Research Article
Herbal Products Use Among Chronic Patients and its Impact on Treatments Safety and Efficacy: A Clinical Survey in the Jordanian Field

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Abstract

Objectives: To assess the current use of herbal products among chronically ill patients in Jordan and to review the impact of the used herbal products on their treatments safety and efficiency. **Materials and Methods:** This study was a questionnaire based cross-sectional study conducted between March and June, 2016. The developed and validated questionnaire consisted of 2 different forms, one for patients with chronic diseases and one for the community pharmacists. Patients and pharmacists were randomly recruited into this study by pharmacy students skilled to perform the data collection. **Results:** About 376 patients were recruited into this study (mean age 43 years, 54% female). About 216 (57.4%) were using 43 different herbal products. The most common chronic diseases suffered by the patients were hypertension, diabetes and hyperlipidemia. Males and older patients were more likely to experience unsafe or inefficient use of herbal products. Only 54.2% of the patients informed their pharmacists of their use of herbal products. A minority of the pharmacists (8.2%) reported very good knowledge of herbal products use and herbs-drugs interactions and only (11.3%) always ask their patients about their use of any herbal products. **Conclusion:** Many chronically ill patients in Jordan use herbal products for the management of their chronic conditions. Inefficient use is common mainly amongst males. Patients and pharmacists are not communicating as needed regarding patients use of herbal products. New strategies need to be implemented in the country to resolve these vital issues.

Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Natural products have been reported since ancient's history to be used by human kind and are still used world wild for health promotion and treatment of diseases[1]. Despite all the recent developments in drug industry, herbs remain to be used often in treatments of common ailments rather than conventional drugs[2]. More commonly, they are used as adjunct therapy to conventional pharmaceuticals, as a safer and more affordable system of health care[3]. Regardless of the reasons, patients using herbal medicines in combination with conventional medications, especially those used for chronic conditions, should be assured that the treatments they are using are safe and effective as what they are supposed to be[4,5].

Pharmacists are found in an ideal position to discuss with their patients the use of herbal supplements when pharmacological treatments are prescribed. Lack of dialog between the pharmacists and their patients about the use of herbal supplements is alarming and has been previously highlighted[6]. Patients with chronic conditions were found unaware of the risks due to the herb-drug interactions, leading to unsafe and inefficient treatments[7]. Studies shed light on the importance of pharmacists asking the patients about their use of any herbal products along with their conventional medications[8]. In addition, patients should be provided with science-based information on dosage, contraindications and efficacy for their herbal treatments by their community pharmacists[9].

Despite significant progress made in implementing the WHO traditional medicine strategy 2014–2023 (http://apps.who.int/iris/bitstream) around the world, there are numerous challenges related to herbal products safety and quality, research and development, education and training of practitioners, in addition to information provision and communication between pharmacists and their patients. To resolve these challenges, provision of education for the pharmacist is essential[10]. More clinical based study is needed to guide towards the appropriate use of herbal medicines in our health systems[11].

Previous studies have shown that herbal products use is very common among Jordanians[12,13]. Many of the herbal products remain untested and their uses are either poorly monitored or not monitored at all[14,15]. Hence, it is important to evaluate the appropriate use of herbal products in the country, especially for patients using medications for treating their chronic conditions at the same time[16].

The aims of this study include determining the prevalence of use of herbal products by patients with chronic diseases living in Jordan, prevalence of inefficient use of these products, role of the pharmacist in this area and factors associated with the use of these products.

MATERIALS AND METHODS

This cross-sectional study was conducted between March and June, 2016. Randomly selected community pharmacies distributed between Eastern Amman and Western Amman (capital of Jordan) were visited and invited to participate in the study. All pharmacists who studied at the same selected pharmacies during the study period were asked to participate in the study. Patients visiting the participating pharmacies were also approached randomly to participate in the study. Patient's inclusion criteria included those who were common customers at the recruited pharmacy and come back to the same pharmacy at least bimonthly to receive their medications, diagnosed with a chronic diseases, above the age of 18 and have been living in Jordan over 1 year.

Pharmacy students enrolled in the phyotherapy course at the Applied Science Private University for the year 2015/2016 (n = 45) were trained to assist in carrying out the data collection part of the study. Each student approached 15-25 pharmacists. Verbal consent was obtained from the participants (pharmacists and patients) before study entry. Ethical approval for the study was obtained from Applied Science Private University, Faculty of Pharmacy research committee.

Data collection tool was a face to face pre-developed questionnaire by the study investigators (Appendix 1). Appendix 1 and 2 show questionnaires for pharmacists and patients respectively, both included closed (using 5 likert scale) and open questions prepared by the principal researchers. Part A of the questionnaire was designed to collect socio-demographic characteristics for the pharmacists/patients, while part B was designed to collect information regarding use of herbal products, source of knowledge about herbal products and overall experience. The questionnaires underwent face validation following its review by expert researchers in the field. The questionnaire was also distributed to pharmacists (n = 10) and pharmacy students (n = 10) to assess the questionnaires for clarity. All submitted comments were taken into consideration by the researchers and used in developing the final version of the questionnaires.

Participating pharmacists were interviewed at their pharmacies and they were asked about their level of education, years of experience, their pharmacy average daily selling rate Jordanian Dinar (JD). Part B investigated

pharmacist's role in advising their patients on the use of prescribed and non-prescribed herbal products simultaneously with patient's chronic medications, their level and source of knowledge regarding the available pharmaceutical herbal products, their involvement in investigating patient's present treatments looking for possible interactions or contraindications, their counseling practices when selling prescribed herbal products to patients with a medical history, the references they use for assessing possible interactions between the conventional medications and herbal products and their experience about the efficiency and safety of the herbal products used by their chronic patients.

For the participating patient's, questions involved documenting their history of herbal use (mainly for treating chronic conditions), indications, source of advice and knowledge on herbal products, whether their health care providers were aware of this use and their experience regarding the efficiency and safety of the herbal products they used for their chronic conditions along their conventional medications.

Following data collection, the reported most frequently used herbal products by the patients were reviewed in term of their efficiency and safety for treating the conditions the patients declare they used it for. Herbs and Natural Supplements-An Evidence Based Guide[17] was used to complete this part of the study, in addition to a number of peer-reviewed published clinical, *in vitro* and *in vivo* studies. In order to rate the claimed efficiencies of the herbal products used by study participants for treating common chronic conditions, a comprehensive list of the herbal products used to treat the top 5 chronic conditions described by the patients was prepared (Appendix 2). The Appendix 2 also shows the gender and the age group of the patients per chronic condition. The Appendix 2 helped in correlating some of the socio-demographic factors associated with the inefficient use of these herbal products among the chronic patients.

Data analysis: Statistical analysis was performed using Statistical Package for Social Sciences (SPSS version 20, Chicago, IL, US). Descriptive analysis was carried out to determine the frequencies calculated for the categorical variables.

Based on the number of licensed pharmacies (1,568) and the number of population (4,000,000) in Amman, sample size was calculated using a margin of error of 5%, confidence level of 95% and response distribution of 50%, a minimum of 309 pharmacies and 385 patients were needed.

RESULTS

Socio-demographic characteristics: Out of the approached pharmacies in the study (294), 200 agreed to participate and complete the questionnaire, resulting in a response rate of 68%. The majority (47.4%) had less than 5 years working experience, while few (22.7%) had a working experience of 5-10 years and some (29.9%) had more than 10 years working experience. All pharmacists had a bachelor of pharmacy degree or higher and all were licensed as a trained pharmacist. The majority (79.4%) of the pharmacists were allocated in Western Amman (higher socioeconomic areas of Amman). The average daily income was above 400 JD (1 US dollars = 0.71 JD) for the majority of pharmacists (65.5%). Some pharmacists (28.4%) reported an income in the range of 200-399 JD and few (6.2%) reported less than 200 JD income.

A total of 376 out of 400 patients who were approached to participate in the study agreed to participate and complete the questionnaire, giving a response rate of 94% with an average age of 42.92±15.21 (Mean±SD) years. Majority of patients were females (54.3%), Jordanians (87.2%) and residence of Western Amman (71.3%). About half of the patients (49.0%) had a university degree.

All patients were using conventional medications for their chronic diseases which involved diabetes mellitus type one and type two (22.3%), hypertension (22.3%) and hyperlipidemia (9.6%). Many patients (45.0%) had diverse health disorders including heart problems, arthritis, hormonal disorders, asthma, obesity, irritable bowel syndrome, atherosclerosis, anemia, migraine and osteoporosis.

Herbal products use by patients: All participating patients (n = 376) had chronic diseases. When these patients were asked how frequent they use herbal products for treating their health conditions (chronic and non-chronic diseases), more than half of the patients (n = 216 and 57.4%) revealed that they use them with frequencies ranging from often-usually-always, with no significant variations between the two genders (Females: n = 128, 63%, males: n = 88, 23.4%). Among the most frequently used products, 43 different herbal products were reported. Table 1 shows the top 10 used herbal products by study patients. The most common reported herbal products used were garlic (n = 28), sage (n = 20), roselle and anise (n = 16).

Factors associated with inefficient use of herbal products: Analyzing the comprehensive list of the herbal products used by the study patients to treat their chronic diseases (Appendix 2), out of all patients reported use of herbal

products (n = 216), 76 out of the 156 cases (48.72%) were found to be using at least one inefficient herbal remedy. A proportion of (45.45%) of the male patients with relatively high frequency (40 cases) were using 10 ineffective products that were not supported by any evidence for their claimed use, (e.g., herbal mixture for treating hypertension with or without diabetes or lipedemia). These patients were equally distributed between the age groups 40-59 and 60+ years old. Regarding female patients, only (28.1%) of them with a frequency of (36 cases) were found using 8 ineffective products to treat their chronic conditions not supported by any evidence. They were distributed between younger age groups (20-60 years), when compared with the male patients (Table 2).

Knowledge and beliefs about herbal products use among patients: In answering the question whether the patients inform their pharmacists when they are using herbs before requesting their medications, majority of patients (54.2%) reported to rarely inform their pharmacists about using herbal products (Fig. 1). Results showed that 58.1 and 50.9% of the male and female patients, respectively had a low awareness regarding the role of their pharmacist in assessing potential herb-drug interactions, with no significant variations among the 2 genders.

Many patients (45.8%) reported that they ask their pharmacist for alternative herbal products that are useful for their medical conditions (with frequencies ranging from often-usually-always). Results showed significant variations ($p \leq 0.05$) between the 2 genders as shown in Fig. 2. Nevertheless, both genders revealed less interest in the role of the pharmacist advising them on alternative herbal products for treating their chronic conditions, with the majority 51.1 and 57.0% of males and females patients respectively, reported to rarely ask their pharmacist for any herbal treatments.

Table 1: Frequencies for the top 10 commonly used herbal products for the treatment of different chronic and non-chronic health conditions by study patients (n = 216)

Herb	Frequency	Percent*	Males	Females
Garlic (*Allium sativum*)	28	20.0	12	16
Sage (*Salvia officinalis*)	20	14.3	8	12
Roselle (*Hibiscus sabdariffa*)	16	11.4	4	12
Anise (*Pimpinella anisum*)	16	11.4	4	12
Thyme (*Thymus vulgaris*)	12	8.6	0	12
Mixture of unknown herbs	12	8.6	4	8
Cinnamon (*Cinnamomum cassia*)	12	8.6	4	8
Mixture of known herbs	8	5.7	0	8
Ginger (*Zingiber officinale*)	8	5.7	4	4
Olive leaves (*Olea europaea*)	8	5.7	0	8
Sum	140		40	100

*No significant differences were found between both genders

Table 2: Association between patient's gender and age with the frequencies and percentages (%) of the reported use of herbal remedies in treating specific chronic conditions by study patients (n = 216)

	No evidences are available to support the claimed use		
Gender	Age group (year)	Frequency*	Percentage relative to the gender population using herbal products*
Male	40-59	20	22.73
	60+	20	22.73
Female	20-29	16	12.50
	30-39	4	3.13
	40-60	16	12.50
	Clinical evidences are available to support the claimed use		
Gender	Age group (year)	Frequency*	Percentage relative to the gender population using herbal products*
Male	40-59	8	9.09
	60+	4	4.55
Female	40-59	12	9.38
	In vivo or *in vitro* studies are available to support the claimed use		
Gender	Age group (year)	Frequency*	Percentage relative to the gender population using herbal products*
Male	40-59	8	9.09
	60+	20	22.73
Female	20-29	8	6.25
	30-39	4	3.13
	Studies with mixed results and conflicts on the efficiency of the herbal remedy used		
Gender	Age group (year)	Frequency*	Percentage relative to the gender population using herbal products*
Male	40-59	4	4.55
	60+	12	13.64
Female	-	0	-

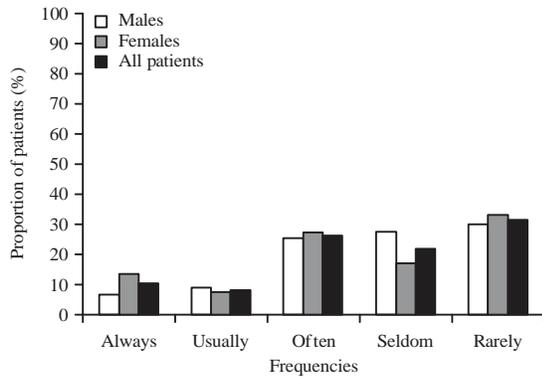*Calculated using data from Appendix 2

Fig. 1: Frequencies of patients who reported informing their pharmacist of their herbal products use before requesting their chronic medications (n = 376)
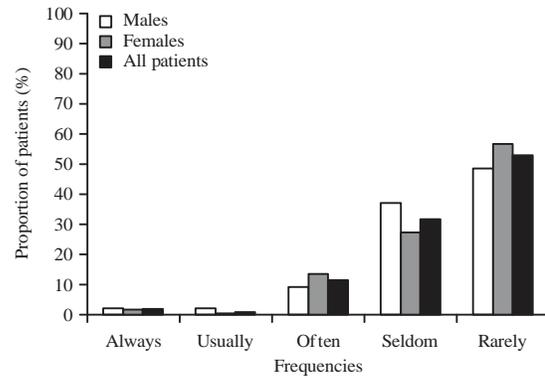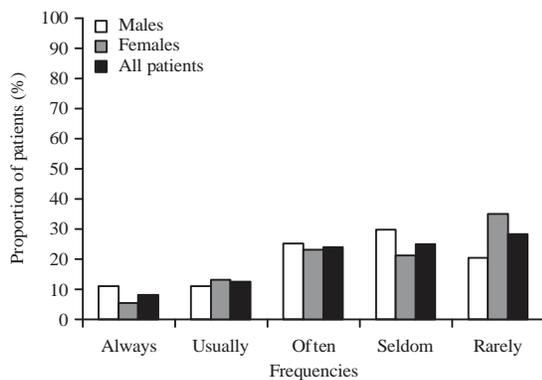

Fig. 2: Frequencies of patients who reported to ask their pharmacists for alternative herbal products that would be useful for treating their chronic conditions (n = 376)

Fig. 3: Frequencies of patients who complained for potential side effects caused by herb-drug interactions (n = 376)
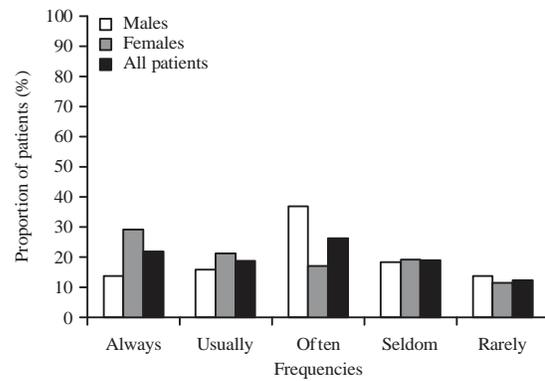

Fig. 4: Proportion of chronically ill patients who believed in the high efficiency of herbal products and their ability to decrease the frequency of conventional medications used (n = 376)

Both genders showed almost similar experiences when they were asked if they have ever suffered from potential side effects, that they could correlate to the use of herbs along with their chronic medications (Fig. 3). While (53.2%) of the patients answered with rarely, a proportion of (14.9%) of the chronic patients said that they experienced some side effects or interactions, which could be caused by using their conventional medications with certain herbs. Comparing the two genders, 56.9 and 48.8% of the female and male patients respectively, showed a rare frequencies of these interactions, with no significant variations.

Among the interviewed patients, (41.4%) of them said that they believe with the high efficiency of treatments by herbal products, which was rated as the major factor for their use. Moreover, these patients also believe with the ability of treatments by herbal products to always or usually decrease the frequencies for conventional medications used to treat the same conditions (Fig. 4). Where (51.0%) of the female patients

said they do always or usually get this benefit from herbal products use, only (30.3%) of the male patients get this benefit, with significant variations (p≤0.05) between the 2 genders.

Regarding the patient's source of knowledge for using medicinal herbs, 40.4% of them said that they depend on the internet. Their second source was the pharmacist (22.3%), followed by their MD which contributed to only (13.8%). A proportion (23.4%) of the patients depend on other sources, including their local herbalist, friends and family, TV, books and magazines or traditional recipes inherited via generations. By comparing both genders, female patients showed to depend more on the internet (females: 41.2% and males: 39.5%). Never the less, male patients showed to depend more on the pharmacist (males: 27.9% and females: 17.6%), with no significant variations among the gender of the patients. Only minority of the female (15.7%) and male (11.6%) patients showed to depend on their MD.

Knowledge and beliefs about herbal products use among the pharmacist: When pharmacists were asked to evaluate their knowledge about the use of herbal products for treating common chronic diseases, the evaluation for the majority of the pharmacists (47.4%) was average, while 25.8% believed they have a good amount of knowledge and only 8.2% believed that they have very good knowledge.

When pharmacists were asked to assess their knowledge about potential herbs-drugs interactions, the majority (39.2%) reported slight knowledge, while 34.0% of them reported average knowledge and only 22.6% of them reported a good/very good level of knowledge.

As for the pharmacist's source of knowledge about herbal products use and their potential interactions with drugs, a majority of pharmacists (33.3%) reported their universities (during their B. Pharmacy degree or D. Pharmacy degree). The rest reported the internet (27.8%), published papers and books (19.4%) and different life experiences from friends, family, medical companies, advertisements and herbalists (19.5%).

When pharmacists were requested to evaluate how frequently they ask their chronically ill patients about their use of any herbal products, only (11.3%) of pharmacists said they always ask, other (58.8%) of the pharmacists reported to usually ask and about 3rd of the pharmacists (29.9%) reported to rarely ask.

Regarding recommending chronically ill patients to use herbal products in combination with their conventional medications, majority of the pharmacists (45.4%) reported recommending herbal use. Other pharmacists (32.0%) reported to sometimes recommend herbal use and the rest of the pharmacists (22.7%) never recommended herbal products use to their patients.

DISCUSSION

This is the first study conducted in Jordan to reveal important information regarding chronically ill patient's use of herbal products. Most of the participants in this study believed in the high efficiency of herbal products, being the driving force for them to use it frequently. The study showed that more than half of the chronically ill patients use at least one herbal product. Female were shown to be more frequent users of herbal products than male patients. This could be due to the fact that female participants use herbal products to treat also acute health conditions as well as chronic diseases. Hypertensive patients, with or without diabetes and dyslipidemia were found to be the most frequent users of herbal products in this study. High use of herbal products

results in higher cases of inefficient use[18] more side effects and interactions with chronic medications[19].

Use of herbal products by chronically ill patients has been acknowledged by previous studies conducted in Jordan and in the Middle Eastern countries. Qunaibi *et al.*[20] reported 48% of patients in Jordan to be using herbal products for treating their medical conditions, mainly hypertension and diabetes. Patients justified their use of the herbal products by the claimed safety and efficiency of the herbal medicine in the country. A study conducted in Palestine showed that majority of hypertensive patients (86%) and more than half of the diabetic patients (52%) used at least one type of medicinal herbs[21].

The herbal products used by the patients in this study were found to be relatively safe plants that are commonly used on daily basis as food or beverage (Table 1). However, according to the literature, many of these products failed to show evidences for their claimed uses. The study sheds light on the inefficient use of herbal products mainly by male patients.

Many of the interviewed patients reported that they experienced some side-effects, which could be a consequence for the reported improper use of the medicinal herbs coincidently with conventional chronic medications. In a recent similar study conducted in Palestine, Al-Ramah *et al.*[7] reported that about 60% of the chronically ill patients used at least one medicinal herb, with about 22% experiencing at least one inefficient herbal product use. Males and older patients were also more likely to experience inefficient use of herbal products[7].

This study unveiled interesting facts about causes leading to the inefficient use of herbal products among chronically ill patients. Patients rarely inform their pharmacists about their use of herbal products. Only 11% of the patients ask their pharmacists to make a recommendation for herbal treatments that can be used to improve their health conditions. Female patients were less interested than males in the role of the pharmacist as an adviser for herbal product's use. Other cause reported in this study leading to the inefficient use of herbal products was the source of patient's knowledge about herbal products use. Most patients depend on the internet to obtain knowledge in this study. The community pharmacist came 2nd in this domain. Nevertheless, only 8% of pharmacists reported to have very good knowledge in this study. Such results are not surprising considering that only about one third of the pharmacists reported receiving education about the safe and efficient use of herbal products through their educational courses at their universities. Majority of the pharmacists depended on other less science-based evidences

and trusted sources such as the internet. Consequently, only 11% of the pharmacists said they always ask their chronically ill patients about their use of herbal products. Hence, chronically ill patients need to be educated about the role of the pharmacist regarding the efficient and safe use of the herbal products. Also, pharmacy students need to receive full education in this area at their pharmacy schools and to have their skills to update and upgrade their knowledge continuously following graduation to become independent long-term self-learners.

Limitations of this study include that the study was performed through a group of pharmacies allocated mainly in the western areas of Amman, Jordan, therefore it might not be representative to the practice in other parts of the city or other cities in the country. The references used to review the claimed efficiencies of the herbal products used to treat the chronic conditions reported in this study were not all very recent, although efforts were made to use the most available recent resources. The data collected were done through pharmacy students. Although, the students were trained well on the collection of data, some issues, such as social bias issues could have immerged. Answers of the pharmacists and patients could have been affected by the researcher being a pharmacist. Study sample size was restricted by researcher's time available for data-gathering.

CONCLUSION

The use of herbal products is a common practice among Jordanian chronically ill patients. Pharmacists should be aware of the common herbal products uses, especially for treating common conditions and to be able to evaluate and discuss its efficiency and safety with their patients using science-based evidences.

A high frequency of scientifically unsupported uses of some herbal products that claimed to treat chronic conditions was found. A substantial proportion of patients did not inform their pharmacists about herbal products use, therefore to avoid any possible negative outcomes, better counseling and communication between patients and pharmacists are recommended.

ACKNOWLEDGMENTS

Appendix 1: Study questioners forms 1 and 2

Pharmacist's questioner (Form 1)
Part A

- Age group (years): 20-29 30-39 40-59 60+
- Gender: Male Female
- Level of education: BSC Master PhD
- Work experience (years): <5 5-10 >10
- Area location: EA WA
- Nationality: Jordanian Non-Jordanian
- Average monthly sale (JD): <100 100-199 200-399 >400

Part B

(1) How do you evaluate your knowledge about the use of herbal products for the treatment of chronic diseases?

Very few   Little   Average   Good   Very good
- If your answer is average or more, what is the source of your information?
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(2) How do you evaluate your knowledge about herbs-drugs interactions?

Very few   Little   Average   Good   Very good
- If your answer is average or more, what is the source of your information?
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(3) How frequent you ask your patients if they use any herbal products along with your chronic medications?

Always   Usually   Often   Seldom   Rarely

(4) Would you recommend your patients to use herbal products in combination with their conventional medicine for the treatment of chronic diseases?

Yes   No   Sometimes

saPatient's questioner (Form 2)
Part A

- Age group (years): 20-29 30-39 40-59 60+
- Gender: Male Female
- Level of education: Primary SC Secondary SC High SC Diploma BSC Master/PhD
- Area location: EA WA
- Nationality: Jordanian Non-Jordanian

Part B

(1) In case you suffer from chronic diseases, what is it?

Diabetes (type 1 and 2)   Hypertension   High cholesterol   Thyroid gland disorders other
- In the case of the answer "Other", mention the name of the disease?
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(2) Do you use herbal products for the treatment of chronic health conditions?

Always   Usually   Often   Seldom   Rarely
- If you're above answer was (Always-Usually-Often); what is the name of the disease and herb used?
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(3) Do you inform your pharmacists when you are using herbs before requesting your conventional medications?

Always   Usually   Often   Seldom   Rarely

Appendix 1: Continued

(4) Do you ask your pharmacist about alternative herbal products that are useful for your medical conditions?

Always   Usually   Often   Seldom   Rarely

(5) Have you ever suffered from potential side effects, which you could correlate to the use of herbal products along with your chronic medications?

Always   Usually   Often   Seldom   Rarely

Appendix 1: Continued

(6) Do you believe that the use of herbal products in the treatment of chronic diseases is effective and have an influence in reducing the dose of the conventional medicine?

Always   Usually   Often   Seldom   Rarely

(7) What is the source of your information about the use of herbal products?

Online   MD   Pharmacist   Other (specify) ----------------

Appendix 2: Top five chronic conditions among the interviewed patients (n = 376), with their self-choices of herbal remedies

Herbal products	Gender	Age	Frequency	Evidences for efficiency
High blood pressure				
Roselle	Male	40-60	8	Roselle (*Hibiscus sabdariffa*): A dose-dependent decrease in systolic and diastolic blood pressure has been demonstrated for aqueous preparations of the *Hibiscus* calyx. Patients with essential but untreated, hypertension demonstrated a decrease in blood pressure with sour tea therapy. Their hypertensive state returned on cessation of therapy[22,23]
Mixture of mustered oil, hawthorn, garlic and fish oil	Male	40-60	4	Mustered oil: No data on hypotensive effect were available[24,25] Hawthorn (*Crataegus oxycantha*): Mixed results were found. Some *in vivo* and *in vitro* research shows that hawthorn might reduce blood pressure but other research shows no benefit. It may exert mild blood pressure-lowering activity, which appears to be as a result of a number of diverse pharmacological effects[26,27] Garlic (*Allium sativum*): No strong evidence for the effect of garlic on blood pressure is available[28] Fish oil: Based on clinical studies, evidence is inconclusive for the effect of fish oils on hypertension and is based on older studies[29-31]
Onion	Male	60+	4	Onion (*Allium cepa*): The peel of onion extract showed hypotensive effect on diabetic rats. This could be due to extract quercetin content, antioxidant activity and inhibiting vascular smooth muscle cells Ca^{2+} influx[32]
Garlic	Female	30-40	12	As mentioned above
	Male	40-60	4	
Flaxseed	Female	20-30	4	Flaxseed (*Linum usitatissimum*): Data available on antihypertensive effect are inconclusive[33]
Olive leaves	Female	40-60	8	Olive leaves (*Olea europaea*): No data available on antihypertensive effect were found[34]
Barley	Female	40-60	4	Barley (*Hordeum vulgare*): No data available on antihypertensive effect[35]
Diabetes				
Mixture of rocket and onion	Male	60+	4	Rocket (*Eruca sativa*): In *in vivo* model of alloxan-induced diabetic rabbits, studies showed significant reduction in glycaemia, also supported by recovery of body weight[36] Onion (*Allium cepa*): According to WHO Monographs on Selected Medicinal Plants 1999, limited trials have shown a decrease in blood glucose levels in healthy volunteers and non-insulin–dependent diabetic subjects using onion extracts[32,37,38]
Olive leaves	Female	30-40	4	Olive leaves (*Olea europaea*): Potentiating of glucose-induced insulin release and increased peripheral uptake of glucose has been demonstrated in alloxan-diabetic rabbits with no clinical evidence have been demonstrated[39,40]
Bitter melon seeds	Male	40-60	4	Bitter melon (*Momordica charantia*): Clinical trials evaluating the effect of bitter melon in type 2 diabetes showed no statistically significant effect versus placebo or glibenclamide[41,42]
Okra	Female	20-30	4	Okra (*Abelmoschus esculentus*): Tomoda *et al.*[43] reported that okra polysaccharide possesses hypoglycemic activity in normal mice. An anti-diabetic activity of okra on alloxan-induced diabetic rats has also been reported by Sabitha *et al.*[44,45]
Garlic and onion	Female	30-40	4	Garlic (*Allium sativum*): In a meta-analysis on diabetic rats, the antidiabetic effects of garlic extract were not significant for lowering glucose concentration and body weight[32]
Cranberry leaves	Female	40-60	4	Cranberry (*Vaccinium macrocarpon*): Cranberry juice may decrease the side effects of diabetes and increase the quality of life for people with diabetes. A small trial on adults with type II diabetes found lower insulin levels compared with placebo[46]
Ginger	Male	60+	4	Ginger (*Zingiber officinale*): There is inconsistent evidence about the effects of ginger on blood sugar control in people with diabetes. Some research suggests

Appendix 2: Continued

				that taking ginger daily in two divided doses for 8 weeks reduces insulin levels, but not blood sugar. Another study shows that ginger affects blood sugar but not insulin levels. Although it's not clear, the conflicting results may be due to the dose of ginger used or the length of time the patients had been diagnosed with diabetes[47,48]
Parsley	Male	40-60	4	Parsley (*Petroselinum crispum*): *In vivo* studies show the leaves of parsley decreased blood glucose level and demonstrated hepatoprotective activity in diabetic rats via antioxidant activity in STZ-induced diabetic rats[49-51]
Cinnamon	Female	20-30	4	Cinnamon (*Cinnamomum cassia*): Evidence is lacking to support the clinical use of cinnamon in the management of diabetes. Researchers have isolated polyphenols from cinnamon that possess insulin-like activity and have demonstrated a dose-dependent increase in glucose utilization in animal muscle tissue[52-55]
Sage, chamomile and marjoram	Female	20-30	4	Sage (*Salvia officinalis*): Studies on animals have shown effects of methanol leaf extracts and sage tea on fasting plasma glucose levels but not on glucose tolerance tests or insulin[56,57] Chamomile (*Matricaria chamomilla*): No data are available[58] Marjoram (*Origanum majorana*): A methanol extract of marjoram leaves strongly inhibited rat intestinal alpha-glucosidase[59]
Mixture of grape fruit, garlic, ginger and olive leaves	Male	40-60	4	Grape fruit (*Citrus paradise*): A well-controlled animal model, which showed that regardless of the amount of fat in the diet, consumption of grape fruit juice markedly, lowered fasting serum insulin. In addition, also its consumption reduced fasting glucose in mice and reduced the rate of weight gain[60]. These outcomes did not depend on reduction of caloric uptake between. The anti-glycemic effect of grape fruit juice occurred within 5 days and was as pronounced as the effect of metformin[61]

Cholesterol

Mixture of green tea, cinnamon and fish oil	Female	40-60	4	Green tea (*Camellia sinensis*): Clinical trials evaluating green tea showed decreases in total and LDL cholesterol for subgroups, decreases in serum triglycerides and a decreased total HDL: Cholesterol ratio[62-65] Cinnamon (*Cinnamomum cassia*): A double blind, randomized, placebo controlled clinical trial was conducted on patients with type 2 diabetes. The levels of fasting blood glucose, HbA1c, triglyceride, weight, BMI and body fat mass decreased significantly compared to baseline, but not in placebo group[66] Fish oil: In 2004, the FDA approved the use of fish oil for reducing very high triglyceridemia in adults as an adjunct to diet[67]
Rosemary	Male	60+	4	Rosemary (*Rosmarinus officinalis*): Aqueous extract perfusion of rosemary was administration to normal and streptozotocin-induced diabetic rats show a decrease in sugar, total cholesterol, triglycerides and LDL-cholesterol levels and an increase in HDL-cholesterol level. The findings of this study indicate that the administration of rosemary resulted in a better lipid profile and decreased blood sugar level in both normal and diabetic rats[68]
Mixture of onion, garlic and artichoke	Male	60+	4	Onion (*Allium cepa*): Hypolipidemic effects have been demonstrated in rats and rabbits and include effect on diet-induced atherosclerosis, hypolipidemic action and inhibitory effects on platelet formation[69-71] Garlic (*Allium sativum*): Some studies have suggested that garlic has no effect in adults with mild to moderate hypercholesterolemia[72,73] Artichoke (*Cynara scolymus*): Based on clinical trials, dry artichoke extract is recommended to treat hyper lipoproteinemia, preventing atherosclerosis and coronary heart disease[74]
Chamomile	Male	40-60	4	Chamomile (*Matricaria chamomilla*): No data are available[58]

High blood pressure with diabetes

Mixture of roca, fenugreek, onion and garlic	Male	60+	4	Rocket (*Eruca sativa*): Studies showed significant reduction in glycaemia as discussed earlier, with no data were available on antihypertensive or antidiabitic effects[75,76] Fenugreek (*Trigonella foenum-graecum*): Results from clinical trials support beneficial effects of fenugreek seeds on glycemic control in persons with diabetes However, no data on antihypertensive effect were available[77]

Appendix 2: Continued

High blood pressure with lipidemia				
Mixture of anise, chamomile and roselle	Male	60+	4	Anise (*Pimpinella anisum*): No data are available[78]
				Chamomile (*Matricaria chamomilla*): People who experience blood pressure spikes due to stress, the tea may contribute indirect benefits. Chamomile tea may help reduce anxiety levels and lower blood pressure slightly[79]. No data on antidiabetic effect were available
				Roselle (*Hibiscus sabdariffa*): In addition to its antihypertensive effect as discussed earlier, the results regarding the hypolipidemic effect are mixed. Some early research suggests that taking *Hibiscus* extract by mouth or consuming hibiscus tea might lower cholesterol levels in people with metabolic syndrome or diabetes. However, other early research shows that taking a specific extract of hibiscus leaves does not improve cholesterol levels in people with high cholesterol[80-82]

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