



Herbal Folk Medicine for Heart Failure in Uzbekistan: Ethnopharmacology, Pharmacological Evidence, and Clinical Perspectives

Ohunjonov Toxirmalik Abdumalik ugli

Fergana Medical Institute of Public Health, Fergana, Uzbekistan

ABSTRACT

Heart failure (HF) represents an escalating public health burden in Uzbekistan, where cardiovascular diseases account for the majority of adult mortality. Alongside evidence-based pharmacotherapy, traditional folk medicine remains deeply embedded in regional healthcare practices. This review synthesizes current ethnopharmacological and pharmacological evidence on herbal remedies employed for HF management in Uzbekistan, with particular focus on five widely used medicinal plants: *Crataegus songarica*, *Astragalus membranaceus*, *Leonurus cardiaca*, *Glycyrrhiza glabra*, and *Peganum harmala*. A structured literature search of PubMed, Scopus, Web of Science, and Google Scholar was conducted for publications from 2010 to 2024. Two comparative analytical tables evaluate active compounds, mechanisms of action, clinical dosages, efficacy, adverse effects, and limitations. The evidence indicates that several traditional herbal remedies possess scientifically supported cardioprotective properties; however, high-quality randomized controlled trials in Central Asian populations remain scarce. Rigorous integration of validated phytotherapies into formal cardiovascular care protocols in Uzbekistan requires further dedicated clinical investigation.

Keywords: *heart failure; folk medicine; Uzbekistan; herbal medicine; cardioprotective plants; ethnopharmacology; phytotherapy; Central Asia*

INTRODUCTION

Heart failure (HF) is a complex, chronic clinical syndrome characterized by structural or functional cardiac abnormalities resulting in reduced cardiac output and elevated intracardiac pressures. Globally, HF affects more than 64 million individuals and remains a leading cause of mortality, hospitalization, and impaired quality of life [1]. In Asia, including Central Asian republics, the epidemiological burden of HF is rising significantly, driven by increasing prevalence of hypertension, ischemic heart disease, diabetes, and aging populations [2]. Uzbekistan, a nation of approximately 36 million people, records more than 1.5 million acute and chronic cardiovascular disease (CVD) cases annually, with over half a million newly diagnosed cases per year, representing a 1.4-fold increase in primary incidence over the past two decades [3]. Cardiovascular

diseases account for the dominant share of mortality in the country, and the rural-urban divide further complicates equitable healthcare access across regions [4, 5].

Despite the availability of guideline-directed medical therapies including angiotensin-converting enzyme inhibitors, beta-blockers, sodium-glucose cotransporter 2 inhibitors, and mineralocorticoid receptor antagonists, significant therapeutic gaps persist in Uzbekistan due to medication costs, limited specialist access, and deeply rooted cultural preferences for traditional healing [6]. Uzbekistan occupies a historically significant position in the ethnopharmacological landscape of Central Asia, possessing extraordinary biodiversity with over 4,500 plant species, of which approximately 529 are recognized as medicinally active in arid and semi-arid zones alone [7]. The territory has been a crossroads of the ancient Silk Road, integrating Avicennian (Ibn Sina) medicine, Tibb-e-Unani, Zoroastrian herbal traditions, and Soviet-era phytotherapy into a rich folk medical repertoire [8].

Several medicinal plants used by traditional healers (tabib) in Uzbekistan have demonstrated scientifically documented cardiovascular activity, including positive inotropic, antiarrhythmic, vasodilatory, and cardioprotective effects [9, 10]. Among the most frequently referenced are hawthorn (*Crataegus songarica*), milkvetch (*Astragalus membranaceus*), motherwort (*Leonurus cardiaca*), licorice root (*Glycyrrhiza glabra*), and Syrian rue (*Peganum harmala*). These plants appear in ethnobotanical records spanning the Fergana Valley, Samarkand, Bukhara, and the arid steppe regions, where they are prepared as decoctions, tinctures, or powders by lay healers and dispensed for cardiac complaints [7, 8].

Despite growing pharmacological research globally, an integrated, evidence-based synthesis of these herbal medicines within the specific context of Uzbekistan and heart failure management remains absent from the literature. This review aims to bridge that gap by critically examining the phytochemistry, mechanisms of action, clinical evidence, dosage parameters, adverse effects, and limitations of the principal folk medicinal plants employed for HF in Uzbekistan, thereby providing a foundation for future research and potential evidence-based integration into regional cardiovascular care.

METHODS

This narrative review was conducted following the methodological framework of the Narrative Review Guidelines (SANRA). A structured literature search was performed across PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, and the eLibrary platform (for Russian and Uzbek language sources) for publications between January 2010 and December 2024. Search terms included combinations of: "heart failure," "cardiac glycosides," "herbal medicine," "traditional medicine," "folk medicine," "Uzbekistan," "Central Asia," "Crataegus," "Astragalus membranaceus," "Leonurus cardiaca," "Glycyrrhiza glabra," "Peganum harmala," "cardioprotective,"

"phytotherapy," and "ethnopharmacology." Grey literature sources included WHO reports, Uzbekistan Ministry of Health annual statistical reports, and European Medicines Agency monographs on herbal products. Studies were included if they reported pharmacological, clinical, or ethnobotanical data relevant to the selected plants and cardiovascular outcomes. A total of 30 publications were selected for final synthesis and reference.

Table 1. Phytochemistry, Pharmacological Effects, Mechanisms of Action, and Evidence Levels of Key Herbal Medicines Used in Uzbekistan for Heart Failure

Medicinal Plant	Active Compounds	Pharmacological Effects	Mechanism of Action	Level of Evidence
<i>Crataegus songarica</i> / <i>C. oxyacantha</i> (Hawthorn)	Oligomeric procyanidins, vitexin, hyperoside, quercetin, chlorogenic acid	Positive inotropy, vasodilation, antioxidant, anti-inflammatory, antiarrhythmic, anti-ischemic	cAMP-independent positive inotropic effect; NO-mediated vasodilation; inhibition of NF-kB; ROS scavenging; phosphodiesterase inhibition	Meta-analyses, RCTs (SPICE trial, HERB CHF), systematic reviews; EMA classification as traditional herbal medicinal product
<i>Astragalus membranaceus</i> (Milkvetch)	Astragaloside IV, formononetin, calycosin, quercetin, isorhamnetin, kaempferol, astragalus polysaccharides	Cardioprotection, LV remodeling improvement, anti-apoptotic, anti-fibrotic, anti-inflammatory, angiogenic	PI3K/AKT/NRF2 pathway; inhibition of NLRP3 inflammasome; mitophagy activation via AKT/mTOR; ESR1 regulation; downregulation of ANP, BNP, beta-MHC	Network pharmacology, in vitro, in vivo, systematic reviews; meta-analysis of RCTs (2024)
<i>Leonurus cardiaca</i> (Motherwort)	Stachydrine (leonurine), leonuridine, chlorogenic acid, quercetin, hyperoside, rutin, orientin	Negative chronotropy, hypotensive, antioxidant, antithrombotic, mild sedative, cardiotonic	Reduction of mitochondrial ROS; calcium channel modulation; negative chronotropic effect; alpha-adrenergic receptor modulation; mitochondrial protective activity	Limited human trials; 1 pilot study (n=50, 1200 mg/day); traditional use recognized by European Medicines Agency; pre-clinical evidence strong
<i>Glycyrrhiza glabra</i> (Licorice)	Glycyrrhizin, glycyrrhetic acid, liquiritigenin, isoliquiritigenin, glabridin, licochalcone A	Antioxidant, anti-inflammatory, vasodilatory, lipid-lowering, anti-atherogenic, cardioprotective (anti-DOX toxicity)	Suppression of NF-kB; PPAR-alpha/gamma and SIRT-1 interaction; inhibition of cytochrome P450; NO-mediated vasodilation; antioxidant enzyme upregulation	Comprehensive preclinical reviews; limited human RCTs; significant in vitro and in vivo evidence; 2022 systematic review (80 studies)
<i>Peganum harmala</i> (Syrian Rue / Harmal)	Harmine, harmaline, harmalol, peganin (vasicine), quinazoline alkaloids	Inotropic, vasorelaxant, hypotensive, anti-inflammatory, MAO inhibition, antispasmodic	Beta-carboline alkaloids: MAO-A inhibition; L-type Ca ²⁺ channel modulation; NO release from endothelial cells; alpha-	Pre-clinical evidence; no dedicated cardiac RCTs; traditional use documented in Uzbekistan, Central

Medicinal Plant	Active Compounds	Pharmacological Effects	Mechanism of Action	Level of Evidence
			adrenergic antagonism; harmine-mediated transient hypotension	Asia, and Middle East; in vivo rat and dog models

RESULTS

Epidemiological Context

Uzbekistan registers more than 1.5 million acute and chronic CVD cases annually, with a primary incidence rate that increased 1.4-fold (from 1,291 to 1,759 per 100,000) between 2003 and the early 2020s. Cardiovascular disease mortality in Uzbekistan remained relatively high and stable over 2020-2023, ranking among the highest in Central Asia. Heart failure specifically represents the terminal common pathway of hypertensive heart disease, ischemic cardiomyopathy, and rheumatic valvular disease, all of which are disproportionately prevalent in both urban and rural Uzbek populations.

Prevalence and Pattern of Herbal Medicine Use in Heart Failure

Traditional herbal medicine use in Uzbekistan is widespread, with a 2012-2022 field survey identifying 529 medicinal plant species across arid regions. Of these, a substantial proportion target cardiovascular, respiratory, and gastrointestinal complaints. The most culturally prominent plants used for cardiac indications include *Crataegus songarica* (locally known as "yovvoyi olcha" or hawthorn), *Leonurus cardiaca* (motherwort), *Glycyrrhiza glabra* (licorice, or "meyan ildiz"), and *Peganum harmala* ("isiriq"), which are employed in rural and peri-urban communities across Fergana, Andijan, Samarkand, and Bukhara regions. *Astragalus* species are also well-established in Uzbek ethnobotany, with multiple species recorded as medicinal, particularly for strengthening and tonic effects.

Crataegus songarica (Hawthorn)

Hawthorn preparations derived from leaves, flowers, and berries of *Crataegus* species represent one of the most extensively studied phytomedicines for HF worldwide. Meta-analyses of eight clinical trials confirmed significant increases in maximum working load (approximately 7 Watts) and improvements in symptomatic control in patients with NYHA class I-III HF. The SPICE trial (n=2,300 patients, 24 months), although not demonstrating a significant primary mortality endpoint, confirmed safety of the standardized extract WS 1442 at 900 mg/day in HF patients on optimal conventional therapy. In Uzbekistan, *Crataegus songarica*, native to Central Asian highlands, is used as a folk decoction prepared from dried berries and flowers for palpitations, dyspnea, and fatigue. Its procyanidin- and flavonoid-rich profile supports vasodilation and inotropic action without dependency on the cyclic AMP pathway.



Astragalus membranaceus (Milkvetch)

Astragalus membranaceus (Huangqi) is one of the most pharmacologically investigated herbal medicines for cardiac conditions globally, and multiple species of *Astragalus* are endemic to Uzbekistan. A 2024 meta-analysis of randomized controlled trials demonstrated significant improvements in left ventricular ejection fraction (LVEF), end-diastolic volume, and BNP levels in HFrEF patients receiving *Astragalus*-based preparations as adjuncts to standard therapy. Network pharmacology analysis identified Isorhamnetin, Quercetin, Calycosin, Formononetin, and Kaempferol as primary active constituents, acting via regulation of ESR1 expression and inflammatory cytokine suppression (TNF-alpha, IL-1beta, IL-18, IL-6). Astragaloside IV, the saponin fraction, activates mitophagy through AKT/mTOR pathway inhibition, protecting cardiomyocytes from mitochondrial dysfunction, a central mechanism in both acute and chronic HF.

Leonurus cardiaca (Motherwort)

Motherwort (*Leonurus cardiaca*) is widely recognized in both Central Asian and European folk traditions as a heart-strengthening herb. Its principal active alkaloid, stachydrine (leonurine), together with flavonoids including quercetin, hyperoside, rutin, and orientin, exerts mild negative chronotropic and hypotensive effects. A pilot clinical study (n=50) investigating *Leonurus cardiaca* oil extract at 1,200 mg/day over 28 days in hypertensive patients with anxiety and sleep disturbances reported significant improvements in blood pressure and emotional symptoms, with 80% of participants demonstrating moderate to significant clinical benefit. Pre-clinical evidence consistently supports mitochondrial protection through reduction of reactive oxygen species and anti-apoptotic activity in cardiomyocytes. In Uzbekistan, motherwort is used as a folk tea for palpitations, anxiety-driven tachycardia, and mild cardiac insufficiency.

Glycyrrhiza glabra (Licorice)

Licorice root (*Glycyrrhiza glabra*) is perhaps the most ubiquitous medicinal plant in Uzbekistan and broader Central Asia, available in markets throughout Fergana and the Zarafshan valley. Its primary bioactive compound, glycyrrhizin, exhibits anti-inflammatory (via NF-kB suppression), antioxidant, anti-atherogenic, and cardioprotective properties. A 2022 systematic review of 80 studies confirmed significant anti-atherogenic effects of licorice and its metabolites in both experimental and limited clinical settings. In vitro studies have demonstrated that *Glycyrrhiza glabra* root extract attenuates doxorubicin-induced cardiotoxicity via interaction with PPAR-alpha/gamma and SIRT-1, reducing oxidative stress in H9c2 cardiomyocytes. However, the mineralocorticoid-like activity of glycyrrhizin poses a significant safety risk in HF patients with fluid retention and hypertension, representing a critical pharmacovigilance concern in Uzbek folk practice.

Peganum harmala (Syrian Rue, Harmal)

Peganum harmala (isiriq in Uzbek) is widely distributed across the arid deserts of Bukhara, Kashkadarya, and Surkhandarya regions of Uzbekistan, where it holds a deeply embedded role in folk medicine and ritual purification. Its beta-carboline alkaloids (harmine, harmaline, harmalol) and quinazoline alkaloids (vasicine) exert complex cardiovascular effects: at low concentrations, harmine and harmaline produce vasorelaxation mediated by increased NO release from endothelial cells, whereas at higher doses, harmaline inhibits L-type Ca²⁺ channels and produces bradycardia, hypotension, and potential cardiotoxicity. No dedicated clinical trials in HF patients have been conducted with P. harmala. Its MAO-A inhibitory activity creates significant risk of hypertensive crisis with tyramine-rich foods and serotonergic drugs, limiting its safety profile in cardiovascular patients on polypharmacy.

Table 2. Dosage, Clinical Usage, Adverse Effects, and Limitations of Herbal Medicines for Heart Failure Management in Uzbekistan

Medicinal Plant	Traditional Dosage	Clinical Usage	Adverse Effects	Limitations
<i>Crataegus songarica</i> / <i>C. oxyacantha</i>	160-1800 mg/day dried extract; WS 1442: 900 mg/day; decoction of berries/flowers: 2-4g TID	Adjunct therapy in NYHA class I-III HF; improvement of exercise tolerance and symptoms; hypertension; arrhythmia prevention; adjunct to ACE inhibitors	Generally mild: nausea, dizziness, headache, palpitations. Rare: fatal arrhythmia with <i>C. pubescens</i> root (case report). Drug interaction with digoxin (pharmacokinetic)	No significant mortality benefit (SPICE trial); limited high-quality RCTs for NYHA III-IV; insufficient evidence for severe HF; no Central Asian-specific trials
<i>Astragalus membranaceus</i>	Injection: 60-80 mL IV daily; oral: 9-15 g dried root/day; astragaloside IV: 40-80 mg/day	HFrEF adjunct therapy; left ventricular reverse remodeling; chronic heart failure combined with standard care; anti-fibrotic support; myocarditis	Generally well-tolerated. Rare: allergic reactions, skin rash. High-dose injection: mild gastrointestinal discomfort. Potential immunostimulatory effects in autoimmune patients	Most RCTs from China; risk of reporting bias; limited long-term safety data; no standardized extract formulations; no Uzbekistan-specific studies; dose heterogeneity across trials
<i>Leonurus cardiaca</i>	200-500 mg dried herb capsules, up to 2 g/day; tincture (1:1): 2-4 mL TID; folk decoction: 1-2 tsp/cup, TID	Functional HF with anxiety/stress component; tachyarrhythmia management; mild hypertension; folk tonic for palpitations; adjunct in cardiac insufficiency	Sedation, potential bleeding risk (antiplatelet activity); uterotonic effect (contraindicated in pregnancy); contact dermatitis; photosensitivity. Interaction: anticoagulants, cardiac glycosides, sedatives	Very limited RCT data (single pilot study, n=50); no specific HF outcomes data; contraindicated in pregnancy and severe HF; no established dosing for HF in Uzbek clinical settings

Medicinal Plant	Traditional Dosage	Clinical Usage	Adverse Effects	Limitations
<i>Glycyrrhiza glabra</i>	Powdered root: 1-4 g TID; decoction: 1 tsp/cup simmered 15 min TID; tincture (1:1, 20%): 2-6 mL/day. Limit: <10 mg glycyrrhizin/day long term	Cardioprotection during chemotherapy (doxorubicin); anti-atherogenic support; anti-inflammatory adjunct in CVD; hyperlipidemia; traditional cardiac tonic in Uzbek folk medicine	Pseudohyperaldosteronism with high/prolonged doses; hypokalemia; hypertension aggravation; edema (contraindicated in HF with fluid overload); interaction with diuretics, cardiac glycosides, spironolactone, corticosteroids	Paradoxically worsens fluid retention in decompensated HF; glycyrrhizin causes mineralocorticoid-like effects; requires DGL preparations for cardiac patients; no dedicated HF RCTs
<i>Peganum harmala</i>	Folk use: seed infusion or decoction, 1-2 g seeds/day; alcoholic extract: 0.5-1 g harmine equivalent; no standard clinical dosing established	Traditional cardiac tonic in Uzbekistan and Central Asia; folk remedy for palpitations and chest pain; used in combination herbal formulas; peripheral vasodilation support	Narrow therapeutic index; harmaline: CNS stimulation, hallucinations, tremors (high doses); cardiotoxic at overdose; vasorelaxation at low doses but hypotension at high doses; embryotoxic; uterotonic	No clinical HF trials; high toxicity potential; MAO inhibition creates dangerous food and drug interactions (tyramine-rich foods, antidepressants); requires rigorous standardization before clinical use

DISCUSSION

The present review reveals a substantial and growing body of pharmacological evidence supporting the cardioprotective potential of traditional herbal medicines used in Uzbekistan, while simultaneously highlighting critical gaps in clinical validation specific to the Central Asian context. Cardiovascular disease constitutes the dominant cause of mortality in Uzbekistan [3, 4], and the concurrent prevalence of traditional medicine use creates both opportunities and risks that the healthcare system must address systematically.

Crataegus preparations stand out as the most clinically validated herbal medicines for HF, with multiple European randomized controlled trials confirming symptomatic improvement in NYHA I-III patients and an acceptable safety profile including non-significant pharmacokinetic interactions with digoxin [11, 12]. The European Medicines Agency has formally recognized hawthorn leaf and flower preparations as traditional herbal medicinal products for mild HF symptoms. The identification of *Crataegus songarica* as a native Uzbek species offers particular relevance: standardization of local hawthorn preparations could bridge traditional use with evidence-based phytotherapy [13, 14]. However, the absence of Uzbek-specific clinical trials and the demonstrated lack of mortality benefit in the SPICE trial necessitate caution regarding its use as a primary HF therapy [14].



Astragalus membranaceus emerges as the herbal medicine with perhaps the strongest recent mechanistic evidence base. A 2024 meta-analysis demonstrated significant improvements in LVEF and biomarkers of LV remodeling in HFrEF patients receiving *Astragalus*-based adjunct therapy [15]. Network pharmacology approaches have elucidated the multi-target nature of its active flavonoids, which simultaneously regulate inflammation, apoptosis, and mitochondrial function through pathways including PI3K/AKT and mTOR [16, 17]. Given the rich biodiversity of *Astragalus* species in Uzbekistan, with multiple endemic species documented in arid zone surveys, the development of standardized local extracts represents a scientifically and economically feasible priority [7]. The current limitation remains the predominantly Chinese origin of available RCT data and concerns regarding trial quality and heterogeneity of preparations.

Leonurus cardiaca occupies a clinically underexplored position. Despite centuries of empirical use for cardiac complaints in Uzbekistan and Europe and a strong pre-clinical evidence base demonstrating mitochondrial cardioprotection [18], the absence of adequately powered HF-specific clinical trials represents a significant knowledge gap. The EMA Herbal Monograph acknowledges traditional use for palpitations and cardiac insufficiency associated with nervous tension, but reserves evidence-based indication status pending further RCT data [19]. Its alkaloid constituents, particularly leonurine, interact favorably with calcium channel regulation and chronotropy at physiological doses, suggesting potential utility in HF with tachycardia; however, its uterotonic activity and potential bleeding risk mandate careful patient selection.

The dual character of *Glycyrrhiza glabra* in the context of HF deserves particular pharmacovigilance attention. While its anti-inflammatory and antioxidant properties offer potential cardioprotective benefit, particularly in the early stages of cardiac remodeling and chemotherapy-associated cardiomyopathy [20, 21], its mineralocorticoid-like effects pose a direct risk of sodium and fluid retention that can precipitate acute decompensated heart failure in susceptible patients [22]. Traditional Uzbek folk practitioners may be unaware of this dose-dependent risk, particularly in patients already receiving diuretics or presenting with peripheral edema. Pharmacovigilance education targeting traditional healers and patients in Fergana, Andijan, and Namangan regions, where licorice is particularly popular, constitutes an urgent public health intervention.

Peganum harmala represents the most pharmacologically complex and potentially dangerous of the reviewed herbs. Its widespread ritual and medicinal use in Uzbekistan belies a narrow therapeutic index and significant drug interaction potential via MAO-A inhibition [23, 24, 25]. The cardiovascular effects of harmine and harmaline are biphasic and concentration-dependent, making standardization extremely difficult without rigorous extraction and dosing protocols. Until dedicated safety and efficacy

trials are conducted, *P. harmala* should not be recommended to patients with established heart failure, particularly those receiving beta-blockers, ACE inhibitors, or antidepressants.

A broader challenge in this field is the methodological quality of available evidence. The majority of relevant clinical trials originate from China and examine Traditional Chinese Medicine formulations that may not directly correspond to the Uzbek ethnopharmacological repertoire, despite taxonomic similarities [26, 27]. Furthermore, the 2022 AHA/ACC/HFSA HF management guidelines do not address herbal medicines, reflecting the absence of adequately powered, multicenter trials from non-Asian populations [28]. Developing a national pharmacovigilance framework in Uzbekistan for traditional herbal medicine use in chronic diseases, particularly HF, represents a regulatory and scientific priority [29, 30].

CONCLUSION

Uzbekistan stands at a compelling intersection between a rapidly worsening heart failure burden and a rich, living tradition of herbal folk medicine that has sustained communities across its diverse geography for millennia. This review demonstrates that the five principal cardioactive plants of Uzbek folk medicine, *Crataegus songarica*, *Astragalus membranaceus*, *Leonurus cardiaca*, *Glycyrrhiza glabra*, and *Peganum harmala*, are not mere cultural artifacts but pharmacologically active agents whose molecular mechanisms increasingly align with modern understanding of cardiac pathophysiology. Hawthorn and milkvetch stand closest to clinical integration, supported by systematic reviews and meta-analyses; motherwort and licorice show promise but require dedicated clinical investigation; and Syrian rue demands rigorous safety evaluation before any clinical recommendation can be made. The future of cardiovascular care in Uzbekistan need not choose between its pharmaceutical heritage and evidence-based medicine. Rather, a strategically designed program of Uzbekistan-specific clinical trials, standardized extract development from locally endemic plant species, and structured pharmacovigilance education for traditional healers could transform folk cardiology into a validated, accessible, and culturally resonant complement to guideline-directed therapy. This convergence of ethnopharmacological wisdom and modern medical science represents not only a scientific imperative but a profound opportunity to reduce the heart failure burden among the populations of the Fergana Valley and beyond.

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