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Original Article

A Cross-Sectional Study of Community Attitude towards Herbal Products against Hepatobiliary Diseases in Northern Cyprus

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ABSTRACT

Aim: The study in Northern Cyprus aimed to improve patient-centered care and healthcare practices by examining community perceptions of Herbal Products (HPs) for liver and biliary diseases. **Materials and Methods:** The self-administered questionnaire utilized in this cross-sectional study, which was carried out in Nicosia, Northern Cyprus from October 2021 to July 2022, allowed 446 participants to provide information on their sociodemographic characteristics and attitudes toward HPs. **Results:** It was observed that liver diseases are common in Northern Cyprus, with 48.2% suffering from some form. HP use was determined at 47.8%. Pharmacies were the most commonly sought-after sources of information at all education levels, followed by physicians. Camellia sinensis was the most commonly consumed plant, followed by Cynara scolymus, Curcuma longa, Taraxacum officinale and Glycyrrhiza glabra. On the other hand, Silybum marianum was unpreferred. **Conclusion:** The knowledge of both the healthcare profession (physicians, pharmacists, etc.) and the community in Northern Cyprus need to be improved on the HPs, however, there exists the need for more studies, and instruction on HPs with particular emphasis on safety.

Keywords Hepatobiliary diseases, Herbal products, Northern Cyprus, Hepatoprotection, *Cynara scolymus*, *Taraxacum officinale*.

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INTRODUCTION

A large number of deaths and morbidities are related to liver diseases and complications, posing an important global economic burden.[1] Among liver diseases are viral hepatitis, Alcoholic or Nonalcoholic Liver Disease (ALD or NAFLD), cholestatic liver disease, cholangiopathies, and autoimmune liver disease, resulting in advanced-stage liver diseases, such as cirrhosis and hepatic malignancies. Despite this, the clinical management of these liver diseases is still quite challenging as a result of late diagnosis, progression, poor understanding of pathogenesis, and a lack of effective therapeutic strategies.[2] Conventional or synthetic drugs used to treat liver diseases often lead to serious side effects, thus there are many debates about treatments of choice, among which are herbal products (HPs), which have been used since ancient times.[3,4] Some of the most commonly used plant(s) and their HPs against liver and biliary diseases are milk thistle (*Silybum marianum* L.),[5] dandelion (*Taraxacum officinale* L.), artichoke (*Cynara scolymus* L.), and turmeric (*Curcuma longa* L.).[6]

There is a paucity of thorough understanding about this particular field of medical practice in Northern Cyprus, which has hampered the development of evidence-based practices and customized interventions, despite the growing recognition of the significance of liver and biliary health, especially in light of their significant impact on overall wellbeing. Due to the lack of empirical evidence concerning medical management of hepatobiliary diseases with HPs, optimal healthcare strategies, therefore highest quality of patient care, cannot be effectively delivered. Data can be generated via studies that closes these gaps in knowledge, evidence-based guidelines generated, and treatment optimizations effected by taking into consideration the healthcare requirements of the population in North Cyprus.

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Studies in other topics have been conducted in North Cyprus before. Studies on HP-based treatment of diabetes mellitus,[7] pregnancy[8] have been conducted before in Northern Cyprus. Also in 2023, a study about Complementary and Alternative Medicines in Northern Cyprus: Public Awareness, Patterns of Use, and Attitudes were conducted in Northern Cyprus.[9]

The aim of this study was to elucidate the perception of HPs against liver and biliary diseases by the community in Northern Cyprus, as well as to perform a cross-sectional evaluation of their current knowledge and attitude concerning the usage of HPs via questionnaire. As far as the authors know, this is the first report on the HPs usage against liver and biliary diseases attitude of the community of Northern Cyprus in specific, and the world in general.

MATERIALS AND METHODS

Study Design and Informed Consent

This cross-sectional self-administered questionnaire study was conducted in the community of Nicosia, Northern Cyprus from October 2021 to July 2022 among the general population. Diversity of backgrounds and life circumstances representative of the community was ensured during data collection. The primary strategy in the sampling volume was accessing as many participants as possible. Therefore, any person with legal standing to provide informed consent was considered to be eligible, so as to provide as diverse a socioeconomic background as possible. Minors were thus excluded from the study. Informed consent was obtained from the participants in both verbal and assumed digital form. Verbal consent was obtained by informing the potential participants of the nature of the study and asking them if they would like to participate. Assumed digital consent was in the form of a disclaimer on the first page of the questionnaire form, detailing the study and the data to be collected, and informing the participants that they should only proceed with the questionnaire if they consented to their information being processed in fitting with the aims of the study.

Population and Setting

The population of Northern Cyprus in 2020 was reported as 382.836. When the needed sample size of the designed study was calculated by Raosoft®, the required sample size needed to be minimum 384 for the present study. In-depth comprehensive literature review was undertaken to verify the relevance, validity and contextual propriety of the questionnaires before their creation. Both the contents and the structure of the questionnaire were created based on the information produced from the literature review. A panel of experts from the community of Nicosia was convened to assess the appropriateness of the questionnaires. The panel consisted of 3 pharmacists with at least 5 years of experience as community pharmacists, 3 physicians with at least 5 years of experience in internal medicine, 3 academics with at least 5 years of experience in the fields of phytotherapy, pharmaceutical botany or pharmacognosy, and 3 individuals randomly selected. Modifications were made to the questionnaires based on the feedback provided by the panel. The questionnaire was presented in the Turkish language, using formal language and the questions were designed to be closed-ended, with definitive answer selections to each question. The questionnaire was designed to be completed in approximately 15 to 20 min.

Once the questionnaire design was finalized, a pilot study was conducted with 20 individuals to identify potential issues and unforeseen challenges, as well as test the measures implemented to mitigate such issues. Also tested were the timing allocated to the questionnaire, the approachability of the subject and the detection of potential linguistic ambiguities. The data obtained from the pilot study was excluded from the study and the data analysis present in this study.

All participants included in the study participated under strict confidentiality and of their own volition. It was clearly explained and understood that their participation was voluntary and entirely anonymous, with all personal information being kept confidential and only the minimum required data being collected. Demographic information was also collected, with basic sociodemographic data such as age, gender and level of education, as well as income, in addition to study-related information such as their source of procurement of HPs and knowledge of said products.

The questionnaire data was collected face-to-face or online using Survey Monkey®. Questionnaires consisted of questions for sociodemographic information and attitudes against HPs. 446 participants responded completely to the questionnaire so the required sample size has been achieved. Although the study was conceived before the COVID-19 pandemic and therefore was a face-to-face questionnaire, the pandemic necessitated a conversion to an online questionnaire form to allow its completion during the pandemic.

Statistical Analysis

The collected data were cleared, entered into, and evaluated using the Statistical Package for Social Sciences (SPSS)/ PASW version 26.0 for Windows (IBM, Chicago, IL).

Ethical Approval

Ethical clearance was obtained from the Near East University Ethics Committee (YDU 2020/86-1250), and consent was obtained from all respondents before participation in the study. The study was also conducted in conformity with international guidelines for human studies. Personal information was deidentified before the data analysis.

RESULTS

Sociodemographic Characteristics

A total of 446 people of the community in Northern Cyprus participated in the study, the majority of them were women (*n*=265, 59.4%) and between the ages of 18-24 years (*n*=97, 21.7%). Most participants work as healthcare professionals (*n*=126, 28.3%) or civil servants (*n*=115, 25.8%). Approximately half of the participants were educated to the level of bachelor's degree (*n*=211, 47.3%). The income level was in the middle segment for more than half of the participants (*n*=250, 56.1%). A minimum of 0-5 years of job experience was held by the vast majority of community/patient participants in the study (24.2%). Table 1 summarizes information about the sex, age, educational level, working area, and work experience and income level of participants.

The results indicated that among the participants (*n*=446), 231 (51.8%) had no diagnosed liver or biliary system ailments, followed by NAFLD with 184 (41.3%). The rest answered with HBV (Hepatitis B Virus) (*n*=15, 3.4%), HCV (Hepatitis C Virus) (*n*=7, 1.6%), alcoholic cirrhosis (*n*=4, 0.9%), and primary biliary cirrhosis (*n*=3, 0.7%). None of the participants had autoimmune hepatitis. Two participants declined to answer. An age-dependent increase in NAFLD was observed among the participants, rising from 9.4% in participants aged 18-24 to 95.3% in participants aged 65 and over. Liver disorders become more prevalent as individuals get older. The age group of 55-65 had the highest percentage of individuals with a liver disorder at 10.4% (*n*=46) except the ones with no diagnosis yet (*n*=10).

The frequency of HPs use was considered to be a crucial factor in determining the attitude of the community toward HPs. The majority of participants (*n*=213, 47.8%) reported using herbal products occasionally, while 34.8% used them very rarely. Only a small percentage either never or always use HPs (*n*=27, 6.1%, and *n*=14, 3.1%, respectively).

Pharmacies are the primary source for approximately a third of the participants (range: 28.4%-31.3%, *n*=131) at all education levels, followed by doctors with a range of 13.8%-25.0% (*n*=67). As the education level increases, the use of the internet as a source of information declines from 14.9% to 3.1%, with an overall 12.6% utilization rate (*n*=56). Herbalists are not widespread sources of information for the participants, with less than 3.6% (*n*=16) among all education levels using them. Families and friends also comprise a significant proportion of information sources, making up 14.6% (*n*=65) of all participants.

The vast majority of participants procure their HPs from the pharmacy (*n*=343). This is followed by herbalists, which serve as the supply for *n*=66 participants, then the internet (*n*=22).Figure 1 provides information on the preference for plant(s) and/or their HPs for hepatobiliary disorders by the community of Northern Cyprus, as well as the absolute numbers and percentages of usage. The participants were given the option to select one or more HPs to indicate their preference.

Table 1: Sociodemographic characteristics of participants.

Variable	Community n (%)
Sex	
Female	265 (59.4%)
Male	178 (39.9%)
Unspecified	3 (0.7%)
Age	
18-24 years	97 (21.7%)
25-34 years	93 (20.9%)
35-44 years	86 (19.3%)
45-54 years	65 (14.6%)
55-64 years	62 (13.9%)
65+years	43 (9.6%)
Educational level[a]	
Associate degree	87 (19.5%)
Bachelor's degree	211 (47.3%)
MSc	116 (26.0%)
MD	32 (7.2%)
Working Area	
Health Care Professional	126 (28.3%)
Community	87 (19.5%)
Civil Servants	115 (25.8%)
Retired	51 (11.4%)
Other	65 (14.6%)
Unspecified	2 (0.4%)
Work experience	
0-5 years	107 (24.0%)
6-10 years	87 (19.5%)
11-20 years	115 (25.8%)
21-30 years	74 (16.6%)
31+ years	60 (13.5%)
Unspecified	3 (0.7%)
Income Level	
Low	162 (36.3%)
Middle	250 (56.1%)
High	30 (6.7%)
Unspecified	4 (0.9%)

[a]Among the participants, no one answered with either "MD Specialist" or "PhD".

It was observed that *Camellia sinensis* (L.) Kuntze (green tea) was the most commonly consumed plant (80.9%) against hepatobiliary diseases by the participants, followed by *Cynara scolymus, Curcuma longa, Taraxacum officinale* and *Glycyrrhiza*

glabra L. at preference rates of 78.0%, 47.1%, 29.6% and 27.1%, respectively. On the other hand, *Silybum marianum* was one of the least preferred plants (5.4%).*C. scolymus* and containing HPs were reported to be used by 67.5% of the participants with no diagnosis yet. Similarly, in alcohol-independent fatty liver disease, the majority of the participants (92.4%) were using this plant and/or containing products. However, it is important to note that the observed increase in usage from 67.5% to 92.4% following the diagnosis of alcohol-independent fatty liver disease does not necessarily imply a causal relationship. Over 70% of the participants diagnosed with HBV (*n*=11), HCV (*n*=5), or alcoholic cirrhosis (*n*=3) reported the usage of *C. scolymus.*

C. longa was preferred for use by less than half of the total of the participants who had no diagnosis yet (*n*=111, 48.1%). The percentage of usage reached its highest with participants diagnosed with alcohol-independent fatty liver disease (48.9%).

S. marianum was reported as "not used" by 94.6% of all participants. Some participants diagnosed with HBV (20.0%) or primary biliary cirrhosis (33.3%), were reported as "using", however the total number of those participants (*n*=15, 3.4% and *n*=3, 0.7%, respectively) was relatively low.

T. officinale is preferred by 70.4% (*n*=314) of all participants. Undiagnosed participants utilized *T. officinale* at a rate of 18.2% (*n*=42), whereas those diagnosed with alcohol-independent fatty liver disease utilized it at a much higher percentage of 41.3% (*n*=76).

C. sinensis was the most commonly consumed plant (80.9%) against liver and biliary diseases among the participants. 73.6% of undiagnosed participants reported (*n*=170) using it while 91.8% of those diagnosed with non-alcoholic fatty liver disease (*n*=169) reported using it. Similarly, the majority of respondents with HBV (80.0%, *n*=12) and HCV (71.4%, *n*=5) reported using green tea. Among the 25.0% of participants with alcoholic cirrhosis (*n*=1) and all the respondents diagnosed with primary biliary cirrhosis reported using green tea (*n*=3).

Among the participants, those with diagnosed liver and biliary diseases had a higher use of *G. glabra* (27.1%) versus those without diagnosis (23.4%). On the other hand, the usage of this plant increased relatively with various diagnoses. Approximately half of the HBV diagnosied participants (46.7%) were reported to use this plant, however, the vast majority of the HVC diagnosed participants (85.7%) reported not using this plant.

The plants and their products reported as "not used" by the majority of the community in Northern Cyprus were *R. officinalis*, rosemary (*n*=380, 85.6%), *A. absinthium*, wormwood (*n*=433, 97.5%), *Helichrysum* spp. (*n*=436, 98.2%), *A. millefolium,* yarrow (*n*=414, 93.2%), *C. asiatica,* gotu kola (*n*=438, 98.7%), respectively.

DISCUSSION

The findings show that approximately half of the community living in Northern Cyprus (*n*=213, 47.8%) report occasionally using HPs, placing a major load on pharmacists and physicians to maintain current knowledge of HPs and their potential interactions with other medications as well as any side effects and cautions. Studies done in the past support this finding.[10-12] Additionally, based on the findings and when compared to other studies, it was discovered that HP consumption varied by nation.[13] As an illustration, 66.8% of people in Nigeria,[14] 63.5% of people in Kuwait,[15] 39.2% of people in Turkey,[16] and 33.9% of people in Malaysia[17] have used HPs.

Prevalence of Liver and Biliary Disorders among Participants

The vast majority of the participants had no diagnosis, however, among the participants who have been diagnosed with a liver and biliary disease, NAFLD (41.3%), HBV (3.4%), and HCV (1.6%)

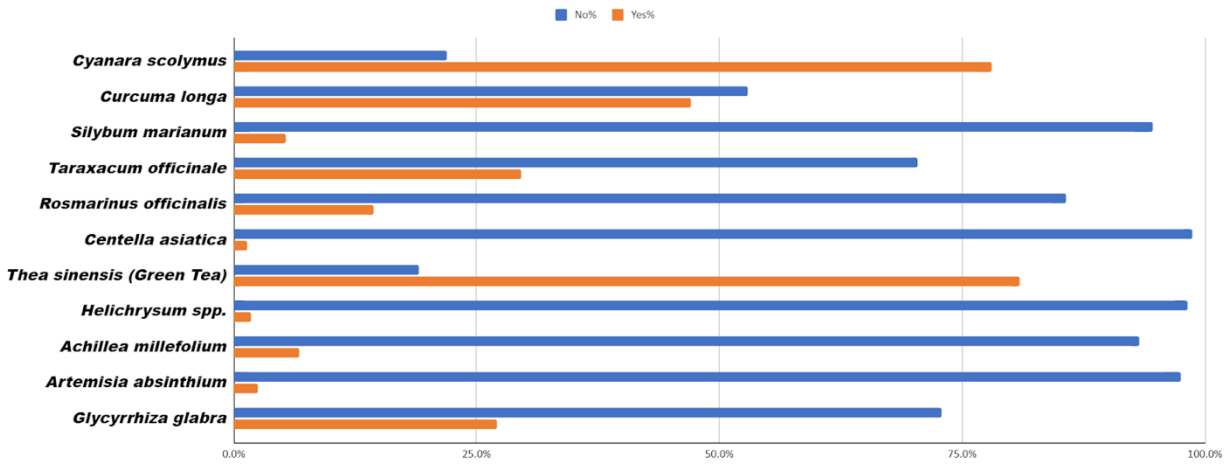

Figure 1: The preference for plant(s) and/or their HPs for hepatobiliary disorders by the participants.

were the most prevalent disorders. Additionally, the prevalence of liver disorders increases with age.

A previous study was conducted in Northern Cyprus, including 25,442 individuals from 113 different nationalities. Of these, 17,529 were male (68.9%) and 7,913 were female (31.1%), with a mean age of 34.32±14.24 years (range: 0-102). While 339 (1.35%) of 25,068 applicants were positive for HBsAg test, the corresponding rates for anti-HCV and anti-HIV were 31 (0.1%) in 24,973 and 9 (0.04%) in 24,044, respectively. When only the seropositivity rates of the citizens of the Republic of Cyprus were analyzed, HBsAg was found to be 0.8%, anti-HCV 0.014% and anti-HIV 0.03%. When HBsAg and anti-HCV seropositivities were compared in terms of gender, no statistically significant difference was found, while those who were anti-HIV positive in the screening tests (100%, *n*=9) were all male.[18]

A cross-sectional study was performed using the data of blood centers of two hospitals (Nalbantoglu General Hospital, Nicosa and Akcicek Military Hospital, Kyrenia) in Northern Cyprus between January 2000 and January 2001. A total of 17,545 people between the ages of 20 and 56 (mean SD, 34.5 10.3) years, including 13,546 males and 3,999 women, were involved in the study. In all groups, the prevalence of HBsAg was 2.46%, anti-HCV was 0.46%, anti-HIV was 0.00%, HBV DNA was 2.25%, and HCV RNA was 0.33%. Group I had the lowest overall HBsAg positive (2.16%). In terms of HBsAg positivity rates, there was a significant difference between groups I and II (2=6.11, *p*=0.047). Anti-HCV prevalence did not differ significantly across groups (2=0.32, *p*=0.852).[19]

Herbal products and/or supplements used for liver and bile diseases

The findings imply that a substantial proportion of participants with liver and biliary problems, notably those with non-alcoholic fatty liver disease, HBV, and HCV, prefer to use mostly *C. sinensis* (green tea) and its products. In the literature, it was shown that *C. sinensis* possesses hepatoprotective effects by reducing liver damage caused by alcohol, viral hepatitis etc. due to a variety of phenols and catechins.[20] However, there might also be an association between green tea and liver damage in some cases. Due to (-)-epigallocatechin gallate or its metabolites which, depending on the patient's metabolism, can possibly induce oxidative stress in the liver and cause hepatotoxicity.[21]

C. scolymus (artichoke) is a widely utilized herbal medicine or supplemental food in liver and biliary disorders. It is a flowering plant in the Asteraceae family with hepatoprotective properties. Studies have shown that artichoke extract may be beneficial in treating various liver conditions, including liver damage caused by AFLD, NAFLD, and hepatitis. It has also been investigated for its potential in improving bile flow and relieving symptoms associated with biliary disorders such as gallstones and cholecystitis. A study in 2015 investigated its hepatoprotective effects against carbon tetrachloride-induced liver damage, demonstrating a reduction in hepatic enzymes and improvements in liver histology in the presence of the extract[22] Biliary tract disorders arise from the reduction of bile secretion and/or difficulty of reaching to intestinal lumen due to the gallbladder stones, atonia of biliary ducts etc., The leaf preparations of *Cynara scolymus,* which is the most advised plant, is supported for dyspeptic complaints by the German Commission E[23] The majority of participants in the present study reported its use in all types of hepatobiliary disorders in Northern Cyprus.

C. longa is used as a spice that contains curcuminoids, such as curcumin, its primary active ingredient, with hepatoprotective,[24] antioxidant and anti-inflammatory properties that can help protect the liver from damage and improve liver function.[25] The U.S. Food and Drug Administration (FDA) has declared *C. longa* to be "generally safe". Jaundice, hepatitis, and other liver diseases are all treated with turmeric. The correlation between *C. longa* and liver damage was confirmed in a systematic review.[26] Further studies reported an association with acute liver injury. One of the studies suggested that *C. longa* usage is becoming popular for weight loss in combination with *Piper nigrum* (black pepper) and its major active constituent piperine, an alkaloid which increases the bioavailability of curcumin. Contaminants in *P. nigrum* were suggested to be responsible for hepatotoxic effects.[27]

S. marianum is one of the well-known plants offered for hepatoprotective effect by the German Commission E. It contains a flavonolignan complex called silymarin, which has antioxidant[28] and anti-inflammatory properties that help to protect the liver from damage and promote liver regeneration. Jaundice, hepatitis, and other liver diseases are all treated by *S. marianum*; however, it was one of the least consumed plants against liver and biliary disease by the participants in the present study. Recently, its mechanism of action against NAFLD was reported. It was reported that the hepatoprotective activity of this plant and its main active compound silymarin was mainly on regulation of biological processes and immune system processes.[7] According to a study, silymarin therapy significantly reduced viral load and liver enzymes in Hepatitis C positive patients when compared to placebo.[29] Similar improvements were observed in individuals with viral hepatitis, according to a meta-analysis of 8 randomized controlled studies.[30] PBC patients receiving silymarin therapy also had significantly improved liver function and reduced liver fibrosis when compared to placebo.[31]

T. officinale roots and leaves are commonly used in herbal medicine to support liver health. It helps stimulate the production of bile, aiding in the digestion of fats and has diuretic properties that can help flush toxins out of the liver.[8] Numerous pharmacological properties of *T. officinale* have been noted, including hepatoprotective, anti-inflammatory, and antioxidant actions. According to a study, *T. officinale* root extract reduced

oxidative stress and improved liver function tests.[32] The study revealed interesting patterns among different participant groups. Among the undiagnosed participants, 18.2% reported utilizing *T. officinale*, suggesting that even individuals without specific medical conditions are aware of its potential benefits and are incorporating it into their lifestyle. A notable observation is the higher utilization rate of *T. officinale* among individuals diagnosed with NAFLD, with 41.3% of them reporting its usage.

G. glabra has been studied for its hepatoprotective properties. Some studies have suggested that certain compounds in it, such as glycyrrhizin and flavonoids, may exhibit antioxidant and anti-inflammatory effects that could be hepatoprotective.[33] A significant portion of the community is aware of the potential benefits of *G. glabra* root and is incorporating it into their treatment practices. It was reported that the long-term usage of *G. glabra*, which was used by almost 30.0% of the community in Northern Cyprus, is moderately toxic, manifesting hypertension and hypokalemia-induced secondary disorders.[34]

CONCLUSION

The participants living in Northern Cyprus have a high proclivity to consult experts such as physicians and pharmacists for assistance and direction concerning HP utilization. According to the present study, many individuals, especially those who had NAFLD, HBV, or HCV, prefer *C. sinensis* and HPs containing this plant. *C. sinensis*'s hepatoprotective effects, attributed to its phenols and catechins, have been documented, although potential associations with liver damage have also been suggested. The knowledge of both the healthcare profession (physicians, pharmacists etc.,) and the community in Northern Cyprus needed to be improved on the HPs used for the protective and therapeutic effects on liver and biliary diseases, as demonstrated by low usage preference for *Silybum marianum*. However, the lack of knowledge of the potential preventive and therapeutic properties of this plant by both physicians and pharmacists in Northern Cyprus may be the cause of the low preference for the usage of this plant and its HPs. Further data analysis is challenging because of the possibility that the individuals used the HPs combined with other drugs or therapies.

The results point to the need for more studies and instruction on herbal medicines used for hepatobiliary diseases in Northern Cyprus, which can be accomplished by raising awareness, strengthening pharmaceutical curricula, and raising the level of knowledge among health professionals and patients through training programs, especially taking into consideration the trust that the population of Northern Cyprus have in their pharmacists and the ease of access to community pharmacies. Particular interest can be paid to the adverse effects of HPs and the safe utilization practices necessary to minimize the manifestation of such effects.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AFLD: Alcoholic Fatty Liver Disease; **ALD:** Alcoholic Liver Disease; **FDA:** Food and Drug Administration; **HBV:** Hepatitis B Virus; **HCV:** Hepatitis C Virus; **HP:** Herbal product; **NAFLD:** Non-Alcoholic Fatty Liver Disease.

CONTRIBUTION OF AUTHORS

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Dudu Özkum Yavuz, Ali H. Meriçli, Duygu Yiğit Hanoğlu and Umut Sözüöz conceived of the presented idea. Fehmi B. Alkaş performed statistical analysis and computations. Azmi Hanoğlu helped supervise the project. All authors discussed the results and contributed to the final manuscript.

SUMMARY

This study in Northern Cyprus looked at community perceptions of Herbal Products (HPs) with the goal of improving patient-centered care and healthcare practices. It was found that 48.2% of people in Northern Cyprus had some kind of liver ailment. At all educational levels, pharmacies were the most frequently requested information sources, followed by doctors. The plant that was most frequently consumed was *Camellia sinensis*. The data showed that both patients and pharmacists lacked sufficient knowledge about the use of herbal medications for hepatobiliary disorders. Still, further research is required, as is education regarding HPs with a focus on safety.

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