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Original article

Libyan Endemic Medicinal Plants for Patients with HCV and Those Undergoing Dialysis: Future Perspectives

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Abstract
This paper focuses on endemic plants in Libya and their medicinal use, particularly their antiviral activity, specifically their antiviral activity in treating HCV cases in Haemodialysis Units (HD). It emphasises the active constituents of these plants and presents data accurately collected from recent research published in trustworthy internet sources, including PubMed, ScienceDirect, Scopus, Google Scholar, and Wiley. Among these publications. Notably, the Asteraceae family emerged as the most dominant family, featuring three species. The literature also presented numerous medicinal plants that effectively managed HCV infections. A comprehensive list of 12 medicinal plants belonging to 8 families showed beneficial action against HCV and kidney illness. The major bioactive compounds implicated in the kidney therapy have been identified. These compounds include Polyphenols such as phenolic acids, flavonoids, and tannins. By recognising the therapeutic properties of these endemic plants, we can enhance treatment options for HCV and related kidney disease complications. Moreover, many of the polyphenols showed anti-HCV activity. The use of these natural compounds is fundamental due to their lower production costs, as they are not chemically synthesised. Understanding these therapeutic properties leads to the development of effective treatment for both HCV and kidney disease complications.
Keywords. Endemic plants, Bioactive compounds, Anti-HCV, Kidney disease, Libya, Efficacy.

Introduction

Medicinal herbs encompass compounds that are not only beneficial to people's health but also provide biological defences against herbivores. Using plant materials in herbal medicine or extracts can help treat various illnesses, alleviate discomfort, and enhance overall well-being. The plant kingdom includes higher plants, microbes, algae, and lichens that are rich in phytochemical bioactive compounds. Interestingly, the number of discovered bioactivities related to antiviral properties is 1500–1600, emphasising the potential of these natural resources in developing new therapies [1, 2, 3]. The estimated numbers of phytochemicals and bioactive compounds in the plant kingdom are shown in (Figure 1).

Moreover, naphthoquinones, alkaloids, polyphenols (e.g., flavonoids), lignans, anthraquinones, phenolic acids and their derivatives, coumarins, nitrogenated compounds, terpenes, and peptides are among the active compounds found in these plants that contribute to phytoantiviral therapy. (Figure 2) depicts the mechanism of what happens in the virus. Herbal medicine, which is known as traditional medicine, is the first source of modern medicine through the extraction of its active ingredients. It is worth noting that the use of biologically active compounds varies worldwide depending on the type of traditional medicine: Ayurveda, the indigenous medical system of India, is based solely on the use of alkaloids and polyphenols; European traditional medicine relies mainly on strychnine, quinine, and morphine; and Chinese traditional medicine focuses on camptothecin and Taxol [4]. Traditional Arabic Medicine (TAM) is a well-known traditional medical system referred to sometimes as Unani medicine, Graeco-Arabic medicine, humoral medicine, or Islamic medicine [5]. Islamic medicine is known to be used for disease prevention and treatment. Because of the rise of Islam and Islamic culture in the seventh century, specifically the spread of the Prophet Muhammad, peace be upon him, Hadith, this type of traditional medicine is widely recognised as Tibb Al-Nabawi [6]. Many of the traditional prophetic medicinal herbs contain bioactive chemicals and have biological activities (antiviral) and are used to treat and prevent viral infections [7].

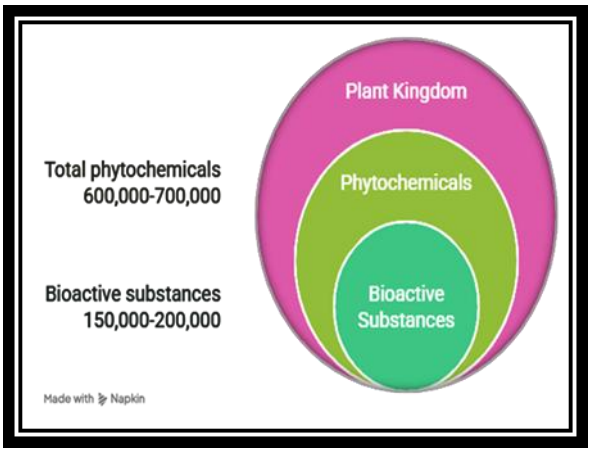


Figure 1. The estimated numbers of phytochemicals and bioactive compounds in the plant kingdom

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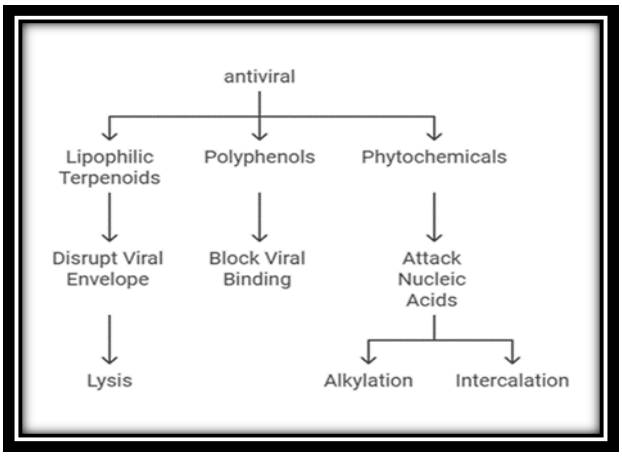


Figure 2. Depicts the mechanism of what happens in the virus

The use of traditional medicine is gaining extraordinary focus from pharmaceutical companies. Furthermore, the World Health Organisation reports that around 20,000 plants are used for illness treatment. The use of medicinal plants has led to significant scientific output, with progress reaching a peak in 2010. Since 2010, publications of components for drug research and synthesis have stabilised at about 5,000 per year [8, 9]. (Figure 3) shows the rate at which people around the globe use these plants for medicinal purposes.

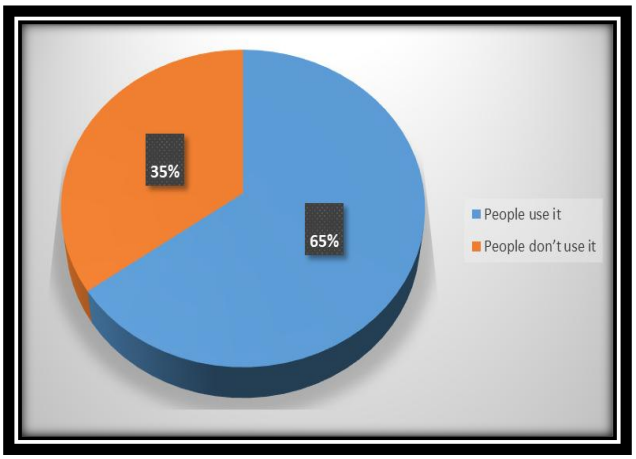


Figure 3. The rate at which people around the world use plants as medicine

In a timely progression, medicinal herbs gained an important role in the innovation of novel medications. From 1950 to 1970, about 100 plant-based novel medications were introduced into the US drug market, including deserpidine, reseinnamine, reserpine, vinblastine, and vincristine, all derived from higher plants. According to the development of science and, more interestingly, novel medications such as etoposide, eguggulsterone, z-guggulsterone, teniposide, nabilone, plaunotol, lectinan, artemisinin, and ginkgolides were introduced to pharmacies all over the world between 1971 and 1990. Moreover, 2.0% of medications were introduced to the medical industry, including paclitaxel, topotecan, gomishin, and irinotecan between 1991 and 1995 [10]. Figure 4 depicts the evolution of medicinal plant discoveries and medication development.

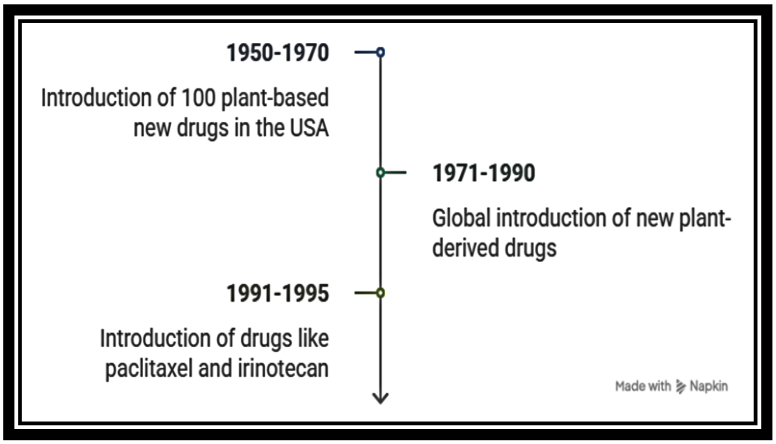


Figure 4. The evolution of medicinal plant discoveries and drugs

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Rainfall in northern Libya fluctuates between 100 and 500 mm/year, whereas in the south, it only reaches 10 mm/year. Libya is noted for its rich and varied geography, which includes plateaus, mountains, valleys, and deserts, influencing the character and diversity of the plant system [13]. Similar to all other cultures worldwide, Libyans use indigenous medicinal herbs to cure a range of illnesses. For thousands of years, the people who live in the Green Mountain region of Libya (Al-Jabal Al-Akhdar) have used the medicinal plants that are grown there, creating a rich folk herbal medicine tradition that has persisted over the years [14]. Based on the flora of Libya, we can divide the three areas into the coastal area, the Jabal Nafusa area, and the Al-Jabal Al-Akhdar area. Coastal areas include Leptis Magna, the Kaam area, Misurata, Wadi El-Ghattara, Jafara Plain (Wadi Ghado), Sidi-Omeer, Misurata (Sassu Valley), Wadi El-Enaghar, Zliten (Wadi El-Zekr), and Zliten coast. The Jabal Nafusa area includes Wadi Kaam and Wadi Malah. Al-Jabal Al-Akhdar area features Wadi Al-Agar, Wadi Derna, Wadi Al-Zagzoog, Wadi Asra, Valley Jarjr-oma, Wadi Haboon, Sidi Abu-Ras, Wadi Zaza Al-Abiar (Sidi Amohamed forest), and Ain Mara. Furthermore, the greatest valley on the Green Mountain (Al-Jabal Al-Akhdar), which is home to Wadi Al-Kouf, is home to a wide variety of aromatic and therapeutic plants. There are 107 species of medicinal plants from 49 families and 93 genera in Wadi Al-Kouf. With 38 families, 79 genera, and 89 species, dicotyledons are the biggest group of angiosperms; in contrast, monocotyledons only have 8 families, 10 genera, and 13 species. With 11, 9, 6, and 6 species each, the Asteraceae, Lamiaceae, Fabaceae, and Solanaceae families have the greatest number of species [3]. In 1989, the Flaviviridae family's enveloped positive single-stranded RNA virus, known as HCV, was identified as the cause of non-A, non-B hepatitis [15].

Infection with HCV puts a heavy burden on healthcare systems around the world. Moreover, hepatocellular carcinoma is primarily caused by a prolonged infection with HCV [16]. High rates of sustained virologic response are achieved by novel treatments based on direct-acting antivirals [17]. HCV infection is a worldwide health concern, resulting in acute or chronic hepatitis. Standard therapy is costly and poorly tolerated. New therapies utilize direct acting antivirals, which are expensive and may not be accessible to all patients. Natural bioactive compounds are being studied for their biological activity, antiviral properties, and potential advantages such as chemical diversity, low production costs, and minimal side effects [18,19]. Additionally, HCV transmission is commonly associated with direct percutaneous exposure to blood, such as blood transfusions, healthcare- related injections, and injectable drug use [20].

In addition, Libya provides free HD maintenance for end-stage kidney illness through a rapidly expanding network of centres, and there is a widespread consensus that patients on HD should be tested for HBV and HCV infections before starting treatment and evaluated every 3–6 months thereafter. Dialysis for seropositive patients is performed on dedicated machines in a separate room or alongside seronegative patients if space is limited. In contrast, haemodialysis patients are at a higher risk of viral hepatitis due to frequent blood transfusions and prolonged vascular access [21,22,23, 24,25,26]. The purpose of this perspective paper is to summarise some important thoughts and findings on medicinal plants endemic to Libya with bioactive compounds to treat hepatitis C and kidney dialysis patients simultaneously. Based on recently obtained literature, this paper will explore several intriguing current trends and prospects for these compounds, which play an essential role in the field of natural product research.

Methods

Data on medicinal plants with antiviral properties and the flora of Libya were gathered from online databases such as PubMed, ScienceDirect, Scopus, Google Scholar and Wiley. The search terms employed were antiviral activity, hepatitis C, kidney dialysis patients, active components, and medicinal plants. The most recent published data from the previous five years on the major outcomes of symptoms and the impact of medicinal herbs on the liver and kidney. On a priority basis, one or two publications are chosen as references for each plant species from the Web of Science journals and the most recent years.

Results

Table 1 provides a summary of medicinal plants. The botanical name, life form, active ingredients, and the methods used are provided for each plant, along with the diseases treated and therapeutic effects. The dominant family was Asteraceae, with 3 species. Additionally, medicinal plants that have been studied and reported in the literature for the treatment and management of Hepatitis C were included. A comprehensive list of 12 medicinal plants belonging to 8 families that exhibit activity against Hepatitis C and kidney disease is presented, with some plants showing efficacy for both conditions.

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Table 1. Medicinal plants endemic in Libya with antivirals

Family	Botanical name	Lifeform	Active ingredients And part of use	Diseases treated	Therapeutic effects	References
Asteraceae	*Onopordum cyrenaicum* Maire & Weiller	*Th	Dehydromelitensin -8-(4'-hydroxy-methacrylate), flavonoids, acetylenic substances, steroids, triterpenes Leaves,seeds,fruits	Hepatitis\ Antimicrobial effects	-	(27,28,3)
	Helichrysum stoechas (L.) Moench	Ch	Arzanol pyranone / flowers	High antioxidant activity, anti-inflammatory, antiviral properties, enhance both liver and kidney function	+	(29,49,50,51)
	Silybum marianum (L.)	Th	Silymarin / seeds	Positive effect on liver and kidney functions	+	(19, 30,31,52,53)
Lamiaceae	*Teucrium polium* L.	Ch	Phenolic microencapsulated / leaves	Improvement in liver and kidney function, antioxidant and antibacterial activities	+	(32,54)
Polygonaceae	*Polygonum maritimum* (L.).	H	Avicularin, gallic acid, polygonic acid, saponins, flavonoid myricetin-3-O-rhamnoside / Seeds	Kidney disorders, diarrhea, bleeding, Hepatitis C, Anti -inflammatory	+	(3, 33, 60)
Solanaceae	*Solanum nigrum(L).*	Th	Solasonine, solanine, solanidine, solamargine/ leaves	Liver complaints, skin infection, constipation, Hepatitis C	-	(3,34)
Asparagaceae	*Asparagus stipularis* Forssk.	Ph	Saponin, asparagine, phenolic; flavonoid / leaves, stem, pericarp	Liver disorder, stomach ache, rheumatism, natural antioxidants, anticancer	-	(3,35)
Fabaceae	*Glycyrrhiza glabra (L.)*	Ch	Glycyrrhizin Polyphenols/ roots	Hepatitis C	-	(19,39)
	Vachellia nilotica (L.)	Ph	Tannins, flavonoids, saponins, lignans, proteins and peptides/ The pods, bark, leaves, and fruits	Hepatitis C antioxidant, antiviral, Anti-mutagenic	**-**	(16)
Oleaceae	*Olea europaea (L.)*	Ph	Polyphenolic compounds / leaves	Against hepatitis, antiviral activity, antimicrobial effect	-	(7, 40)
Cucurbitaceae	*Ecballium elaterium (L.)*	H	Flavonoids/ fruits and fruit juice, flowers and leaves	Antiviral activity, antioxidant effect	-	(36, 37) (38)
	Citrullus colocynthis (L.)	H	Phenolic compounds / fruit	Antiviral activity, antioxidant and antimicrobial	-	

**Phanerophytes (Ph), Chamaephytes (Ch), Therophytes (Th), Hemicryptophytes.+ Both the liver and kidney can be used, except for Teucrium polium, which requires medical supervision.- Not assessed except for Glycyrrhiza glabra. Does not give.*

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Prevalence of The Plants

Asteraceae has been documented as the most dominant family in Libya, representing 237 species [41,42]. It can be found in various locations throughout Libya. In the east, it was the largest family in the Sedy Boras region, represented by 130 species [3,43]. Moreover, Asteraceae was found to dominate the valley of Wadi Belkaf with 18 species [44]. Generally, Asteraceae was recorded as the family with the highest number of endemic genera in Al-Jabal Al-Akhdar [3,45]. In addition, according to the flora of Libya, *Onopordum cyrenaicum* Maire & Weiller Wild, native to north-eastern Libya, is endemic to the coastal area of Wadi El-Enaghar, as seen in (Figure 5).



Figure 5. Onopordum cyrenaicum

Also, *Helichrysum stoechas* (L.) Moench Wild has a native range in the W. & Central Mediterranean regions. It is a medicinal plant and an endangered species in Libya. The Jabal Nafusa area (25 km W. of Khoms), Rumia (15 km from Yefren), Tagma (5 km from Yefren), Bir El Ghanum, El Naggazah, Msallata National Park (Shaafeen), Tarhuna (Msaaed, Msabha), Msallata-Garaboulli Province, and Gharyan (Sedrores Mountains) are notable locations. Moreover, in the coastal areas of Tripoli, Leptis Magna, Sabrata, and Misurata, there are regions of coastal areas, Tripoli Beach dunes in Karkurah, and the Zliten coast. *Helichrysum stoechas* is visible in (Figure 6).



Figure 6. Helichrysum stoechas

In addition, the plant *Silybum marianum* (L.) Wild, native to the Mediterranean, Central Asia, and Ethiopia, is a medicinal plant. Jabal Nafusa area Al-Amamra (10 km) E. of Al-Kussbat, Msallata (Shaafeen), Msallata National Park (Shaafeen), Msallata-Garaboulli Province, Gharyan (Sedrores Mountains), Wadi Kaam (Dam & Lake, Main Course, Headwaters), Coastal Area, Leptus, Megna, Kaam Area, Sabrata, Al-Hdaba Treatment Plant Tripoli, Sabratha, Coastal of Tripoli, Wadi El-Enaghar, Zliten (Wadi EL-Zekr). (Fig. 7 depicts *Silybum marianum*. So, Asteraceae, the most dominant family in Libya, can be a good source of antivirals.

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Figure 7. Silybum marianum

Figures 8 to 16 also include *Teucrium polium*, *Polygonum maritinum*, *Asparagus stipularis*, *Solanum nigrum*, *Ecballium elaterium*, *Citrullus colocynthis*, *Glycyrrhiza glabra*, *Vachellia nilotica*, and *Olea europaea*. They belong to the Lamiaceae, Polygonaceae, Solanaceae, Asparagaceae, Cucurbitaceae, Fabaceae, and Oleaceae, respectively.



Figure 8. Teucrium polium



Figure 9. Polygonum maritinum

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Figure 10. Asparagus stipularis



Figure 11. Solanum nigrum



Figure 12. Ecballium elaterium



Figure 13. Citrullus colocynthis

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Figure 14. Glycyrrhiza glabra



Figure 15. Vachellia nilotica



Figure 16. Olea europaea

Discussion

This study emphasised the potential of medicinal plants as antiviral medications, paying special emphasis to compounds such as polyphenols, which include flavonoids, phenolic acids, tannins, Dehydromelitensin-8-(4'-hydroxy-methacrylate), acetylenic substances, steroids, triterpenes, caffeoylquinic acids and Silymarin.The genus *Onopordum* L. contains about fifty species of the tribe Cardueae (Asteraceae family).Sesquiterpenoids, flavonoids, acetylenic substances, steroids, triterpenes, lipids, and chemicals containing nitrogen are among the metabolites that have been identified from *Onopordum* species [27]. Furthermore, a number of substances found in *Onopordum* species have good or exceptional biological qualities. For instance, polyphenols and caffeoylquinic acids. It's worth noting that caffeoylquinic acids isolated from *O. illyricum* have been linked to antibacterial and antifungal, hepatoprotective, choleretic, diuretic, and bile-expelling properties, as well as the inhibition of HIV integrase, a crucial component of HIV replication and its insertion into host DNA, and the defence of proteins, lipids, and DNA against oxidative damage brought on by free radicals. Choleric, diuretic, bile-expelling, hepatoprotective, and antifungal and antibacterial properties [46].

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In addition, [47,48] these two studies report that *Helichrysum stoechas* extracts, administered as infusions in rat models, significantly reduced kidney stone formation and improved urinary biochemical parameters in sodium oxalate-induced urolithiasis. Both preventive and curative effects were observed, with the greatest preventative efficacy at a dose (156mg/kg) (stone formation score: 1.16), while the sodium oxalate group had the largest frequency of kidney stones (stone formation score: 2.66). The available evidence from these two studies supports the traditional use of *Helichrysum stoechas* for kidney stone prevention and treatment. Furthermore, the evidence base is limited by the small number of studies, lack of mention of sample sizes, and absence of detailed statistical analyses or adverse effect reporting in animal models. Moreover, evidence for hepatic effects remains insufficient based on these two investigations.

In contrast, Arzanol, a phloroglucinol α-pyrone compound from *Helichrysum italicum*, has potent anti-inflammatory and antiviral properties. It inhibits NF-κB and suppresses pro-inflammatory cytokines, inhibits HIV-1 replication in T cells, and has strong antioxidant activity. It also inhibits the mPGES-1 enzyme and PGE2 biosynthesis, contributing to its anti-inflammatory effects [49, 50]. In diabetic rat animal models, the benefits of *Silybum marianum* extract, another plant in the Asteraceae family, seem to enhance both liver and kidney function. The doses between 200 and 400 mg/kg of extract for 14 days decrease liver enzymes.

Additionally, it may offer protection against renal and hepatic diseases [51]. Moreover, silymarin treatment reduced the severity of hepatic damage when compared to that observed after APAP treatment, decreasing neutrophil infiltration in the hepatic tissue, which further indicated its significant hepatoprotective effect. [52]. In this respect, developing innovative therapeutic techniques, such as antioxidant supplementation with the flavonoid silymarin, aims to protect against the damage caused by ischemia and reperfusion in kidney tissues [53].Probably, several phenolic compounds, ranging from 121.6 to 975.3 µg/g DW, including ferulic acid, cinnamic acid, gallic acid, caffeic acid, salicylic acid, catechin, ellagic acid, and chrysin, were found in *Teucrium polium*, belonging to the Lamiaceae family, according to the phytochemical analysis. This is another intriguing piece of information to talk about. The microencapsulated phenolics indicated improvement in the growth, liver function, and morphometric parameters of the ileum and antioxidant- and inflammation-related gene expression [32]. On the other hand, excessive dosages of this drug may be harmful to the kidneys and liver. However, due to the toxicity of medicinal plants, their unsupervised use should be avoided [54]. In such studies, one of the main bioactive substances found in *Polygonum* L. plants, including *P. chinense*, *P. capitatum*, *P. amphibium*, *P. salicifolium*, and *P. hydropiper*, which belongs to the family Polygonaceae, is quercetin (QCN) [55]. However, the researchers here did not mention *Polygonum maritimum* (L.). So, the researchers should search for it. QCN demonstrated safety and resulted in a 25% reduction in viral load for some patients. In a Phase I clinical trial with patients who have the hepatitis C virus [56]. In another study, at a dosage of 1.25 mg/ml, an in vitro investigation demonstrated a 95% inhibition of NS3 serine protease and a 70% reduction in viral replication [57]. QCN's oral bioavailability in humans varies greatly, ranging from 0% to 50%, and is subject to phase I and II metabolism in organs such as the small intestine, liver, and kidneys, which leads to metabolic breakdown in the gastrointestinal tract. [58, 59].

In addition, according to Custorio, the flavonoid myricetin-3-O-rhamnoside (8.135 mg/g), which is thought to have anti-inflammatory properties, predominated in acetone extracts produced from the aerial organs of micropropagated *P. maritimum*. [60]. It is evident that several plant-derived compounds, such as polyphenolic and flavonoid compounds, demonstrated potent inhibition of hepatitis C virus replication in vitro. The mechanism of antiviral action of these polyphenolic compounds mainly depends on their diverse abilities to neutralise cytotoxic oxidants, to inhibit essential host or viral enzymes, to inhibit viral binding and penetration into cells, and to trigger the host immune system. [52]. Antiviral medications obviously lower the risk, as evidenced by the recently released haemodialysis (HD) research findings [23]. Although Abdullahinia et al. [61] noted that infection rates in Libya fall into population-based categories rather than reflecting clinical infection, they stressed that these conclusions should not be taken at face value. Libyan researchers like Khalaf [24] reinforced this statement by pointing to infection among population-based categories as one of the causes. On the other hand, Ahmad et al. [25] and Ali et al. [26] emphasised the necessity of implementing measures in hemodialysis clinics.Furthermore, more studies are needed to thoroughly understand clinical and demographic risk factors, according to Abubakeer et al. [62]. This result is in line with Atampugbire et al. [63], who claim that to fully realise the potential of therapeutic plants, research is required to improve the selectivity of plant extracts and reduce toxicity levels. Moreover, future research may examine biosurfactant-based formulations to improve the solubility, stability, and delivery of these compounds, potentially boosting their antiviral activity.

Conclusion

In conclusion, this is the first study that illuminates endemic plants in Libya, which possess substantial bioactive components like polyphenols that exhibit anti-HCV activity. The latest literature review is relevant to both HCV patients and those in dialysis clinic patients. Moreover, the current study provides a list of 12 medicinal plants from eight families that demonstrate efficacy against HCV and kidney disease, with some plants serving as remedies for both. The predominant family was Asteraceae. Medicinal plants have a promising future because they are low-cost to produce and do not require chemical synthesis. Substantial bioactive components could be vital in the treatment of HCV cases and kidney disease complications.

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Conflict of interest
The author declares no conflict of interest.

Data availability
All data were provided in the manuscript.

Disclaimer
The manuscript is the author's original work and has not been published previously, nor is it under consideration for publication elsewhere.

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