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Exploring The Concurrent Use and Potential Interactions Between Prescription Drugs and Health Supplement Products Among Patients With Chronic Diseases

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ABSTRACT

The concurrent use of prescription drugs and health supplement products (HSP) is a concern among patients with chronic diseases. This study aimed to investigate the concurrent use of prescription drugs and HSP among patients with chronic diseases in suburban and rural area of Sarawak, Malaysia. The potential drug-HSP interactions were also assessed.

This was a cross-sectional multicenter study involved seven government districts hospitals. Patients who prescribed with three or more chronic prescription drugs were recruited from the outpatient pharmacy of the hospitals by using convenient sampling. The patients' perceptions and practices of HSP consumption were assessed by a questionnaire. The patients' current used of prescription drugs and HSP were also assessed.

A total of 350 patients were recruited in this study and 84 patients (24.0%) found to have actively using HSP. Slightly more than half (55.7%) of the patients perceived that there were potential interactions between HSP and prescription drugs. Nevertheless, 56.0% of the patients never consult their healthcare providers regarding potential drug-HSP interaction. Besides, 54.0% of patients never search for information about the potential interaction. A total of 80 cases of potential drug-HSP interactions were identified. The interactions were mostly involved antihypertensive drugs (66.3%) and antidiabetic agents (17.5%). Vitamin B3 (niacin) (33.8%) and fish oil (omega-3) supplements (26.3%) were the most common HSP involved in the interactions.

In conclusion, the patients have lack of awareness regarding potential drug-HSP interactions. Healthcare providers should be alert about the concurrent use of HSP and prescription drugs among the patients.

Keywords: Health supplement products, prescription drugs, concurrent use, public health

Introduction

The concurrent use of prescription drugs and health supplement products (HSP) always exposes patients to the risk of drug-HSP interactions. It was found that when the patients consumed more types of HSP, the risk of drug-HSP interactions is increased exponentially (1). A previous study revealed that the risk of drug-HSP interactions was 6.0% when two HSP were consumed but it increased to 50.0% when five HSP were consumed. The risk of drug-HSP interactions achieved maximum 100.0% when patients consume more than eight HSP with their prescription drugs (1). It was found that potential HSP and prescription drugs interaction was as high as 11% according to a study done among dementia patients in Norway (2). This was especially found among patients with chronic diseases and elderly patients for which 2% of them were potentially at risk of having major drug-HSP interactions (3). Half of these potential interaction were involved anticoagulant. Besides, in another study conducted among anticoagulant or antiplatelet drugs users who concurrently using HSP, half of them were found to have risk of potential drug-HSP interactions (4).

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Healthcare providers should alert about the concomitant use of HSP and prescription drugs as the consequence of drug-HSP interactions could be severe. For example, ginkgo biloba which has been commonly taken for prevention of memory loss among geriatrics has found to be able to induce cytochrome P450 liver enzyme (5). Patients who were concurrently taking the antiepileptic drugs and ginkgo biloba were found to had experienced fatal seizure because of increased drug's metabolism rate that was induced by ginkgo biloba (6). Moreover, concurrent use of gingko biloba and prescription drugs such as warfarin, aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) will increase the tendency of bleeding among patients (7-9). Hence, patient's usage of HSP should be documented in the patient's medical record in order to alert the clinicians about the potential interaction between prescription drugs and health supplements (10).

Currently, there is a lack of studies on concurrent use of prescription drugs and HSP in Asian countries as most of the studies were conducted in Western population (11). In Malaysia, the previous studies that investigated concurrent use of prescription drugs and HSP were single centre (4, 12), involved patients with specific disease (12) or interaction with specific type of medicines (13). Notably, all these studies were conducted more than a decade ago (4, 12, 13) and there is no latest data available for the current usage of HSP in Malaysia. In addition, none of the past studies included samples from Sarawak, which has the largest territories in Malaysia. Therefore, more studies are needed in order to provide evidences on the extent and manner of concurrent use of prescription drugs and HSP. This in return will enhance the Malaysian healthcare professionals' capability in identifying and managing patients at risk of drug-HSP interaction. In order to bridge the gap in the literature and to provide practical implications for Malaysian healthcare professionals, this study aimed to investigate the prevalence of concurrent use of prescription drugs and HSP among patients with chronic disease from the government district hospitals in suburban and rural area of Sarawak. The potential drug-HSP interactions were also assessed in this study.

Materials and Methods

This was a cross-sectional multicenter study conducted from June 2018 to August 2018. This study has granted ethics approval from the Medical Research & Ethics Committee, Ministry of Health Malaysia (approval number: NMRR-17-943-35773(IIR)). A total of seven hospitals including Saratok Hospital, Bau Hospital, Kanowit Hospital, Marudi Hospital, Dalat Hospital, Betong Hospital, and Daro Hospital were involved in the study. All patients who visited the outpatient pharmacy of the hospitals were screened for eligibility to be enrolled in this study during the entire study period. Patients who consumed three or more chronic prescription drugs were included in this study by using convenient sampling. In order to reduce recall bias, this study only included the HSP mentioned by the patients which they were currently actively using it. Patients who were less than 18 years old, pregnant women, admitted for inpatient care or inpatients were excluded from this study. Patients who had language barrier and unable to give consent for participation in this study were excluded as well.

The sample size was determined by using formula for prevalence study. Previous study showed that the prevalence of HSP consumption among Malaysian were approximately 30% (14) and a total of 323 patients are required for 95% confidence interval and 5% margin of error. A data collection form was developed based on the objectives of the study using information from a literature review. The data collection form consists of four parts. The first part consists of patient demographic data. The second part involved a questionnaire to assess the prevalence of HSP consumption, perceptions and practices of the patients with regards to HSP. Meanwhile, part three records the prescription drugs that patients received from the hospital. The prescription drugs were recorded based on the information provides from the patients and subsequently compared with the patients' medical card record. Part four was to assess the patient's current use of HSP, which included the names, dose and frequency of consumption. The data collection form has gone through face and content validation by two experts and three practicing clinical pharmacists with at least five years of working experiences in hospital. The data collection forms were further adjusted after pre-testing with 32 patients.

The data collection was performed by the pharmacists from respective hospitals involved in this study. Prior to the data collection, training session were conducted with all the pharmacists to ensure the standardization in the data collection. The patients who collected medications from outpatient pharmacy department of the selected hospitals were screened by the pharmacists. Those

who fulfilled the inclusion criteria were invited to participate. The objectives of the study were explained, and the patients were asked for consent to participate in the study. Subsequently, the data collection forms were filled in by the pharmacists through face to face interviews. When the patients were asked about the type of HSP that they were consuming, they would be requested to bring their HSP for identification if they cannot recall the products' names.

In this study, HSP is defined as manufactured dietary supplements products contains one or more dietary ingredient such as vitamins, minerals, herbs, amino acids, fatty acids, enzymes and other bioactive substances used for general wellbeing (15). The collected data were analysed using IBM SPSS® Statistics Version 23. Descriptive statistics were used to report the pattern of concurrent use of prescription drugs and HSP among the patients. The potential interaction between the HSP used by the patients and the prescribed drugs were evaluated based on a literature search on primary journal and secondary source such as meta-analysis and review articles. Besides, tertiary database which summarized the clinically significant of the interaction were used in the assessment of drug-HSP interaction as well. The tertiary database used in the assessment of drug-HSP interaction were Micromedex, Stockley's Drug Information (Medicines Complete) and Lexicomp® Drug Information Handbook.

Results

Patient's demographic characteristics: A total of 350 patients were recruited in this study. Slightly more than half (52.3%) of the patients were aged more than 55 years old while 43.1% were aged between 36 to 55 years. The patients were mainly female (56.0%). Considering the education levels, 19.7% of the patients did not receive any formal education. Meanwhile, the number of patients who received primary and secondary education were 34.9% and 36.0% respectively. A total of 37 patients (10.6%) were active smokers while 61 patients (17.4%) were alcohol drinkers. When assessing the type of chronic diseases of the patients, majority (86.9%) found to have hypertension, followed by diabetes mellitus (52.9%) and dyslipidaemia (34.3%) (Table 1).

Prevalence of Use and Concomitant Use of HSP With Prescription Drugs: Less than half (42.3%) of the patients stated that they have experiences in using supplement products. Nevertheless, only 84 patients (24.0%) were currently active HSP users. Slightly more than half (56.9%) of the patients would not consider taking HSP in the future. When specifically assessing the 84 patients who were active HSP users, 65.5% of them found to have concomitantly consumed supplement products with their prescription drugs (Table 2).

Patients' Perceptions and Practices With Regards To The Potential Drug-HSP interaction: All the 350 patients were assessed on their perceptions towards potential interaction between prescription drugs and HSP. Slightly more than half of the patients perceived that there are potential interactions between HSP with their prescribed drugs (55.7%) and the potential interactions increase when taking prescribed drugs together with HSP (52.9%). Majority (73.7%) of the patients expressed agreement towards the important to search for information about potential drug-HSP interactions. Besides, the patients mostly (72.5%) perceived that it is important to read the HSP leaflet about the potential drug-HSP interaction before consuming HSP. Most (81.5%) of the respondents also agreed or strongly agreed that it is important to consult their healthcare providers regarding potential drug-HSP interactions (Table 3).

The 148 patients who have experiences in consuming HSP plus two patients who were new HSP users were grouped together (total of 150 patients) to investigate on the practices regarding potential drug-HSP interaction. Approximately half (56.0%) of the patients never consult their healthcare providers regarding this issue. Besides, about half of them never search for information about potential drug-HSP interaction (54.0%) and never read the product leaflet for this information as well (51.3%) (Table 3).

Category of Prescription Drugs Involved In The Potential Drug-HSP Interactions: The potential drug-HSP interaction were mostly involved antihypertensive drugs (66.3%) and followed by antidiabetic agents (17.5%). Among the antihypertensive drugs, calcium channel blockers (22.5%) and ACE inhibitor (15.0%) were mostly involved. Whereas, biguanides (12.5%) was the antidiabetic drug class which mostly involved in the interaction (Table 4).

The Rate of Potential Drug-HSP interaction: The rate of potential drug-HSP interaction according to the prescription drugs involved in the interaction are shown in table 5. Amlodipine was among the most used prescription drugs among the 84 active HSP users (54.8%, n = 46).

Table 1. Demographic Characteristics of The Patients

Demographic characteristic	n (%)
Age, years	
18 - 35	16 (4.6)
36 - 55	151 (43.1)
> 55	183 (52.3)
Gender	
Female	196 (56.0)
Male	154 (44.0)
Education	
No formal education	69 (19.7)
Primary school	122 (34.9)
Secondary school	126 (36.0)
Diploma/degree	33 (9.4)
Cigarette smoking	
Smoker	37 (10.6)
Ex-smoker	57 (16.3)
Non-smoker	256 (73.1)
Alcohol consumption	
Drinker	61 (17.4)
Ex-drinker	37 (10.6)
Non-drinker	252 (72.0)
Chronic diseases	
Hypertension	304 (86.9)
Diabetes mellitus	185 (52.9)
Dyslipidaemia	120 (34.3)
Chronic kidney disease/end stage kidney disease	13 (3.7)
Others	83 (23.7)

Table 2. Prevalence of use and concomitant use of health supplement products with prescription drugs among the patients

	Survey Questions	Yes, n (%)	No, n (%)
1	Do you ever take any health supplement products?	148 (42.3)	202 (57.7)
2	Are you consuming any health supplement products now?	84 (24.0)	266 (76.0)
3	Would you consider taking health supplement products in the future?	151 (43.1)	199 (56.9)
4*	Concomitant use of health supplement products (less than half an hour pre-medication or less than 2-hour post-medication) with prescribed medicines.	55 (65.5)	29 (34.5)

*This question involved only patients who were currently active HSP users (n = 84)

Among the 46 HSP users whom prescribed with amlodipine, 15 potential drug-HSP interaction were identified. Hence, the rate of potential drug-HSP interaction for amlodipine among the active HSP users was 32.6%. Conversely, simvastatin was prescribed among 51 active HSP users but only 5 cases (9.8%) of potential drug-HSP interaction were identified.

HSP Involved In Potential Drug-Hsp Interaction: A total of 15 supplement products were involved in the potential interaction with the prescribed drugs among the active HSP users. Vitamin B3 (33.8%) and fish oil (omega-3) supplements (26.3%) were most commonly involved in the interaction (Table 6).

Potential Drug-HSP Interaction: A total of 80

Table 3. Perceptions and Practices of The Patients With Regards To The Potential Interaction Between Prescription Drugs and Health Supplement Products

Questions (perceptions)*		Strongly Disagree n (%)	Disagree n (%)	Neutral n (%)	Agree n (%)	Strongly Agree n (%)
1.	There are potential interactions between health supplement products and prescribed medicines.	3 (0.9)	38 (10.9)	114 (32.6)	179 (51.1)	16 (4.6)
2.	The potential drug-health supplement products interactions increase when taking prescribed medicines together with health supplement products.	1 (0.3)	30 (8.6)	134 (38.3)	163 (46.6)	22 (6.3)
3.	It is important to search for information about potential drug-health supplement product interactions before using health supplement products.	1 (0.3)	22 (6.3)	69 (19.7)	217 (62.0)	41 (11.7)
4.	It is important to read the health supplement product leaflet about potential drug-health supplement products interactions before using health supplement products.	2 (0.6)	27 (7.7)	67 (19.1)	208 (59.4)	46 (13.1)
5.	It is important to consult my doctors or pharmacists about the potential drug-health supplement products interactions.	2 (0.6)	23 (6.6)	40 (11.4)	227 (64.9)	58 (16.6)
Questions (practices)†		Never n (%)	Sometimes n (%)	Frequently n (%)	Always n (%)	
6.	Do you ever consult your doctors or pharmacists about the potential drug-health supplement products interaction?	84 (56.0)	26 (17.3)	20 (13.3)	20 (13.3)	
7.	Do you ever search for information about potential drug-health supplement products interaction?	81 (54.0)	28 (18.7)	24 (16.0)	17 (11.3)	
8.	Do you ever read the health supplement products leaflet for any potential drug-health supplement products interactions before using health supplement products?	77 (51.3)	35 (23.3)	14 (9.3)	24 (16.0)	

*This section involved all the patients (n = 350)

†This section involved patients who have experiences in using HSP and new HSP users (total n = 150)

cases of potential drug-HSP interactions were identified in this study. The summary of the potential interactions are illustrated in table 7. There were interactions which potentially affected the absorption of the drug or health supplement. Two patients (2.5%) were concurrently using aspirin and ascorbic acid. The absorption of ascorbic acid can be reduced by aspirin. Besides, calcium supplement may decrease absorption of atenolol and this potential interaction was found in one patient (1.3%). Some of the potential interaction were involved the risk of adverse effects. There were two cases (2.6%) of concurrent used of ginseng extract and hypoglycaemic drugs which may increase the risk of hypoglycaemia. Besides, concurrent used of vitamin D and hydrochlorothiazide were noticed in two patients (2.5%) and the hypercalcaemic effect of vitamin D might be enhanced. Six patients (7.6%) were found to have concurrently

Table 4. Category of Prescription Drugs Involved In The Potential Drug-Health Supplement Products Interactions

No.	Category of prescription drugs	n (%)
1.	Antihypertensive	
	Calcium antagonists	18 (22.5)
	ACE inhibitors	12 (15.0)
	Diuretics	9 (11.3)
	Beta-blockers	8 (10.0)
	Angiotensin II antagonists	5 (6.3)
	Alpha blockers	1 (1.3)
	Sub-total	53 (66.3)
2.	Antidiabetic agents	
	Biguanides	10 (12.5)
	Sulfonylurea	3 (3.8)
	Insulin preparations	1 (1.3)
	Sub-total	14 (17.5)
3.	Antiplatelet	6 (7.5)
4.	Dyslipidaemic agents (HMG-CoA reductase inhibitor)	6 (7.5)
5.	Anticoagulant	1 (1.3)
Total		80 (100)

used vitamin B3 (niacin) and HMG-CoA reductase inhibitor. This combination may cause myalgia, myositis and increase the risk of rhabdomyolysis.

There were interactions which may lead to increase in the prescription drug's effect. Fish oil (omega-3) supplement may enhance hypotensive effect of antihypertensive drugs and there were 19 cases (24.1%) of this potential interaction. Stevia is another herb which may enhance hypotensive effect and the used of stevia and antihypertensive drugs were noticed in two patients (2.6%). Conversely, some of the potential interaction may decline the prescribed drugs' effect. For instance, four diabetes mellitus patients (5.0%) who prescribed with metformin were consuming vitamin B3 (niacin). Vitamin B3 (niacin) may cause insulin resistance and reduce the glucose control of antidiabetic drugs. Radix glycyrrhizae (licorice) may cause fluid retention and reduce the blood pressure lowering effect of antihypertensive drugs. These potential interactions were found in two patients (2.5%) who concurrently consumed Radix glycyrrhizae (licorice) and antihypertensive drugs.

Discussion

Generally, the drug-HSP interactions could be segregated into pharmacokinetic and pharmacodynamic (1, 7). In pharmacokinetics interaction, the absorption, distribution, metabolism and excretion of a drug are affected (1). Whereas, the pharmacodynamic interaction involved the combined pharmacological effect of the drugs and HSP (1). In the present study, both types of pharmacokinetics and pharmacodynamic interactions were found. An example of potential pharmacokinetics interaction was between the concurrent use of aspirin and ascorbic acid. Aspirin reduces the absorption of ascorbic acid. Hence, the daily dose of ascorbic acid may need to increase during long term aspirin therapy (16).

Considering the pharmacodynamic type of potential drug-HSP interactions, interactions which involved synergistic effect were found in this study. For instance, there are potential interactions between fish oil supplements and antihypertensive drugs. Fish oil supplements which contain omega-3 fatty acids can lower blood pressure through inhibiting angiotensin II dependent vasoconstrictions (17) and could have additive effect to antihypertensive drugs (18). Besides, concomitant used of niacin (vitamin B3) and antihypertensive drugs were observed in this study. Niacin found to have additive effect on reducing blood pressure and possible cause hypotension with the use with antihypertensive drugs (18). Therefore, close monitoring of patients' blood pressure is required. Besides, four incidents of potential pharmacodynamic antagonism interaction were found between niacin with metformin as niacin decreases glucose

Table 5. The Rate of Potential Drug-Health Supplement Products Interaction

No.	Prescription drugs that identified possess potential drug-HSP interaction	Number of active HSP users whom prescribed with the drugs n (%)*	Potential drug-HSP interaction rate (%)†
1.	Amlodipine	46 (54.8)	15 (32.6)
2.	Perindopril	34 (40.5)	11 (32.4)
3.	Metformin	39 (46.4)	10 (25.6)
4.	Hydrochlorothaizide	20 (23.8)	8 (40.0)
5	Aspirin	10 (11.9)	6 (60.0)
6.	Simvastatin	51 (60.7)	5 (9.8)
7.	Gliclazide	22 (26.2)	3 (13.6)
8.	Metoprolol	20 (23.8)	3 (15.0)
9.	Atenolol	9 (10.7)	3 (33.3)
10.	Valsartan	3 (3.6)	3 (100.0)
11.	Losartan	5 (6.0)	2 (40.0)
12.	Nifedipine	3 (3.6)	2 (66.7)
13.	Bisoprolol	5 (6.0)	1 (20.0)
14.	Furosemide	5 (6.0)	1 (20.0)
15.	Propranolol	3 (3.6)	1 (33.3)
16.	Enalapril	2 (2.4)	1 (50.0)
17.	Felodipine	2 (2.4)	1 (50.0)
18.	Insulin (Mixtard)	2 (2.4)	1 (50.0)
19.	Warfarin	2 (2.4)	1 (50.0)
20.	Rosuvastatin	1 (1.2)	1 (100.0)
21.	Terazosin	1 (1.2)	1 (100.0)
	Total (number)	285	80

*****Number and percentage of patients who prescribed with the drug. The percentage was calculated based on the total number of active HSP users (n = 84).

†Number and percentage of patients who have potential drug-HSP interaction based on the prescribed drug

tolerance and may lead to hyperglycaemia (19). A recent meta-analysis highlighted that type 2 diabetes mellitus patients were associated with higher blood sugar level if they were prescribed with higher dose of niacin (20). Concurrent used of glucosamine and antidiabetic agents were also found in this study. Glucosamine affects the absorption of peripheral glucose and might reduce the effectiveness of the antidiabetic agents (21, 22).

A total of six patients were using statins (HMG-CoA reductase inhibitor) together with niacin in this study. Using statins together with niacin may increase the risk of a rare but serious condition called rhabdomyolysis that involves the breakdown of skeletal muscle tissues (23). This interaction was found to be dose-dependent particularly in high dose of niacin (24, 25). Chinese descents were found to have higher risk for this interaction. It is unknown whether other Asian populations share the same risk as the Chinese patients (26). The use of these combinations needs to be cautious. The patients need to be monitored for any signs of myopathy or rhabdomyolysis, such as muscle pain, tenderness, or weakness. Patients' creatine kinase should be monitored periodically. Statins should be discontinued immediately if myopathy or rhabdomyolysis is suspected (26). Besides, one patient was found to have used Angelica sinensis (dong quai) together with aspirin. Dong quai increases risk of bleeding and slow blood clotting (27). Dong quai may potentiate the effects of antiplatelets which subsequently could increase

Table 6. Health Supplement Products Involved In Potential Drug-Hsp Interactions

No.	Health supplement	n (%)
1.	Vitamin B3 (niacin)	27 (33.8)
2.	Fish oils (omega-3) supplements	21 (26.3)
3.	Calcium supplements	5 (6.3)
4.	Glucosamine	5 (6.3)
5.	Ascorbic acid	4 (5.0)
6.	Potassium supplements	3 (3.8)
7.	Stevia	3 (3.8)
8.	Ginseng extract (America)	2 (2.5)
9.	Momordica charantia (bitter melon)	2 (2.5)
10.	Radix glycyrrhizae (licorice or liquorice)	2 (2.5)
11.	Vitamin D	2 (2.5)
12.	Angelica sinensis (dong quai)	1 (1.3)
13.	Garlic	1 (1.3)
14.	Panax ginseng	1 (1.3)
15.	Turmeric	1 (1.3)
	Total	80 (100)

the risk of bleeding. Dong quai has been reported to exert an antithrombotic effect by inhibiting platelet activation and aggregation (28). These combinations should be used with caution and close monitoring are necessary (27).

Concurrent use of potassium supplement and angiotensin II receptor blockers (ARBs) were noted in this study. This combination may increase the risk of hyperkalemia (29). The inhibition of angiotensin II results in decreased aldosterone secretion and causes potassium retention (30). The combination should generally be avoided in patients with kidney disease, diabetes mellitus, old age, severe or worsening heart failure, dehydration, or concurrent treatment with other medicines that increase serum potassium. This combination should be avoided unless the benefits outweigh the potential risks. Serum potassium and kidney function should be checked prior to initiating therapy and regularly thereafter. The patients should be counselled on the potential risk of excessive potassium in the diet. Besides, advises on appropriate levels of potassium and fluid intake should be given. Patients should seek medical advice if signs and symptoms of hyperkalemia occurred (30).

This study detected several drug-HSP interactions. This finding reflected that the patients might be ignorant about the potential drug-HSP interactions when concurrently consumed HSP together with prescription drugs. The patients may never or rarely consult their healthcare providers regarding the use of HSP (31). There might be lack of communication between healthcare providers and the patients on the use of HSP (32). Besides, half of the patients in this study did not refer to the product leaflet for any information regarding potential drug-HSP interactions. These findings were in accordance to previous studies showing that family, relatives and friends have huge influence on patients' choices of HSP as they are the main source of information (33, 34). However, the information provided may be not accurate and would be catastrophic to patient's health. Healthcare providers should be alert about the consumption of HSP among the patients. The patients should be counselled about the potential drug-HSP interactions.

The prevalence of drug-HSP interactions is extensive but the exact prevalence was remained unknown. This was because most of the study reported was mainly the potential HSP and prescription drug interactions. It was rather difficult to trace the association of an adverse event which were suspected to be related to drug-HSP interaction retrospectively. Despite of the variation in the clinical significance of drug-HSP interaction, it is important to bear in mind that any interaction has the potential to cause harm (35). Hence, reporting of any experienced adverse reaction resultant from HSP interactions is essential. Unfortunately, reports of adverse events and drug-HSP interactions were relatively low due to under-reporting. This was largely contributed by the patients' assumption on the HSP was safe

Table 7. Potential Drug-Health Supplement Product Interaction Identified Among Active Hsp Users

Potential Drug-HSP Interaction			n (%)	Summary of interaction
No.	HSP	Prescribed drug		
1.	Angelica sinensis (dong quai)	1. Aspirin	1 (1.3)	Concurrent use may increase risk of bleeding.
2.	Ascorbic acid	1. Aspirin	2 (2.5)	Aspirin reduces the absorption of ascorbic acid. The daily dose of 30 – 60 mg ascorbic acid may need to increase to 100 – 200 mg during long term aspirin therapy.
		2. Propranolol	1 (1.3)	Concurrent use may decrease bioavailability of propranolol.
		3. Warfarin	1 (1.3)	Concurrent use may decrease effect of warfarin.
3.	Calcium supplements	1. Amlodipine	3 (3.8)	Calcium may decrease the hypotensive effect of verapamil. The effects of other calcium-channel blockers might also be reduced.
		2. Atenolol	1 (1.3)	Calcium may decrease absorption of atenolol.
		3. Hydrochlorothiazide	1 (1.3)	Concurrent use of moderately large amount of calcium (with or without high doses of vitamin D) and thiazide may cause hypercalcaemia and possibly metabolic acidosis.
4.	Fish oils (omega-3) supplements	1.Perindopril	6 (7.5)	The hypotensive effect of antihypertensive drugs might be enhanced by fish oil.
		2. Amlodipine	4 (5.0)	
		3. Hydrochlorothiazide	2 (2.5)	
		4. Atenolol	1 (1.3)	
		5. Bisoprolol	1 (1.3)	
		6. Enalapril	1 (1.3)	
		7. Felodipine	1 (1.3)	
		8. Losartan	1 (1.3)	
		9. Metoprolol	1 (1.3)	
		10. Nifedipine	1 (1.3)	
		11. Aspirin	2 (2.5)	Fish oils have some antiplatelets effects which might be additive with aspirin. Bleeding is more likely with high-dose fish oils (more than 3 g daily omega-3 fatty acids).
5.	Garlic	1. Losartan	1 (1.3)	The hypotensive effect of antihypertensive drugs might be enhanced by garlic.
6.	Ginseng extract (America)	1. Gliclazide	1 (1.3)	Concurrent use may increase risk of hypoglycemia.
		2. Metformin	1 (1.3)	

Table 7. Continued

Potential Drug-HSP Interaction			n (%)	Summary of interaction
No.	HSP	Prescribed drug		
7.	Glucosamine	1. Metformin	4 (5.0)	Glucosamine may increase blood glucose levels in patients with diabetes mellitus.
		2. Gliclazide	1 (1.3)	
8.	Momordica charantia (bitter melon)	1. Gliclazide	1 (1.3)	Concurrent use may increase risk of hypoglycaemia.
		2. Metformin	1 (1.3)	
9.	Panax ginseng	1. Nifedipine	1 (1.3)	Concurrent use of panax ginseng and nifedipine may increase serum concentration of nifedipine and risk of nifedipine side effects.
10.	Potassium supplements	1. Valsartan	2 (2.5)	Concurrent use may increase risk of hyperkalemia.
		2. Perindopril	1 (1.3)	
11.	Radix glycyrrhizae (licorice or liquorice)	1. Amlodipine	1 (1.3)	Liquorice may cause fluid retention and reduce the effects of antihypertensives.
		2. Metoprolol	1 (1.3)	
12.	Stevia	1. Amlodipine	1 (1.3)	Stevia may reduce blood pressure. Concurrent use of stevia and antihypertensive drugs may increase antihypertensive effect.
		2. Hydrochlorothiazide	1 (1.3)	
		3. Insulin (mixtard)	1 (1.3)	Stevia may reduce blood glucose. Concurrent use with antidiabetic drugs may increase risk of hypoglycemia.
13.	Turmeric	1. Aspirin	1 (1.3)	High dose of turmeric may have additive antiplatelet effect.
14.	Vitamin B3 (niacin)	1. Amlodipine	6 (7.5)	Concurrent use of Vitamin B3 (niacin) and antihypertensive drugs may increase antihypertensive effect.
		2. Perindopril	4 (5.0)	
		3. Hydrochlorothiazide	2 (2.5)	
		4. Atenolol	1 (1.3)	
		5. Furosemide	1 (1.3)	
		6. Metoprolol	1 (1.3)	
		7. Terazosin	1 (1.3)	
		8. Valsartan	1 (1.3)	
		9. Simvastatin	5 (6.3)	Concurrent use of vitamin B3 (niacin) and HMG-CoA reductase inhibitor may cause myalgia, myositis and increase the risk of rhabdomyolysis.
		10. Rosuvastatin	1 (1.3)	
		11. Metformin	4 (5.0)	Vitamin B3 (niacin) may cause insulin resistance and reduce glucose control of antidiabetic drugs.
15.	Vitamin D	1. Hydrochlorothiazide	2 (2.5)	Concurrent use of vitamin D and hydrochlorothiazide may enhance hypercalcaemic effect of vitamin D.
Total				80 (100)

and natural, and felt reluctant to report an adverse effect from a self-medicated substance (8, 35). Under-reporting on the adverse reactions could cause significant loss of valuable safety data, which subsequently contribute to the lack of knowledge about drug-HSP interactions.

Lacking scientific evaluation on HSP interaction is a challenge for the safe use of supplement products. There is limited information about the pharmacokinetics, pharmacodynamics, efficacy, and safety of HSP. Evaluation such as randomized controlled trials was either not available, not demanded by consumers or health care practitioners, and some of the time not required by regulatory agencies (35). In additional, unethical marketing techniques give raise of tons of false advertisements about the safety and efficacy of the herbs were spreading unfiltered to the general population (35, 36). This will eventually cause HSP being promoted for treatment based on word-of-mouth traditions and beliefs that ignoring scientific evidence (36). This could be extremely dangerous especially among vulnerable groups such as geriatric patients. A previous study revealed that 46% of the patients from geriatric clinic were taking supplements with anticoagulation properties. Most (73%) of them were also taking a prescription anticoagulant and were unaware of the potential interactions (35).

Limitation: The convenience sampling in this study might possibly cause selection bias. Besides, there might be recall bias as the data collection were mainly based on self-reporting of the patients.

Conclusion: The concurrent use and potential interactions between prescription drugs and HSP were prevalent among patients with chronic diseases in suburban and rural areas of Sarawak. The patients have lack of awareness regarding potential drug-HSP interactions. Healthcare providers should be alert about the concurrent use of HSP and prescription drugs among the patients. Educational interventions are needed to raise the concern and understanding among the patients towards the safe use of HSP and prescription drugs.

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