

Herb–Drug Interactions in Traditional Cardiovascular Therapy: Pharmacokinetic Mechanisms and Safety Integration in Folk Medicine

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Abstract

Herbal cardiotonics occupy a prominent place in Central Asian traditional medicine, and their concurrent use with conventional cardiovascular pharmacotherapy is common among patients with heart failure and related conditions in Uzbekistan. This narrative review synthesizes current evidence on herb–drug interactions relevant to traditional cardiovascular remedies, with emphasis on pharmacokinetic mechanisms, cytochrome P450-mediated metabolism, and clinical safety considerations. Herbal constituents commonly used in Uzbek folk cardiotonic preparations can modulate hepatic enzyme activity, alter the bioavailability of anticoagulants, antiarrhythmics, and cardiac glycosides, and interact through both pharmacokinetic and pharmacodynamic pathways. Reported interactions range from clinically silent enzyme induction to potentiation of bleeding risk and altered drug clearance. Systematic clinical evaluation of these interactions remains limited despite widespread concurrent use. Structured safety monitoring, clinician awareness, and pharmacovigilance frameworks are needed to support the responsible integration of traditional cardiovascular remedies with modern pharmacotherapy in regional healthcare settings.

Keywords: herb-drug interactions; cytochrome P450; traditional medicine; cardiovascular pharmacology; pharmacokinetics; folk medicine; Uzbekistan; patient safety

Introduction

Traditional herbal cardiotonics remain deeply embedded in the clinical culture of Central Asia, where plant-derived preparations are frequently used alongside, rather than instead of, conventional cardiovascular pharmacotherapy [7], [8]. In Uzbekistan, endemic and cultivated species with documented cardiovascular activity are widely available and commonly self-administered by patients managing heart failure, hypertension, and related chronic conditions, often without disclosure to their treating physicians [1], [2], [9]. As the evidence base supporting the pharmacological activity of these preparations has expanded, so too has recognition that their concurrent use with prescription cardiovascular agents introduces a distinct and clinically relevant risk: herb–drug interaction [3].

Herb–drug interactions arise through two principal mechanisms: pharmacokinetic interactions, in which herbal constituents alter the absorption, distribution, metabolism, or excretion of a co-administered drug, and pharmacodynamic interactions, in which herbal and pharmaceutical agents act on overlapping physiological targets to produce additive, synergistic, or antagonistic effects [4]. Pharmacokinetic interactions mediated through the cytochrome P450 (CYP450) enzyme system are of particular concern in cardiovascular therapeutics, since many first-line agents — including warfarin, digoxin, statins, and several antiarrhythmics — possess narrow therapeutic indices and are highly sensitive to changes in hepatic metabolic clearance [5].

Despite growing recognition of these risks in the general herb–drug interaction literature, evidence specific to the herbal cardiotonics used in Uzbek and broader Central Asian folk medicine remains fragmented, and systematic clinical evaluation of their interaction potential with standard heart failure pharmacotherapy is limited [6]. This narrative review synthesizes current pharmacological and clinical evidence on herb–drug interactions relevant to traditional cardiovascular remedies, with particular attention to mechanisms of CYP450 modulation, documented interactions with

anticoagulants and cardiac glycosides, and the implications for safe clinical integration of herbal cardiotonics with conventional therapy in regional healthcare settings.

Methods

This was a narrative review of peer-reviewed literature addressing herb–drug interactions relevant to traditional cardiovascular and cardiotonic remedies, with particular attention to publications examining Central Asian and Uzbek folk medicine practices. Sources were identified through targeted review of pharmacology, ethnopharmacology, and clinical pharmacology literature published primarily between 2025 and 2026, supplemented by foundational studies characterizing the herbal species used in regional cardiovascular folk medicine. Material was organized thematically around three domains: pharmacokinetic mechanisms of herb–drug interaction, including CYP450 enzyme modulation; documented or plausible interactions between specific herbal cardiotonic constituents and conventional cardiovascular drug classes; and clinical safety frameworks for monitoring and mitigating interaction risk. Table 1 summarizes the organizing framework used to structure the review.

Review Domain	Focus	Representative Sources
Pharmacokinetic mechanisms	CYP450 induction/inhibition, absorption and clearance effects	Mechanistic and pharmacokinetic reviews
Drug-class-specific interactions	Anticoagulants, cardiac glycosides, antiarrhythmics, GI-active agents	Herb–drug interaction case and mechanism reports
Regional cardiotonic context	Uzbek and Central Asian herbal cardiotonic species and use patterns	Ethnopharmacology and folk medicine reviews
Clinical safety integration	Monitoring, disclosure, pharmacovigilance frameworks	Clinical safety and evidence-based practice evaluations

Table 1. Organizing framework for the review of herb–drug interactions in traditional cardiovascular therapy

Results

Pharmacokinetic interaction was the most consistently reported mechanism linking traditional cardiovascular herbal remedies to altered drug exposure. Constituents of several commonly used cardiotonic and adjunctive herbal preparations were reported to modulate CYP450 isoenzyme activity, most notably CYP3A4 and CYP2C9, both of which govern the metabolic clearance of warfarin, several statins, and calcium channel blockers [5]. Enzyme induction was associated with reduced plasma concentrations and diminished therapeutic effect of the co-administered drug, while enzyme inhibition was associated with elevated plasma concentrations and increased risk of toxicity, an effect of particular concern for narrow-therapeutic-index agents such as digoxin and warfarin [3], [4].

Interactions with anticoagulant therapy were among the most frequently documented and clinically significant. Herbal constituents with intrinsic antiplatelet or mild anticoagulant activity were reported to potentiate the effect of warfarin and other vitamin K antagonists, increasing bleeding risk when used concurrently without dose adjustment or enhanced monitoring [4], [6]. Interactions affecting cardiac glycoside therapy were similarly notable: several herbal preparations were reported to alter digoxin absorption or renal clearance, narrowing the margin between therapeutic and toxic serum concentrations [5].

Gastrointestinal-active herbal constituents, frequently co-administered with cardiovascular remedies in traditional practice for digestive complaints, were associated with additional interaction risk through altered gastric pH, intestinal transit time, and first-pass metabolism, each

of which can influence the oral bioavailability of concurrently administered cardiovascular drugs [4]. Ethnopharmacological surveys of Uzbek and Central Asian herbal cardi tonic use confirm that patients with heart failure and related cardiovascular conditions commonly combine multiple herbal preparations with prescribed pharmacotherapy, frequently without medical supervision or awareness of interaction potential, reflecting both the cultural embeddedness of traditional cardi tonic species such as *Crataegus turkestanica* and the limited integration of interaction screening into routine clinical practice [1], [2], [7], [8], [9]. Table 2 summarizes representative interaction mechanisms and their clinical implications for major cardiovascular drug classes.

Drug Class	Interaction Mechanism	Clinical Consequence	Risk Level
Anticoagulants (warfarin)	Additive antiplatelet/anticoagulant effect; CYP2C9 modulation	Increased bleeding risk, altered INR stability	High
Cardiac glycosides (digoxin)	Altered absorption and renal clearance	Narrowed therapeutic margin, toxicity risk	High
Statins / calcium channel blockers	CYP3A4 induction or inhibition	Reduced efficacy or increased toxicity	Moderate
Antiarrhythmics	Pharmacodynamic overlap, hepatic clearance changes	Altered drug exposure, arrhythmia risk	Moderate
GI-active adjuncts	Altered gastric pH and intestinal transit	Variable bioavailability of co-administered drugs	Low–Moderate

Table 2. Representative herb–drug interaction mechanisms and clinical implications by cardiovascular drug class

Discussion

The findings synthesized in this review indicate that herb–drug interaction is not a peripheral concern but a central safety consideration for the integration of traditional cardiovascular remedies with conventional pharmacotherapy. CYP450-mediated pharmacokinetic interaction emerges as the dominant mechanism of concern, consistent with broader pharmacological literature establishing hepatic enzyme modulation as the primary route through which herbal constituents alter drug exposure [3], [5]. The particular vulnerability of narrow-therapeutic-index cardiovascular agents — warfarin and digoxin foremost among them — means that even modest pharmacokinetic perturbation can translate into clinically meaningful bleeding or toxicity risk [4].

These interaction risks take on particular significance in the Central Asian clinical context, where herbal cardi tonics such as *Crataegus turkestanica* and related species are used not as occasional supplements but as culturally embedded components of cardiovascular self-care, frequently alongside prescribed heart failure therapy [1], [2], [8], [9]. The evidence reviewed here suggests that the same bioactive mechanisms responsible for the therapeutic promise of these preparations — modulation of vascular tone, calcium channel activity, and hepatic enzyme function — are frequently the mechanisms underlying their interaction potential, underscoring that pharmacological activity and interaction risk are two sides of the same mechanistic coin rather than independent concerns [7].

Clinical integration of herbal cardi tonics therefore requires more than an assessment of standalone efficacy; it requires systematic evaluation of interaction potential with each patient's existing pharmacotherapy regimen. Structured medication reconciliation that explicitly asks about herbal and traditional remedy use, clinician education regarding the interaction mechanisms most relevant to cardiovascular pharmacotherapy, and pharmacovigilance systems capable of capturing

herb–drug interaction events represent practical steps toward safer integration [6]. Formulation standardization also warrants attention, since inconsistent bioactive compound concentrations across traditional preparations complicate both efficacy assessment and interaction risk prediction [9].

Several limitations of the current evidence base should be acknowledged. Much of the interaction literature relevant to Central Asian herbal cardiotonics is extrapolated from mechanistic and pharmacokinetic studies of related plant constituents rather than direct clinical interaction trials conducted in regional populations. Prospective clinical studies specifically evaluating interaction outcomes in patients using both traditional cardiotonic remedies and guideline-directed heart failure therapy remain scarce. Future research prioritizing pharmacokinetic characterization in regional populations, structured pharmacovigilance data collection, and clinician-directed screening tools would substantially strengthen the evidence base supporting safe integration of traditional and conventional cardiovascular therapeutics.

Conclusion

Herb–drug interaction represents a clinically significant and insufficiently addressed dimension of traditional cardiovascular therapy in Central Asian healthcare settings. Pharmacokinetic mechanisms, particularly CYP450-mediated enzyme modulation, underlie the majority of documented interactions between herbal cardiotonic preparations and conventional cardiovascular drug classes, with anticoagulants and cardiac glycosides carrying the greatest risk of clinically meaningful consequence. As traditional herbal cardiotonics continue to be used widely alongside prescribed heart failure therapy in Uzbekistan and the broader region, structured safety monitoring, clinician awareness, and open patient–provider communication about herbal remedy use are essential to preserving the benefits of both therapeutic traditions while minimizing avoidable harm. Advancing the evidence base through targeted pharmacokinetic and pharmacovigilance research will be central to achieving this balance.

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