Firdaws), Мəнафиу'н-Нас (Book of Benefits), Гəјəтү'л-Бəјан

(Ghayat al-Bayan), *Китабүл-Һәшәјиш* Дискоридес (Dioscorides), and Нүсрәт Әфәнди (Nüsrət Əfəndi) — suggests a highly literate author or compiler.

The objective of this article is not merely to validate or debunk these claims but to understand the mechanism of action envisioned by the traditional healer and the actual pharmacokinetics involved.

Materials and Methods

This critical appraisal article isolates four distinct clinical practices described in the booklet, collectively spanning multiple medical disciplines, and subjects them to rigorous modern scientific scrutiny:

1. Neuropsychiatry: A practice for treating “madness” and spiritual/mental illness using *Peganum harmala* (Syrian rue) seeds boiled with doshab (grape molasses).
2. Infectious Disease/Surgery: A treatment for gangrene using a decoction of *Lawsonia inermis* (henna) and sugar.
3. Orthopedics/Rheumatology: A 40-day regimen of *Lens culinaris* (lentil) consumed with its husk for chronic finger and extremity pain.
4. Emergency Medicine: A method for arresting epistaxis using a peeled *Ficus carica* (fig) stick.

Each of the four identified therapeutic practices was evaluated for pharmacological plausibility and potential risks. The analysis focused on identifying the principal bioactive constituents associated with the specified plant materials, including alkaloids, polyphenols, glycosides, and enzymatic components, as reported in the scientific literature.

Particular attention was given to the preparation methods described in the booklet—such as boiling, concentration with sugars, or direct mechanical application—and their expected impact on the extraction, solubility, and bioavailability of these constituents. Based on established pharmacological knowledge, the interaction of the identified compounds with relevant human physiological pathways was examined in order to assess the intended therapeutic rationale.

Finally, each practice was evaluated with respect to known safety profiles, dose-related risks, and documented adverse effects, allowing for a critical appraisal of both potential benefits and toxicological concerns in a contemporary biomedical context.

Results

Practice I: The Neuro-Psychiatric “Rue and Doshab” Regimen

The first practice addresses “mental illnesses” and “madness” (delilik), recommending a decoction of *Peganum harmala* seeds and doshab (grape molasses). The manuscript specifies a dosage of approximately 3 grams of seeds boiled in water with 75 grams of doshab, to be consumed over a 7-day period.

Peganum harmala, known locally as “üzerlik,” holds a sacred status in Turkic folklore, primarily as an apotropaic agent against the evil eye (nazar).[3] It is ubiquitous in the steppe regions of Azerbaijan and Central Asia.[4] However, the booklet moves beyond the common ritualistic fumigation to systemic oral administration. The term “delilik,” as used in late 19th- to early 20th-century vernacular medical contexts, likely encompassed a broad spectrum of conditions ranging from severe mood disorders and psychotic states to seizure-related and neuropsychiatric disturbances.[5]

The seeds of *Peganum harmala* are among the richest known natural sources of β -carboline alkaloids.[6] The alkaloid profile most relevant to the described practice is dominated by harmine, a potent and reversible inhibitor of monoamine oxidase A, together with harmaline, its dihydro derivative with well-documented psychoactive properties.[7] In addition, tetrahydroharmine contributes a serotonergic component through its activity as a serotonin reuptake inhibitor,[8] collectively providing a coherent pharmacological basis for the central nervous system effects

historically attributed to *P. harmala*. These alkaloids constitute 2-7% of the seed's dry weight.[9,10] A 3-gram dose, therefore, contains approximately 60-210 mg of total alkaloids. This quantity exceeds levels generally considered sufficient to produce central nervous system effects in humans, indicating that the preparation falls within a pharmacologically active range.[8]

The genius of this specific practice lies in the solvent. Doshab is a concentrated grape molasses produced by boiling down grape must. While it serves as a sweetener to mask the intensely bitter taste of the alkaloids,[11] its pharmacological role is far more critical. Doshab is an acidic medium, rich in tartaric and malic acids.[12] Beta-carboline alkaloids in their natural plant state often exist as free bases or bound to lignocellulosic material.[13] Free base alkaloids generally have poor water solubility. The chemical reaction occurring during the boiling process is an acid-base extraction. By boiling the seeds in this acidic, hypertonic solution, the practice effectively converts the lipophilic free bases into highly water-soluble salts (e.g., harmine tartrate).[14] This process significantly increases the bioavailability of the alkaloids compared to a simple aqueous tea. Furthermore, the high sugar content of the doshab creates a hypertonic environment that facilitates cell lysis of the seed coat, maximizing extraction efficiency.

The proposed mechanism of action of this “madness cure” can be retrospectively linked to the inhibition of monoamine oxidase A (MAO-A). Harmine and harmaline are well-characterized reversible MAO-A inhibitors, binding to the enzyme responsible for the degradation of monoamine neurotransmitters, including serotonin, norepinephrine, and dopamine.[15] By limiting monoamine catabolism, such inhibition would be expected to increase synaptic monoaminergic availability. Within the historical clinical spectrum subsumed under the term “madness” —encompassing melancholic withdrawal, psychomotor retardation, catatonic stupor, and lethargic states— an acute enhancement of monoaminergic signalling could plausibly manifest as behavioural activation, improved affective responsiveness, and increased motor engagement. In this context, the apparent “restoration of vitality” may have been interpreted as a therapeutic reversal of madness. The dopaminergic component of this monoaminergic surge, in particular, offers a mechanistic rationale for the reported use of the preparation in states characterized by profound lethargy or psychomotor inhibition. Additionally, recent studies indicate that harmine upregulates brain-derived neurotrophic factor, suggesting a potential neuroprotective and neuroplastic role that extends beyond immediate symptom relief.[16] This could theoretically aid in the repair of neural circuits in chronic psychiatric conditions.

Despite its theoretical efficacy, this practice presents severe potential risks that justify its abandonment in modern unsupervised practice. Harmaline is psychoactive and can produce perceptual disturbances[17] in patients with schizophrenia-spectrum disorders or manic states, augmenting monoaminergic tone can plausibly worsen agitation and psychosis, turning the historical “fire-with-fire” logic into a predictable hazard. The interaction between MAOIs and tyramine-rich foods can cause hypertensive crises.[18] While the reversible nature of harmine makes it safer than older pharmaceutical MAOIs (like phenelzine), the high dose (3g of seeds) reduces this safety margin. Concomitant use with serotonergic antidepressants introduces a well-documented risk of serotonin syndrome, which can be life-threatening.[19] High doses of harmaline are tremorogenic, causing severe tremors and ataxia by affecting the inferior olive in the brainstem.[20] The practice's 7-day duration may increase the risk of cumulative neurotoxicity.

Practice II: The Gangrene Treatment with Henna and Sugar

The second claim involves a treatment for gangrene: boiling 100 grams of *Lawsonia inermis* (henna) with 200 grams of sugar in 1.5 liters of water, to be consumed orally. This recommendation is particularly startling given that henna is almost exclusively used topically in modern and traditional herbalism.

The primary bioactive component of henna (*Lawsonia inermis*) leaves is lawsone (2-hydroxy-1,4-naphthoquinone), which is typically present at concentrations of approximately 1–2% in dried leaf material.[21] While the booklet describes preparation of a decoction using relatively large

amounts of plant material, it explicitly indicates that the resulting liquid was intended to be consumed in small quantities rather than as a single bolus. Nevertheless, under such preparation conditions, boiling facilitates hydrolysis of hennoside glycosides, releasing free lawsone (the aglycone) and increasing its solubility in the aqueous phase.[22] Heat-accelerated hydrolysis therefore has the potential to increase the proportion of bioavailable lawsone in the final preparation.

The inclusion of sucrose in the preparation warrants particular consideration. Although the quantity of sugar added reflects traditional practices aimed at improving palatability and tolerability, its use in the context of gangrene—most commonly associated with diabetes mellitus or peripheral vascular disease—raises physiological concerns.[23] Even moderate increases in systemic glucose availability may impair neutrophil chemotaxis and phagocytosis, potentially compromising host defense mechanisms in infected ischemic tissue and favoring microbial proliferation.[24,25] From a toxicological perspective, the principal concern relates to lawsone itself. As a naphthoquinone, lawsone can undergo redox cycling in vivo, generating reactive oxygen species through semiquinone intermediates.[26] In individuals with glucose-6-phosphate dehydrogenase deficiency—prevalent in Mediterranean and Caucasian populations—reduced glutathione reserves limit the capacity of erythrocytes to neutralize oxidative stress.[27] Under such conditions, exposure to naphthoquinones may precipitate oxidative hemolysis, with secondary risks of hemoglobinuria and acute kidney injury. Cases of hemolytic anemia and renal failure following ingestion of henna preparations have been reported, underscoring the narrow margin between traditional use and toxic exposure.[28,29]

The inclusion of this practice in the booklet can be understood in light of contemporary medical reasoning rather than an appreciation of its toxicological risks. Lawsone exhibits documented antibacterial activity in vitro, including activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa*. [30,31] It is therefore plausible that practitioners extrapolated these local antimicrobial effects to a broader systemic action, interpreting the preparation as a means of “cleansing” the blood of putrefactive elements within a humoral framework. In addition, the practice likely functioned as a therapeutic measure of last resort in cases with an otherwise fatal prognosis. Under such circumstances, treatment outcomes were subject to survival bias: deaths were attributed to the severity of the gangrene itself, whereas rare survivals were retrospectively credited to the remedy.

Practice III: The “40-Day Lentil” Cure for Finger Pain

The third claim describes a dietary regimen for chronic pain affecting the fingers and extremities, consisting of the daily ingestion of a single husked lentil (*Lens culinaris*) over a period of forty days. The text attributes this practice to a “Təzkirə,” a term commonly used to denote a general medical compendium rather than a specifically identifiable work.

From a phytochemical perspective, the seed coat of *Lens culinaris* contains a substantial proportion of the seed’s total bioactive compounds, particularly condensed tannins and flavonoids such as catechin and epicatechin.[32] As the primary protective barrier of the seed against environmental stressors, including pathogens and ultraviolet radiation, the husk is naturally enriched in defensive secondary metabolites. Many of these polyphenolic compounds have been shown to modulate inflammatory pathways through inhibition of cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, providing a plausible anti-inflammatory rationale for their traditional use in chronic pain conditions.[33–35]

The instruction to ingest the lentil husk whole further suggests an implicit slow-release mechanism: the indigestible fiber matrix may protect polyphenols during upper gastrointestinal transit, allowing their subsequent transformation by gut microbiota into smaller, bioavailable metabolites with anti-inflammatory activity.[36,37] Finally, the prescribed forty-day duration resonates with recurrent temporal frameworks in Galenic and Islamic medical traditions, often associated with humoral adjustment.[38] While this timeframe should not be interpreted as a precise pharmacokinetic requirement, it is consistent with the prolonged dietary exposure typically required to influence chronic inflammatory processes.

In contrast to the henna- or rue-based practices, this regimen appears to carry a comparatively low toxicological burden. Lentil husks are not associated with intrinsic toxicity under normal dietary conditions, aside from potential contamination concerns. The prescribed intake of a single husk per day represents a pharmacologically minimal exposure, suggesting that any observed benefit is unlikely to arise from direct high-dose biochemical effects. Instead, the practice may plausibly operate through nonspecific mechanisms, such as low-level dietary modulation or hormetic responses, whereby mild and repeated exposure to bioactive compounds elicits adaptive physiological effects.

Practice IV: The “Fig Stick” for Epistaxis

The final practice describes a method for stopping nosebleeds: peeling the bark of a *Ficus carica* (fig) twig and inserting it into the nasal cavity. The booklet explicitly attributes this method to Ibn al-Baytar, the great Andalusian botanist.[39]

This practice is notable in that it combines a mechanical intervention with the application of a biologically active plant material. The use of a stick functions primarily as a mechanical tamponade, applying localized pressure to the anterior nasal septum, particularly the region of Kiesselbach’s plexus, which represents the most common source of anterior epistaxis.[40] Equally significant is the instruction to peel the stick prior to use. Species of the genus *Ficus* possess a well-developed laticifer system, consisting of canals that rapidly exude latex when the bark is disrupted.[41] By peeling the stem, the practitioner effectively creates an applicator coated with fresh plant latex, thereby combining mechanical pressure with direct contact of latex-derived constituents at the bleeding site.

Fig latex is a rich source of ficin (or ficain), a cysteine endopeptidase enzyme.[42] Ficin has powerful effects on the coagulation cascade. Research indicates that ficin can activate coagulation factor X, a pivotal protein in the blood clotting cascade.[43] Activated factor X (Xa) converts prothrombin to thrombin, which then converts fibrinogen to fibrin, forming the clot.[44] Plant latex proteases also exhibits thrombin-like activity, directly acting on fibrinogen to promote gelation and clotting, independent of the body’s own enzymatic rate-limiters.[45]

Beyond potential enzymatic effects on coagulation, fig latex exhibits pronounced biochemical reactivity at the tissue level. The latex of *Ficus* species is rich in proteolytic enzymes capable of degrading surface proteins upon direct contact with mucosal tissue. Such proteolytic activity may result in localized tissue injury, functionally resembling a mild chemical cauterization at the site of bleeding. This mechanism bears conceptual similarity to the controlled chemical cauterization achieved with silver nitrate sticks in otolaryngological practice, whereby superficial tissue destruction contributes to vessel sealing.[46] In addition, fig latex contains tannins with astringent properties, which promote protein precipitation and localized tissue contraction, thereby further supporting hemostasis through mechanical vessel constriction.[47]

Although this practice may achieve hemostasis, it does so in a relatively non-selective manner and is associated with safety concerns. The proteolytic activity of fig latex is not confined to the bleeding vessel and may extend to surrounding mucosal tissue, increasing the risk of localized necrosis. In addition, fig latex is a well-recognized allergen within the context of latex–fruit syndrome, and direct application to bleeding mucosa introduces a non-negligible risk of systemic hypersensitivity reactions.[48] Finally, fig latex contains psoralens (furocoumarins), compounds capable of inducing phototoxic reactions;[49] accidental spread of latex onto perinasal or labial skin followed by sunlight exposure may result in phytophotodermatitis characterized by erythema and blistering.

Discussion

The analysis of the four therapeutic practices presented in the Ganja booklet reveals a heterogeneous body of medical knowledge rather than a unified theoretical system. Classical dietary and humoral concepts coexist with later procedural and extractive approaches, reflecting the layered transmission of medical traditions within vernacular practice. Rather than representing a linear

transition from “ancient” to “modern” medicine, the booklet illustrates how older authorities, post-classical texts, and local experience were selectively combined according to perceived practical utility.

Within this context, the reference recorded as Ghayat al-Bayan plausibly points to the continued circulation of post-classical Ottoman medical literature associated with figures such as Ibn Sallum, whose works incorporated elements of early iatrochemical thought alongside Galenic frameworks.[50–52] This influence may help explain the presence of preparation methods that go beyond simple herbal decoction, such as acid-mediated extraction in the rue–doshab practice, which treats plant material as a source of chemically active constituents rather than solely as a dietary or humoral agent.

By contrast, the lentil regimen reflects a markedly different conceptual approach, emphasizing prolonged dietary modulation through minimal and repeated exposure. Its forty-day duration resonates with established temporal frameworks in Galenic and Islamic medicine, wherein gradual adjustment of bodily balance was favored over acute intervention. From a contemporary perspective, this practice aligns more closely with nutritional and adaptive physiological mechanisms than with direct pharmacological action.

The fig-stick practice represents yet another therapeutic logic, one oriented toward immediate mechanical and chemical control of bleeding. Its reliance on localized tissue injury and pressure places it within a category of empirically derived emergency measures that prioritize rapid effect over safety margins. While potentially effective in arresting hemorrhage, its non-selective action underscores the risks inherent in such approaches when evaluated by modern clinical standards.

Taken together, these practices highlight the importance of contextual evaluation when engaging with historical or traditional medical sources. While the booklet constitutes a valuable cultural and intellectual artifact, its contents cannot be indiscriminately translated into contemporary practice. The henna-based treatment for gangrene, in particular, illustrates how historically understandable attempts to manage severe infection relied on agents now recognized as carrying significant toxicological risk. At the same time, other elements—such as the chemically informed extraction strategy seen in the rue preparation—invite more nuanced appreciation, suggesting a level of practical chemical reasoning that parallels, in limited ways, modern pharmaceutical principles.

Ultimately, the booklet exemplifies both the ingenuity and the limitations of vernacular medical knowledge. Its careful study offers insight not only into historical therapeutic reasoning but also into the methodological caution required when interpreting traditional remedies through a modern biomedical lens.

Conclusion

This analysis positions the Ganja medical booklet as a vernacular compilation reflecting layered medical traditions, practical experience, and local adaptation rather than a unified theoretical system. The four practices examined display substantial heterogeneity in plausibility and risk: the lentil regimen aligns with low-intensity dietary modulation, the rue-based preparation reflects chemically informed plant processing, the fig-stick application represents a pragmatically motivated but non-selective emergency measure, and the henna-based treatment for gangrene illustrates the toxicological limitations of historical approaches to systemic infection. Collectively, these findings demonstrate that such sources can yield meaningful insight into empirically grounded therapeutic reasoning, provided their claims are interpreted through critical biomedical evaluation rather than adopted uncritically into contemporary practice.

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