

ORIGINAL ARTICLE

Concurrent Use of Herbal Medicines and Prescription Drugs and Potential Herb-Drug Interactions: A Cross-Sectional Study

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ABSTRACT:

Background: Herbal medicine use is widespread amongst people with chronic conditions, and this could be a potential concern for herb–drug interactions. This study aimed to evaluate the prevalence of concurrent herbal medicine use and factors associated with possible interactions among adult patients who were on long-term pharmacotherapy. **Method:** This study included 220 adults attending outpatient departments at a tertiary care hospital and using prescribed medicines for ≥ 3 months. Data on chronic diseases, prescribed and herbal medicines, medication disclosure, information sources, self-medication, and adverse effects were collected through interviewer-administered questionnaires and medical records. Potential herb–drug interactions were identified using published evidence. Descriptive statistics and multivariable logistic regression were performed, with $p < 0.05$ considered statistically significant. **Results:** The mean age was 47.5 ± 13.2 years, and 58.2% were female. 96 (43.6%) of participants reported using herbs concurrently, and 28 (29.2%) disclosed that they used herbs to their physicians. 37 (38.5%) of herbal users were identified as having potential herb–drug interactions. The most frequently reported adverse effects were gastrointestinal symptoms 16 (16.7%), followed by altered glycaemic control 11 (11.5%). Independent predictors were use of three or more prescribed medicines (AOR=3.18, 95% CI: 1.45-6.98; $p=0.004$), physician unawareness (AOR=2.81, 95% CI: 1.18-6.69; $p=0.019$), age ≥ 60 years (AOR=2.39, 95% CI: 1.04-5.47; $p=0.041$), and self-medication (AOR=2.22, 95% CI: 1.01-4.91; $p=0.047$). **Conclusion:** Use of herbal medicine was widespread, often unacknowledged, and had potential interaction risks. Medication safety should be adopted through routine enquiry and pharmacist-supported medication review.

Keywords: Chronic Disease; Herb-Drug Interactions; Phytotherapy; Polypharmacy; Prescription Drugs; Self Medication

INTRODUCTION

People with chronic illnesses receiving long-term pharmaceutical treatment are increasingly using herbal medicines to supplement their treatment¹. Recent studies report a high prevalence among those who have chronic disease: pooled prevalence of 56.9% among people with chronic disease in Ethiopia, 51% in adults with diabetes worldwide, and 43% in adults with chronic kidney disease^{2,3}. Female gender, older age, longer disease duration, perceived safety, and sociocultural factors have been linked to use of herbal treatment⁴.

The co-occurrence of bioactive components in herbs and their potential to interact with therapeutic drugs during absorption, metabolism, transport, or elimination, or by additive pharmacological effect, is clinically relevant⁵. Drug interactions with cytochrome P450 enzymes and drug transporters can decrease effectiveness or cause more side effects⁶. Several issues, including changes in glycaemic control with antidiabetic drugs and increased bleeding with the use of ginkgo, ginger, cranberry, chamomile, or St John's wort, are of concern⁷. Older adults and older patients receiving polypharmacy, multiple herbal products, anticancer therapies, and/or narrow-therapeutic index drugs are at higher risk⁸. Poor communication is a limitation for clinical detection. Reviews have demonstrated that many users are not willing to report use of complementary medicine, which may affect the practice and treatment of clinicians⁹. Lack of knowledge about interactions or the perception that "natural" products are safe can further reduce awareness of interaction risks¹⁰. Multicenter outpatient evidence also suggests that concurrent use is associated with greater self-reported adverse effects, which also supports routine medication reconciliation¹¹.

At the same time, there are limited data available from hospital settings to describe use patterns, disclosure, and adverse effects and interactions between chronically treated adults. There is a need for local evidence to inform counselling and safer prescribing¹². The aim of this study was to establish the prevalence and the pattern of this concurrent use of herbal medicine with prescribed medicine in adults who have been on long-term pharmacotherapy treatment. It examined disclosure practices, sources of recommendations, and the self-reported adverse effects. It also determined factors linked with possible herb–drug interactions.

METHODOLOGY

A hospital-based cross-sectional observational study (August 2020-January 2021) was conducted to assess the pattern of herbal medicine use among adult patients ($n=220$) receiving prescribed medicines and to identify factors associated with documented potential herb–drug interactions

(MS018/2020). Patients with treatment for chronic medical problems were sampled consecutively. The sample size was calculated using OpenEpi Version 3.0.2 (Atlanta, GA, USA; RRID:SCR_021913) based on the single population proportion method. The formula $n = Z^2P(1-P)/e^2$ was applied, where n is the required sample size, Z is the standard normal deviate, P is anticipated prevalence, and e is the absolute precision. Using a prevalence of 38.5% for potential herb–drug interactions, a 95% confidence level, an absolute precision of 6.5%, and a design effect of 1.0. The calculated minimum sample size was approximately 215 participants, which was rounded to 220 participants to ensure an adequate sample size ¹³.

Participants were eligible if they were aged >18 years and were taking at least one prescription drug for at least 3 months. Patients who were unable to provide reliable information, had acute medical emergencies, or refused to participate were excluded from the study. Structured interviewer-administered questionnaires and medical records were used to collect data. Demographic data, primary chronic disease, number of prescribed medications, length of time on medication, use of herbal medicines before the investigation, commonly used herbal medicines, reasons for using herbs, where the person heard about the herbal medicine, disclosure of use of herbal medicine to health professionals, and the presence of self-reported adverse effects were documented. For this study, herbal medicines were defined as plant-derived products used for therapeutic, preventive, or health-promoting purposes, whether used alone or concurrently with prescribed medicines.

The presence of possible herb–drug interactions was identified by searching the herbal products reported in the participants' home medicine cabinets against the drugs reported that they were prescribed and published literature to see if there were any known interactions with the medication. Adverse effects, including gastrointestinal issues, glycaemic changes, dizziness, blood disorders, and allergic reactions, were reported. The number of prescribed medications used concurrently was defined as polypharmacy, defined as taking three or more.

All participants gave written informed consent. All the patient data were treated confidentially throughout the study, and all procedures were done following the principles of the Declaration of Helsinki ¹⁴. The Statistical Package for the Social Sciences (SPSS) Version 26.0 (Released 2021; IBM Corp., Armonk, NY, USA; RRID: SCR_016479). was used to enter and analyze the data. Continuous data were presented as mean ± SD, and categorical data were presented as frequencies with percentages. The Chi-square test or Fisher's exact test (as appropriate) was used to assess associations between participant characteristics and potential herb–drug interactions. A multivariable logistic regression model was performed, which included the variables that were statistically significant from the univariate analyses, to assess independent predictors. Odds ratios (ORs) were calculated with 95% confidence intervals (CI), and p-values <0.05 (two-tailed) were considered statistically significant. Given the cross-sectional design, these associations were not interpreted as causal relationships or temporal predictors.

RESULTS

A total of 220 adult patients taking long-term prescription drugs were included in this study. The mean age was 47.5 ± 13.2 years, and 128 (58.2%) were female. Overall, 96 (43.6%) of the participants reported using herbal medicines concurrently with prescribed medicines, and patients with diabetes and hypertension used the most herbs. The percentage of herbal users who reported current herbal medicine use to their physicians was 28 (29.2%). The gastrointestinal disturbances and changes in glycaemic control were the most commonly reported adverse effects related to the potential herb–drug interactions in 37 (38.5%) of those taking herbs. As shown in **Table I**, the most prevalent chronic conditions that needed continuous pharmacological treatment were diabetes mellitus 82 (37.3%) and hypertension 61 (27.7%).

Table I: Demographic and Clinical Characteristics of Participants (N=220)

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
18–39	58	26.4
40–59	104	47.3
≥60	58	26.4
Gender		
Male	92	41.8
Female	128	58.2
Primary Chronic Disease		
Diabetes mellitus	82	37.3
Hypertension	61	27.7
Cardiovascular disease	34	15.5
Arthritis	25	11.4
Other chronic diseases	18	8.1
Mean age (years)	47.5 ± 13.2	

Table II shows that 96 (43.6%) of the participants reported concurrent herbal medicine. Among users of herbal medicines, 68 (70.8%) had not discussed the use of the herb with their treating physicians, 71 (74.0%) had self-medicated, and 76 (79.2%) acquired the herbal medicines without a prescription. Parents' recommendation was cited most often as an information source, suggesting that parents' use of herbs is outside of supervision. Family/friends' recommendations were the most frequently reported source of information, indicating that herbal medicine use was commonly initiated outside formal healthcare supervision.

Table II: Pattern of Herbal Medicine Use Among Participants(N=96)

Variable	Frequency (n)	Percentage (%)
Concurrent herbal medicine use	96	43.6
Physician informed	28	29.2*
Physician not informed	68	70.8*
Self-medication with herbs	71	74.0*
Family/friends recommendation	49	51.0*
Social media/Internet recommendation	31	32.3*
Herbal products purchased without prescription	76	79.2*

*Percentages calculated among herbal medicine users (n=96)

The two most commonly used herbal products were ginger 28 (29.2%) and turmeric 24 (25.0%), mostly to treat digestive ailments and inflammatory disorders, as shown in **Table III**. Other commonly used herbs included garlic, fenugreek, and Nigella sativa for blood pressure, blood glucose control, and/or general health maintenance.

Table III: Frequently Used Herbal Medicines and Therapeutic Purposes (n=96)

Herbal Medicine	Users n (%)	Common Purpose
Ginger	28 (29.2)	Digestive complaints
Turmeric	24 (25.0)	Joint pain/inflammation
Garlic	18 (18.8)	Blood pressure/cholesterol
Fenugreek	14 (14.6)	Blood glucose control
Black seed (<i>Nigella sativa</i>)	12 (12.5)	General health/immune support

Thirty-eight percent 37 (38.5%) of herbal medicine users could have had herb–drug interactions. The most common gastrointestinal symptoms 16 (16.7%) with clinically relevant safety concerns were followed by altered glycemic control 11 (11.5%) and dizziness 8 (8.3%), increased bleeding tendency 5 (5.2%), and allergic reactions 3 (3.1%), as shown in **Table IV**. These adverse effects were reported by participants and were not clinically assessed for causality or specifically attributed to the identified potential herb–drug interactions.

Table IV: Potential Herb–Drug Interactions and Reported Adverse Effects(N=96)

Variable	Herbal Users (n=96)
Potential herb–drug interaction identified	37 (38.5%)
No interaction identified	59 (61.5%)
Reported Adverse Effects	
Gastrointestinal symptoms	16 (16.7%)
Altered glycemic control	11 (11.5%)
Dizziness	8 (8.3%)
Increased bleeding tendency	5 (5.2%)
Allergic reaction	3 (3.1%)

As shown in **Table V**, the potential interactions between herbs and drugs were significantly higher in older adults, self-medicating patients, and patients who were not aware of talking about herbal medicine with their doctor (all $p < 0.05$), but not in patients who took 3 or more drugs or patients with diabetes mellitus ($p > 0.05$).

Table V: Factors Associated with Potential Herb–Drug Interactions(N=96)

Variable	Interaction Present (n=37)	No Interaction (n=59)	p-value
Age ≥ 60 years	17 (45.9%)	13 (22.0%)	0.015
≥ 3 prescribed medications	24 (64.9%)	21 (35.6%)	0.005
Diabetes mellitus	19 (51.4%)	18 (30.5%)	0.039
Self-medication	32 (86.5%)	39 (66.1%)	0.026
Physician unaware of herbal use	31 (83.8%)	37 (62.7%)	0.031

Figure 1 presents independent predictors of potential herb–drug interactions based on multivariable logistic regression analysis. It presents adjusted ORs and 95% CIs for ≥ 3 prescribed medications, physician unawareness of herbal use, age ≥ 60 years, self-medication, and diabetes mellitus. Use of ≥ 3 prescribed medications showed the strongest association (AOR=3.18, 95% CI: 1.45–6.98, $p=0.004$), followed by physician unawareness of herbal use, age ≥ 60 years, and self-medication. Diabetes mellitus was not significantly associated with potential herb–drug interactions ($p=0.079$). The number of prescribed medications (three or more) was the strongest independent predictor of potential herb–drug interactions (AOR=3.18, 95% CI: 1.45–6.98, $p=0.004$). However, lack of knowledge regarding the use of herbal medicine by physicians, advanced age, and self-medication were also independently associated with increased risk of clinically significant drug–herb interactions, as shown in **Table VI**.

Table VI: Multivariable Logistic Regression of Predictors of Potential Herb–Drug Interactions

Predictor	Adjusted OR	95% CI	p-value
≥ 3 prescribed medications	3.18	1.45–6.98	0.004
Physician unaware of herbal use	2.81	1.18–6.69	0.019
Age ≥ 60 years	2.39	1.04–5.47	0.041
Self-medication	2.22	1.01–4.91	0.047
Diabetes mellitus	1.96	0.92–4.15	0.079

Overall, concurrent use of herbal and prescription medicines was common among the study population, while disclosure of herbal use to physicians was limited. Potential herb–drug interactions were identified in a substantial proportion of herbal medicine users, with polypharmacy, older age, physician unawareness, and self-medication showing independent associations. These findings provide a basis for examining the clinical and medication-related implications of concurrent use.

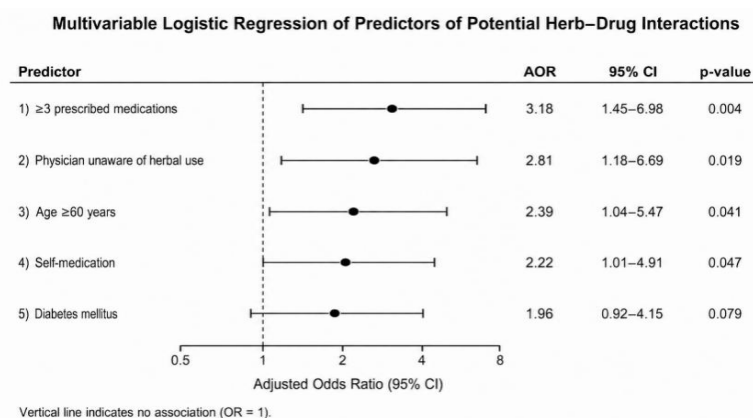


Figure 1: Multivariable logistic regression analysis of predictors of 30-day hospital readmission. Points represent adjusted odds ratios, and horizontal lines represent 95% confidence intervals

DISCUSSION

The present study revealed that 43.6% of adults taking long-term prescription therapy were also taking herbal medicines. 29.2% of herbal user had informed their physician, and 38.5% had one or more possible herb-drug interactions. The estimated worldwide prevalence of 51% among adults with diabetes using complementary medicine¹⁵. It was comparable to the 43% pooled prevalence in adults with chronic kidney disease¹⁶.

The low disclosure rate is clinically significant, as prescribers do not assess exposures that were not disclosed. There was little professional supervision, with almost 75% of users self-medicating and most products being bought over the counter. Family and friends were the most common source of recommendations, and social media had some impact on use. The disclosure rate in the present study was 29.2%, which was comparable to the pooled disclosure rate of 33% (95% CI: 24%–43%) reported for biologically based complementary medicine use¹⁷. Patients may not speak up because they believe herbs are harmless, natural, or outside of the realm of prescribed treatments. Systematically, limited public and professional knowledge of interaction risks has been identified¹⁸.

A significant concern for potential Herb–Drug interactions was identified in 38.5% of the herbal users, but it could not be determined if these interactions were clinically significant. Patients undergoing chemotherapy treatment often have multiple medications and complex treatment regimens, which may increase the risk of medication-related problems and potential interactions¹⁹. Adverse events have also been observed amongst those taking Chinese medicine and Western medicine concurrently in Singapore for active surveillance²⁰. The most common symptoms were gastrointestinal symptoms, followed by changes in glycaemic control and dizziness²¹. These effects are feasible due to the ability of herbal ingredients to irritate the gastrointestinal tract or to alter the absorption, metabolism, transport and pharmacodynamic activity of the drug²². The most frequently used were ginger, turmeric, garlic, fenugreek and *Nigella sativa*, possibly useful for blood pressure or glucose control, which could result in additive hypotensive or hypoglycaemic effects^{23,24}. The interactions of the cytochrome P450 enzymes, transporters and glucose-lowering pathways are described in reviews of diabetes²⁵.

Prescribed drugs were independently associated with possible herb–drug interactions. Participants taking more than three prescribed medicines had higher odds of a possible herb–drug interaction than those taking three or fewer medicines (AOR 3.18). This finding should not be interpreted as indicating that the odds of interaction progressively increased with each additional medicine, because the number of prescribed medicines was analyzed categorically. Medication burden or polypharmacy is a problem in older adults and is linked to worse outcomes in this population²⁶. Other factors such as age ≥ 60 years were also independently associated with increased risk, which may be due to multimorbidity, drug handling, and long-term exposure to treatment. The use of multiple herbals at the same time has also been recently shown to be a medication safety issue in older cancer patients and elderly adults with chronic disease²⁷. Several factors, including physician unawareness and self-medication, continued to be predictors, highlighting that communication and behavior were also factors besides biological vulnerability²⁸.

This study had a cross-sectional, single-hospital design, which limited the causal inferences and generalizability. The adverse effects were self-reported and might have been confounded by recall error, non-disclosure, or incorrect identification of the product. The observed associations should therefore not be interpreted as evidence of causality. Multi-center prospective studies are needed to confirm ingredients and dosages, incorporate standardized interaction instruments, and correlate ingredients/exposures with clinical and laboratory findings. Routine clinician inquiry, pharmacist review, patient education, and electronic alerts should be evaluated in intervention studies for their efficacy in preventing herb–drug harm.

CONCLUSION

This study showed that the use of herbal medicine in combination with prescription medication was common; many patients did not report their use to their physicians. Potential herb–drug interactions, identified based on published evidence, were observed in a substantial proportion of herbal medicine users. The presence of more than three prescribed medicines, older age, physician unawareness, and self-medication were independently associated with potential herb–drug interactions. The findings indicate a need for routine screening, counselling of patients, and improved communication between patients and healthcare professionals to enhance medication safety in practice. Future prospective, multicenter studies are needed to confirm the clinical significance of these potential interactions and to evaluate the effectiveness of pharmacist-based interventions, monitoring, and patient education in reducing clinically significant adverse events.

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