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Journal of Hepatocellular Carcinoma

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EXPERT OPINION

Al-Hijamah (Prophetic Wet Cupping Therapy) is a Novel Adjuvant Treatment for Viral Hepatitis That Excretes Viral Particles and Excess Ferritin Percutaneously, Synergizes Pharmacotherapy, Enhances Antiviral Immunity and Helps Better HCC Prevention and Treatment: A Novel Evidence-Based Combination with Prophetic Medicine Remedies

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Abstract: Viral hepatitis progresses to liver cirrhosis and HCC. Several challenges are facing Sovaldi treatment to viral C hepatitis, eg, viral resistance, difficulty to treat all genotypes, and inability to access treatments in low-income countries. Also, current treatments to Hepatitis B are still challenging. Ideal treatments to viral hepatitis should decrease the viral load, enhance antiviral immunity and repair the viruses-induced tissue damage. That is still beyond reach. High serum ferritin in viral hepatitis correlates with chronicity, increased necro-inflammation, hepatotoxicity, progression to cirrhosis, unresponsiveness to treatments and viremia. Previously, Al-hijamah (wet cupping therapy of prophetic medicine) significantly cleared thalassemic children of causative pathological substances (CPS), eg, excess ferritin, free radicals and serum lipids. Moreover, Al-hijamah significantly increased the antioxidant power and potentiated the natural antiviral immunity, eg, increasing CD4 count, CD8 count and CD4/CD8 ratio. Likewise, the author suggests Al-hijamah as a novel promising adjuvant treatment for viral hepatitis (B and C) for percutaneous excretion of CPS as hepatitis viral particles, excess ferritin, inflammatory mediators, free radicals, and antigen-antibody complexes. Published reports proved that Al-hijamah exerted tissue-protective effects, and cleared blood through the fenestrated skin capillaries in a pressure-dependent and size-dependent manner (a kidney-like manner). That collectively may decrease the viral load for better HCC prevention and supports the evidence-based Taibah theory (Taibah mechanism). Same therapeutic benefits apply to other viral illnesses as AIDS. Even after HCC development, Al-hijamah is quite mandatory for excretion and clearance of CPS that favor malignancy, eg, lactate (Warburg effect), growth factors, metalloproteinases, and others. Al-hijamah-induced immune potentiation benefits HCC patients. Combining Al-hijamah with other natural antioxidant remedies of prophetic medicine, eg, nigella sativa, costus, natural honey, Zamzam water and others will maximize the therapeutic benefits. In conclusion, Al-hijamah and other prophetic medicine remedies are recommended adjuvants to current pharmacological treatments to viral hepatitis and HCC.

Keywords: hepatitis viruses, Al-hijamah, wet cupping therapy, prophetic medicine, Taibah theory, fenestrated skin capillaries and serum ferritin

Background

Hepatitis B and C viruses are oncogenic viruses due to incorporation of their nucleic acids into the hepatocytes' genome. Hepatitis B virus is a DNA virus that directly incorporates into the hepatocytes' genome. Hepatitis C virus is an RNA virus where DNA can be produced from RNA by activity of reverse transcriptase enzyme. Newly produced viral DNA genome can integrate into genome of infected hepatocytes and become oncogenic. Malignant transformation through viral hepatitis infection may occur mainly through the activation of cancer genes (proto-oncogenes) and suppression of tumor suppressor genes.[1,2] Viral hepatitis is a common potentially fatal health problem due to its long-term sequelae, especially in developing countries. Hepatitis B and C may progress to chronic hepatitis and liver cirrhosis. Hepatocellular carcinoma is a possible complication of liver cirrhosis and may complicate the chronic viral infection itself.[3]

Unfortunately, several challenges are facing sofosbuvir (Sovaldi) treatment to viral C hepatitis including viral resistance, difficulty to treat all the genotypes, and inability to provide treatment access in low-resource countries and in special populations.[4] Over the past few decades, the hepatitis C virus (HCV) epidemic has spread to many nations. According to estimates, 34,000 persons in the United States alone died in 2017 as a result of serious hepatitis C consequences such as cirrhosis and liver cancer. Drug injection is responsible for 43% of the hepatitis C virus disease burden globally and 79% of the disease burden in high-income nations. The World Health Organization (WHO) created a worldwide health strategy to eradicate hepatitis C virus infection as a public health issue by 2030 as a result of the development of extremely effective direct-acting antiviral therapies for the disease in recent years.[5]

Diagnosis of Viral Hepatitis Infection

Raised liver enzymes may support the diagnosis of hepatitis. Detection of HCV antibodies (HCV Ab) or HBV surface antigen (HBs Ag) using enzyme-linked immuno-sorbent assay (ELISA) is diagnostic. Polymerase chain reaction (PCR) is better than ELISA as a diagnostic tool as it diagnoses the presence of nucleic acids of hepatitis viruses (DNA in hepatitis B and RNA in hepatitis C). Diagnosis and monitoring the increase in the number of hepatitis viral copies in patients' sera can be done using PCR and is helpful to monitor and predict the future and outcome of the treatment. HBs Ag is a sign of active disease and is detected during the incubation period while HBV envelop antigen (HBe Ag) appears during the incubation period and is detected in the acute stage of the disease and in some chronic carriers.[2,6]

Current Management of Viral Hepatitis Still Faces a Lot of Obstacles

Current treatment for HBV infection includes alpha interferon together with lamivudine and adefovir (both are nucleoside analogues that inhibit HBV replication through inhibiting HBV-DNA polymerase). Unfortunately, they are not quite effective. Current treatment for HCV infection includes Sovaldi (the golden standard), alpha interferon and ribavirin. Treatment for viral hepatitis is so expensive, time-consuming and with serious side effects.[7–11] Unfortunately, several challenges are facing Sovaldi treatment to viral C hepatitis including viral resistance, difficulty to treat all genotypes, and inability to provide treatment access in low-resource countries and in special populations.[4] This may necessitate introducing new adjuvant treatments as Al-hijamah that can work by different mechanisms to treat viral hepatitis as will be discussed here.

Hepatocellular Carcinoma Exhibits the Warburg Effect

Hepatocellular carcinoma (HCC) is the third most common cancer in the world and a primary liver cancer with over 90% are primary HCC. HCC's occurrence and progression are tightly correlated with the Warburg effect (permanent production of lactate from glucose even in the presence of oxygen). Warburg effect is tumors' unique glucose oxidation to give the pro-oxidant lactate (but not the antioxidant pyruvate) even in the presence of oxygen.

Warburg Effect and Cancer Cells' Products in HCC

Like most solid tumors, HCC cells exhibit the Warburg effect (Figure 1). HCC cells follow the same cancer biology criteria as other tumors, eg, increased glucose uptake, increased glycolysis (glucose oxidation), restricted mitochondrial oxidative

Otto Warburg

Warburg effect in HCC

= tumors' unique glucose oxidation to give the pro-oxidant lactate (but not the antioxidant pyruvate) even in the presence of oxygen.

- In the presence of oxygen, normal hepatocytes utilize glucose and produce pyruvic acid that enters Krebs cycle. Totally, 38 ATP molecules/one glucose are formed.
- In the absence of oxygen, normal hepatocytes utilize glucose and produce lactate & 2 ATP molecules/one glucose.
- Even in the presence of oxygen, HCC cells utilize glucose and produce lactate & 2 ATP molecules/one glucose.

Figure 1 HCC cells exhibit the Warburg effect.

phosphorylation, increased pentose phosphate pathway, and enhanced glutamine breakdown. High serum lactate in cancer patients (Warburg effect) mediates chemoresistance, radioresistance, angiogenesis, metastasis and invasion.[12,13]

Prophetic medicine is the body of knowledge about medicine that has been derived from the teachings, customs (sunnah), ahadith (sayings), actions, and agreements of Prophet Muhammad, peace be upon him. All prophetic medicine remedies are natural antioxidants. Both therapeutic and preventive aspects are present in prophetic medicine. All therapies from prophetic medicine are natural antioxidants, including Al-hijamah (prophetic medicine's wet cupping therapy), which works by clearing the body of harmful pathological chemicals by excreting excess oxidants. The medical literature is currently fertile ground for innovative studies on the subject of prophetic medical cures.[14]

Examples of prophetic medicine remedies include Al-hijamah (wet cupping therapy of prophetic medicine that clears blood using the fenestrated skin capillaries) (Figure 2A), Ajwa dates of Aliah (from Al-Madinah, Saudi Arabia), nigella sativa, costus (saussurea lappa), oral honey, sana (senna, cassia angustifolia), sanut (fennel, foeniculum vugulare), and other natural treatments. All are abundant in dozens of all-natural antioxidant compounds that prevent the oxidative stress-related cellular and tissue damage that individuals with viral hepatitis frequently experience.[15]

Expert Opinion: Al-Hijamah (Combined to Other Prophetic Medicine Remedies) as a Promising Adjuvant Treatment to Current Hepatitis Treatments

Al-hijamah is a promising adjuvant treatment for viral hepatitis (B and C) for percutaneous excretion of hepatitis viral particles, excess ferritin (Box 1), inflammatory mediators, free radicals, and antigen-antibody complexes and potentiating the antiviral immunity (Box 2).

Details of this expert opinion include:

1. Hepatitis patients have excess serum viral particles, ferritin, inflammatory mediators, oxidants, free radicals and antigen-antibody complexes that cannot be excreted in urine through the kidneys. Al-hijamah is a reported general clearance treatment for serum, interstitial fluids and tissues,[16,36–40] so that Al-hijamah is highly recommended for treating hepatitis patients (Figures 2B and 3).
2. Hepatitis patients maximally and significantly benefit from Al-hijamah (wet cupping therapy of prophetic medicine) as did thalassemia patients in clearing the serum and the body from disease-causing substances as reported in our previous publications.[16,18,31,33,36–40]

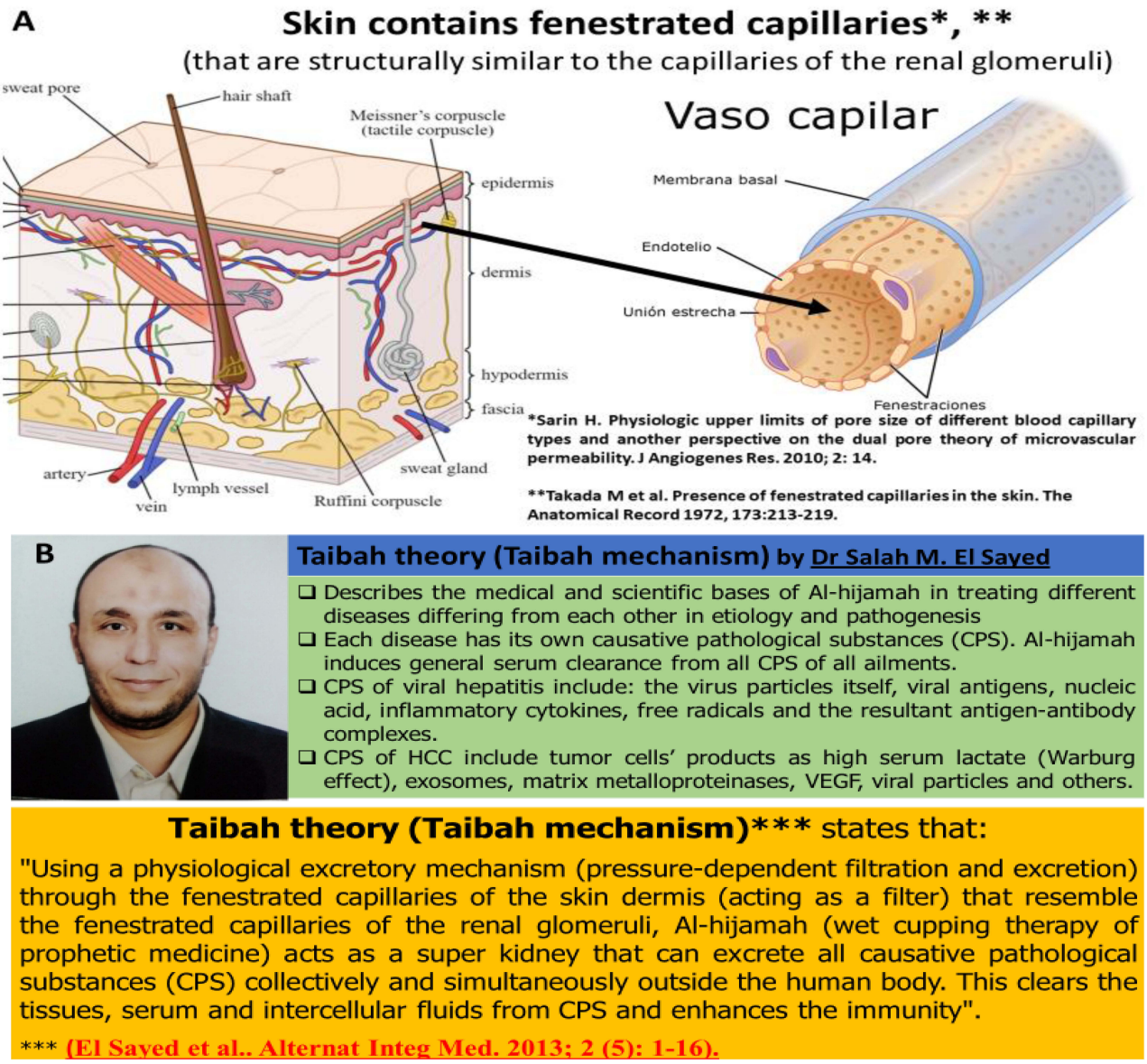

Figure 2 There is a structural similarity between the fenestrated capillaries in the skin dermis (superficial subepidermal capillary plexus) and the renal glomerular capillaries. **Notes**: (**A**) The skin may act as a super-kidney during Al-hijamah for proper excretion of the disease-causing substances. (**B**) Scientific bases of Taibah theory for explaining how Al-hijamah (wet cupping therapy of prophetic medicine) works in treating different diseases. Data from these studies.[16,17].

3. Based on biochemical, pharmacological, histological and Al-hijamah backgrounds, Al-hijamah can excrete the hepatitis viral particles, excess ferritin, inflammatory mediators, free radicals, and antigen-antibody complexes via the percutaneous route (Figure 3).
4. High serum ferritin is a major problem in both hepatitis patients and thalassemia patients. High serum ferritin in viral hepatitis correlates with chronicity and viremia. In thalassemic patients, Al-hijamah effectively cleared thalassemic children of causative pathological substances (CPS) that included excess ferritin.[18] So, Al-hijamah will do the same (blood clearance of serum ferritin) in hepatitis patients.
5. Al-hijamah excretes and clears thalassemic patients of free radicals[18] and serum lipids.[16,18,31,33,36–40]
6. Al-hijamah significantly increased the antioxidant power (deficient in hepatitis patients).[18,36] So, Al-hijamah will do the same (blood clearance of serum from excess lipids) in hepatitis patients.

Box 1 Importance of Decreasing Serum Ferritin in Patients Having Viral Hepatitis. Serum Ferritin Was Significantly Decreased via Direct Excretion Using Al-Hijamah

- Serum ferritin is a strong predictor of treatment response in viral hepatitis.[19]
- Increased serum ferritin is in chronic hepatitis C patients is associated with a decreased response to interferon therapy.[20]
- Patients with chronic hepatitis C may be more sensitive to iron hepatotoxicity than patients with hemochromatosis.[21]
- Increased serum ferritin marks iron-induced oxidative stress that contributes to chronicity of hepatitis C, non-alcoholic and alcoholic liver diseases.[22]
- Hyperferritinemia and hepatic iron overload are commoner in chronic hepatitis B and more severe in patients co-infected with hepatitis D virus.[23]
- Increased serum ferritin correlates with severe necro-inflammatory activity in hepatitis patients.[24]
- High serum ferritin, ALT, γ-glutamyl transpeptidase, liver iron concentration, and increased liver stiffness are markers of HCV viremia.[25]
- Iron overload plays a role in hepatic fibrogenesis and carcinogenesis. Hyperferritinemia in hepatic patients can be explained by cellular necrosis, synthesis increase, inflammation and iron overload.[26]
- Increased iron accumulation in the liver is a risk factor for hepatocellular carcinoma in patients with alcoholic cirrhosis ± nonalcoholic hepatosteatosis.[27]
- Phlebotomy (decreases serum ferritin and iron overload) improves therapeutic response to interferon in patients with chronic hepatitis C.[28]
- Iron depletion was associated with a biochemical response in 22% of patients who did not respond to interferon monotherapy.[29]
- Iron depletion in patients with chronic hepatitis C who have elevated serum ferritin values induces a significant reduction in necro-inflammatory activity (notable decrease in average alanine aminotransferase values) and improves their response to subsequent treatment with interferon.[30]

Note: Data from This Study.[18]

Box 2 Suggested Therapeutic Benefits of Al-Hijamah to Viral Hepatitis Patients

1. Increasing the antiviral immunity[31]
2. Excreting viral particles percutaneously (Taibah mechanism).
3. Excreting disease-causing substances as ferritin and free radicals.[18]
4. Potentiating the pharmacological effects of current therapeutics.
5. Exerting tissue-protective effects.[32]
6. Normalizing serum liver enzymes.[32]
7. Excreting excess lipids, eg, cholesterol and triglycerides.[32]
8. Excreting abnormal proteins as antigen-antibody complexes (Taibah theory).
9. Treating associated co-morbidities that may augment hepatitis and other viral infections, eg, immune suppression.[33,34]
10. Alleviating some drugs-induced side effects, eg, Ribavirin reduces absolute lymphocytes counts in Hepatitis C virus infection[35] while Al-hijamah induces lymphocytosis.[31]

7. Al-hijamah potentiated the natural antiviral immunity in thalassemic children, eg, increasing CD4 count, CD8 count and CD4/CD8 ratio. So, Al-hijamah will do the same (increasing the antiviral immunity) in hepatitis patients. All these reported benefits are quite beneficial and helpful to hepatitis patients.
8. In thalassemic children, Al-hijamah proved to be tissue-protective via inducing a significant decrease in serum oxidants (as malondialdehyde), iron overload,[18] liver enzymes and excess serum lipids.[36] So, Al-hijamah will do the same tissue-protective effects in hepatitis patients.
9. Al-hijamah alleviates some drugs-induced side effects, eg, Ribavirin reduces absolute lymphocytes counts in Hepatitis C virus infection[35] while Al-hijamah induces lymphocytosis.[31] So, Al-hijamah will be hepato-protective in hepatitis patients.
10. Other viral diseases like AIDS can benefit from the same treatment advantages. Al-hijamah is absolutely necessary for the excretion and removal of CPS that promote cancer, such as lactate (the Warburg effect),[41] growth factors, metalloproteinases, and others, even after cancer (as HCC) has developed.[13] Immune potentiation brought on by al-hijamah is very beneficial to cancer patients as HCC.[13,31]
11. 11. To maximize the therapeutic effects, combine al-hijamah with other natural antioxidant remedies of Prophetic medicine, such as nigella sativa, costus, natural honey, Zamzam water, and others.[14,16,36]

Current evidences supporting this expert opinion:

- High serum ferritin in viral hepatitis reflects disease chronicity, increased necroinflammation, hepatotoxicity, progression to cirrhosis, unresponsiveness to treatments and viremia (Box 1). Excretion of serum ferritin through Al-hijamah was confirmed in thalassemia patients[18,31,36] and will benefit hepatitis patients so much via reversing excess ferritin effects.
- Current evidence includes the published reports that Al-hijamah generally clears the human body of disease-causing substances as serum oxidants (malondialdehyde) and potentiates the immunity.[16,18,31,33,36–40]
- The reported results that Al-hijamah causes immunological potentiation, excretion of CPS, and clearance of blood and interstitial spaces[18,31,36] through the fenestrated skin capillaries[16,33,37,38,40] confirmed its therapeutic benefits to hepatitis patients.
- The evidence-based Taibah mechanism (Taibah theory) strongly supports this expert opinion that Al-hijamah excretes all the diseases-causing substances[16,18,31,33,36–40] related to viral hepatitis that may include viral particles.
- Al-hijamah has three major steps applied to the skin: suction, scarifications (shartat mihjam in Arabic) and suction, ie, triple S technique. Al-hijamah benefits from the skin histological structure to excrete CPS through the fenestrated skin capillaries in a pressure-dependent and size-dependent manner (a kidney-like manner), which agrees with the evidence-based Taibah theory (Taibah mechanism).[16,18,31,33,36–40]
- CPS differs from disease to disease according to disease etiology and pathogenesis, so CPS of viral hepatitis include high serum viral particles, viral antigens, viral nucleic acids, inflammatory mediators and high serum ferritin.
- Our previous publications confirmed the success of Al-hijamah to significantly increase the antioxidant power (based on decreasing serum ferritin and free radicals)[18] and potentiating the natural antiviral immunity, eg, increasing CD4 count, CD8 count and CD4/CD8 ratio.[36] Such immunological benefits significantly increase CD4/CD8 ratio in thalassemic patients via increasing total antioxidant capacity/malondialdehyde (TAC/MDA) ratio that takes place via excreting the excess serum oxidants via the percutaneous route.[31] This confirms the therapeutic benefits that can be gained by Al-hijamah treatment to patients having viral hepatitis.

Suggested Mechanisms of Al-Hijamah as a Percutaneous Excretory Procedure That May Clear Serum and Interstitial Fluids of Hepatitis Patients from Disease-Causing Substances

Causative pathological substances (CPS) in viral hepatitis (both HBV and HCV infections) include the virus particle itself (B or C especially during stage of viremia), viral antigens (eg, HBs Ag and HBe Ag), viral nucleic acid (DNA in hepatitis B and RNA in hepatitis C), inflammatory cytokines, free radicals and the resultant antigen-antibody complexes (in hepatitis B) (Figure 3).[7–11] Taibah mechanism for medical bases of Al-hijamah strongly suggests Al-hijamah for treating viral hepatitis. Taibah mechanism states that: "Using a physiological excretory mechanism (pressure-dependent filtration and excretion) through the fenestrated capillaries of the skin dermis (acting as a filter) that resemble the fenestrated capillaries of the renal glomeruli, Al-hijamah (wet cupping therapy of prophetic medicine) acts as a super kidney that can excrete all the CPS collectively and simultaneously outside the human body. This clears the tissues, serum and intercellular fluids from CPS and enhances the immunity (Figure 2A)".[16,39,40]

Taibah Mechanism (Theory) Supports This Expert Opinion (Percutaneous Excretion of Viral Particles and Clearance of Blood and Tissues Using Al-Hijamah)

Based on Taibah theory, CPS for hepatitis patients include the high serum viral particles, viral nucleic acids, free radicals (reactive oxygen species), inflammatory mediators, ferritin and immune complexes. CPS for HCC patients include the high serum tumor cells' products as massive lactate production (Warburg effect),[41] metalloproteinase (MMP) enzymes (facilitating invasion and metastasis), vascular endothelial growth factor (facilitating angiogenesis), free radicals (reactive oxygen species and reactive nitrogen species), and others. Among the MMP family, only MMP1, MMP3, MMP8,

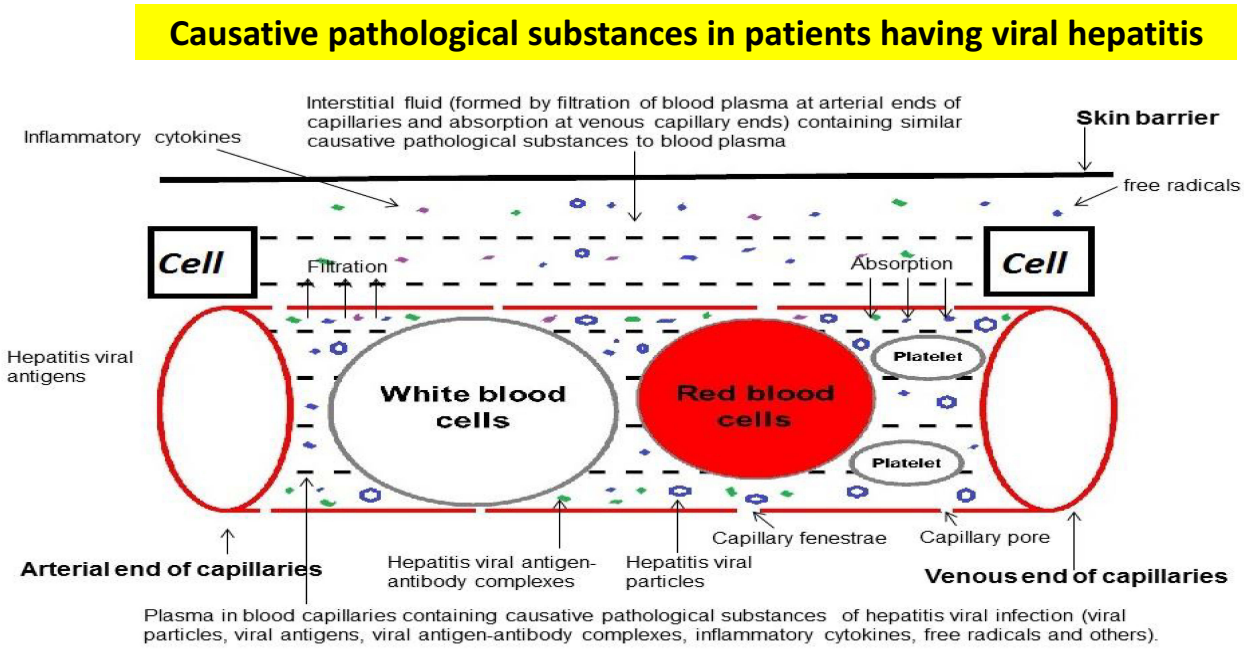

Figure 3 Pathogenesis of hepatitis viral infection.
Notes: Causative pathological substances of viral hepatitis (viral particles, viral antigens, viral antigen-antibody complexes, inflammatory cytokines, free radicals and others) are present in the blood of hepatitis patients and may leak into the interstitial fluids (interstitial fluids are formed through filtration of blood plasma). They cannot be excreted in urine and become retained favoring a chronic viral hepatitis status. Al-hijamah is capable of excreting all the causative pathological substances.

MMP9, MMP11, MMP12, MMP14, MMP15, MMP20, MMP21, and MMP24 significantly increased in HCCs compared with adjacent tissues. Crucially, survival and univariate analyses indicated that only MMPs 1, 9, 12, and 14 predict poor overall survival.[14]

As interstitial fluids are formed by filtration of capillary blood at the arterial ends of capillaries and then become absorbed again at the venous capillary ends,[16,40] the interstitial fluids may contain the same CPS present in the blood plasma in hepatitis patients as evidenced by the presence of infectious hepatitis viral particles in some body fluids, eg, semen and vaginal secretions[7–11] (Figure 4A–F). Puncturing the skin upliftings and applying the second suction step can excrete the collected fluids (Figure 5A–D) and hence decrease the viral hepatitis CPS significantly. The sucking pressure applied during cupping therapy was reported to be from −150 to – 420 mmHg. This suction pressure (filtration force through scarifications created in skin barrier) is transmitted to around the skin capillaries to be added to another less strong filtration force, ie, capillary hydrostatic pressure (−33 mmHg at arterial end of capillaries and −13 mmHg at venous end of capillaries) (Figure 6A–D). Both work as excretory forces against a relatively weaker absorption force, ie, capillary osmotic pressure (+20 mmHg).[16,40] This creates a pressure gradient and a traction force across the skin to drain out the collected and filtered fluids. Suction traction pressure also creates a pressure gradient around the capillaries and increases the filtration at the arterial end of capillaries at a net pressure of −163 to −433 mmHg and at the venous ends of capillaries at a net pressure of −143 to −413 mmHg (Figures 3–6). This results in clearance of blood from CPS and restoration of homeostasis (Figure 7).[16,40]

Prophetic Medicine Remedies as Promising Adjuvants for Treating Viral Hepatitis and HCC

Remedies of prophetic medicine are quite promising for treating viral hepatitis (Figure 8A–C). Among the most important antioxidants in nigella sativa are thymoquinone, carvacrol, and pinene. Moreover, nigella sativa decreases hepatitis viral load, improves response to oxidative stress and improves the clinical condition and glycemic control in

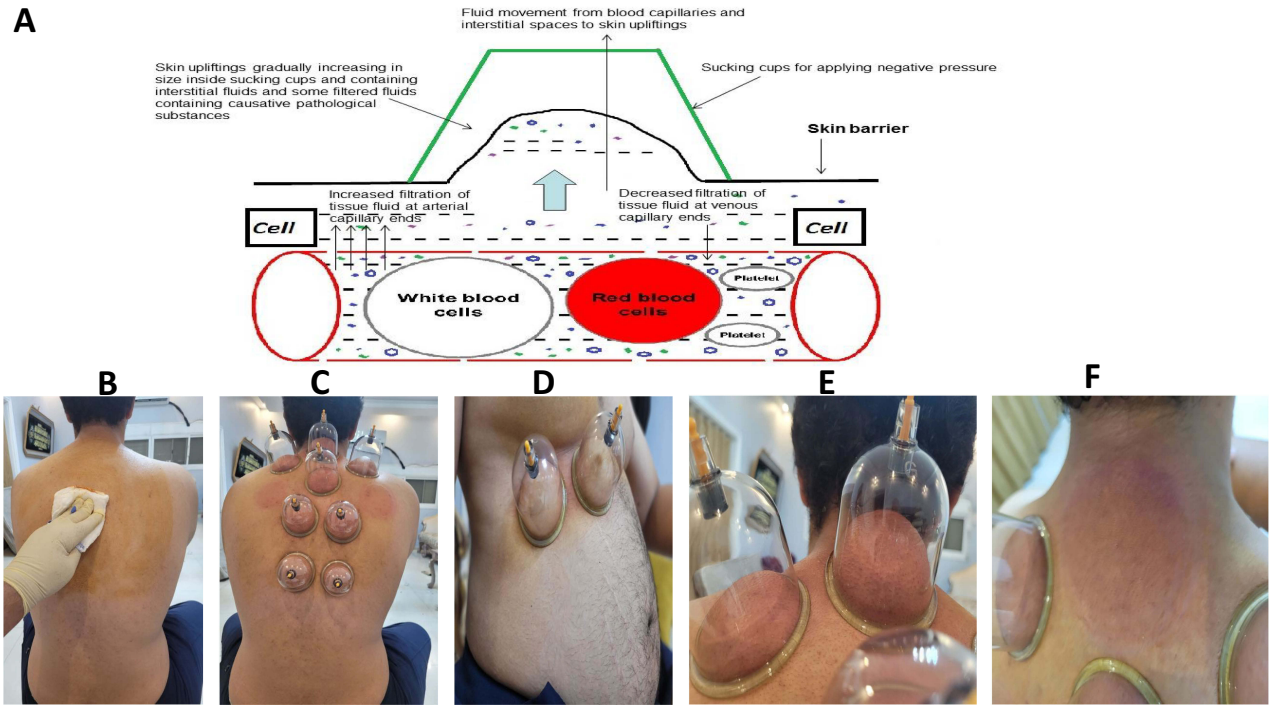

Figure 4 First suction step during Al-hijamah.

Notes: (**A**) Applying suction pressure (inside sucking cups) causes creation of skin upliftings that gradually increase in size inside the skin upliftings. Skin upliftings inside sucking cups contain interstitial fluids, some filtered fluids and causative pathological substances. (**B**) Skin sterilization. (**C**) Applying sucking cups to the upper back region. (**D**) Applying sucking cups to the right hypochondrium (right subcostal region). (**E**) Formation of the skin upliftings where the skin enters inside the sucking cups causing widened peri-capillary spaces and increased filtration of the fenestrated dermal capillaries (beneath the skin barrier). (**F**) Cup margins leave a temporary sign immediately after removal of the cups and before scarification step.

hepatitis patients (Box 3).[42] Natural honey is rich in polyphenols and flavonoids that are strong antioxidants and exert tissue-protective effects (Box 4). Santamarin, dehydrocostus lactone, and costunolide are the principal antioxidants present in costus (Box 5).[15] The preventive and therapeutic benefits of such remedies to the liver include combating hepatitis viruses, reducing hepatitis inflammatory responses, exerting potent antioxidant effects, exerting potent antitoxic effects, exerting potent anti-fibrotic effects, exerting hepatic tissue repair, suppressing carcinogenesis, reverting hepato- 200
cellular carcinoma cells to normal or near normal phenotype, and boosting the natural immunity.[15]

Among the prophetic medicine remedies that were reported to enhance immunity (in addition to Al-hijamah)[31] are natural honey (increased bone marrow cellularity and lymphocyte count) (Box 4),[37] nigella sativa (increased lymphocytes count, CD4 & CD8 lymphocyte count).[32] Costus (saussurea lappa increased the number of macro- phages or lymphocytes),[85] and camel milk (decreased hepatitis C virus load and converted IgG isotype profile to 205
Th1 immunity).[86]

Interestingly, Ajwa dates transformed the malignant phenotype of hepatocellular cancer cells into a phenotype that was very similar to that of normal hepatocytes.[87] This is completely in line with the prophetic hadith that suggested Ajwa date fruit as a remedy and cure for toxins (Box 6).[88] The highly recommended treatment mechanism is the antagonistic relationship between Ajwa antioxidants and toxins-induced oxidant production. 210

How to Quantitate the Therapeutic Benefits of Al-Hijamah to Patients Having Viral Hepatitis (B or C) or HCC?

As we cannot evaluate what we do not measure, quantitative assessment of the therapeutic benefits of Al-hijamah should be performed. That can be done using Al-hijamah indices that were previously reported.[18,93] The five indices for evaluating Al-hijamah and the hijamatologist (the therapist who performed Al-hijamah) are: 215

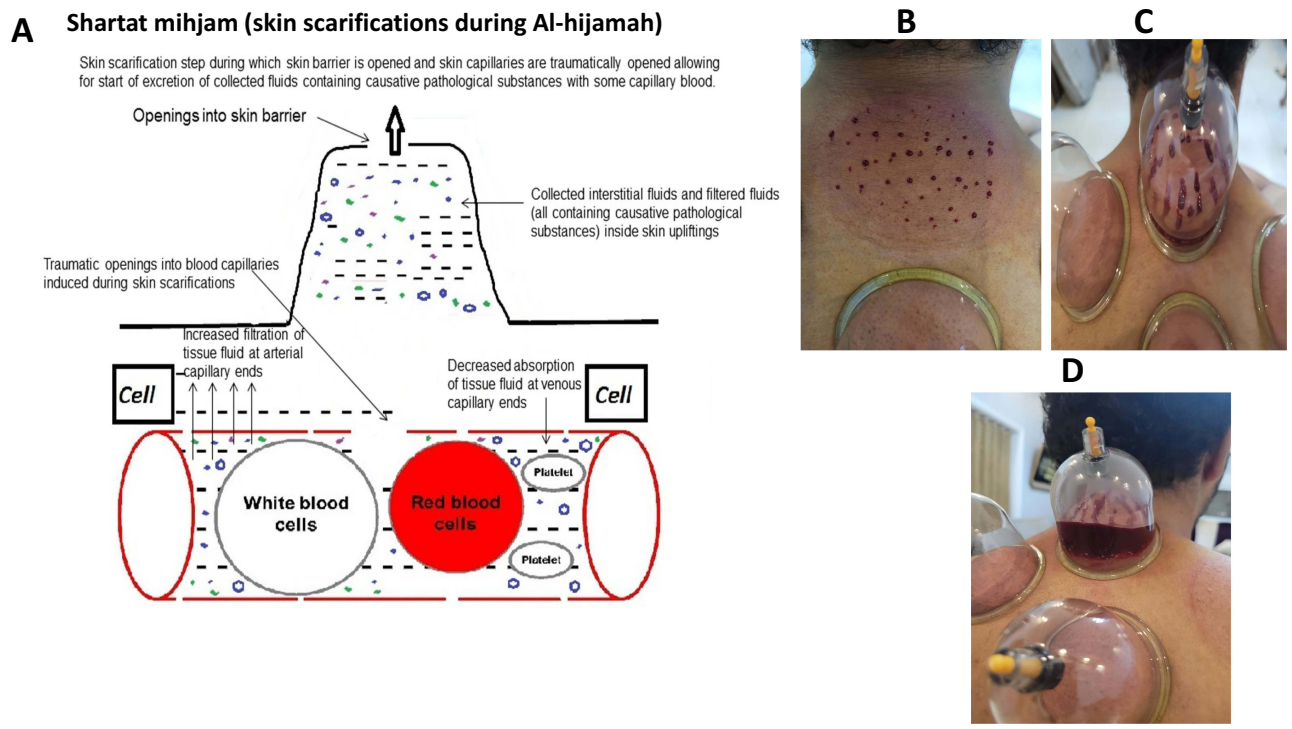

Figure 5 Skin scarification step (shartat mihjam).
Notes: (**A**) Scarifying the skin superficially helps opening the skin barrier and excretion of the collected fluids with causative pathological substances (in agreement with Taibah mechanism). (**B**) Ideal skin scarifications (reflect the hand skills of the hijamatologist) are superficial, longitudinal, vertical, productive, in parallel rows, to the inside of the cup margin, equally done and distributed and covers the whole cup position. (**C**) The bloody excretion increases when adding the sucking cups. (**D**) The bloody excretion is the sum of the excretion coming from all the skin scarifications.

1. Excretion index
2. Clearance index (Purification index)
3. Pharmacological potentiation index
4. Immunological index
5. Clinical therapeutic index

Unfortunately, resistance characterization was reported to ledipasvir and velpatasvir in treating hepatitis C virus genotype 4.[94] Al-hijamah (a minor dermatological and surgical procedure) and other prophetic medicine remedies (nutritional treatments) are simple potentiating natural therapies that synergize the given treatments (and never antagonize them) to patients having viral hepatitis and HCC. The need for Al-hijamah and other prophetic medicine remedies maximizes upon facing drug resistance, treatment failure or co-infection with AIDS.

Practical Example 1: Pharmacotherapy Combined with Al-Hijamah and Other Prophetic Medicine Remedies for Treating Viral Hepatitis and AIDS (for Continuous Medical Education)

Mr XXX is a 48-years-old patient having chronic hepatitis C infection genotype 4. Unfortunately, he was reported to have resistance to ledipasvir and has co-infection with AIDS (unresponsive to highly active antiretroviral therapy, HAART). First blood samples (before ledipasvir administration) indicated that his hepatitis viral load was 3,600,000 copies/mL and his AIDS viral load was 2,000,000 copies/mL. Second blood samples (after ledipasvir administration) indicated that his hepatitis viral load was 3,200,000 copies/mL and his AIDS viral load was 1,500,000 copies/mL. His CD4 count was 198 cells/mm^3 (normal range: 500–1500 cells/mm^3). The physicians decided to keep on the current treatments without change and to add some prophetic medicine remedies as adjuvants. Al-hijamah (wet cupping therapy of prophetic medicine) was done for him by an expert

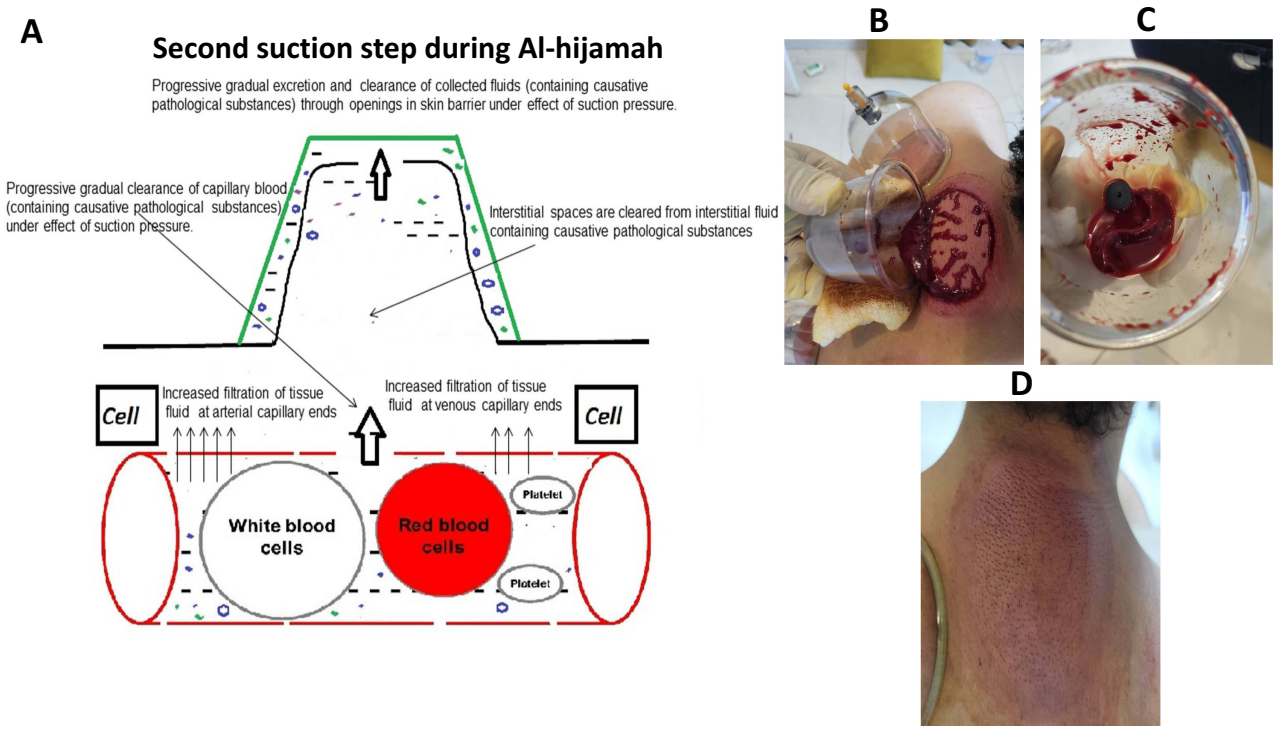

Figure 6 Upon applying the sucking cups again (with opening skin barrier), collected fluids containing causative pathological substances get out completely.
Notes: (**A**) Negative (suction) pressure is transmitted to around the skin capillaries to increase the capillary filtration at both capillary ends, which results in clearance of the capillary blood from causative pathological substances (in agreement with the evidence-based Taibah theory). (**B**) The bloody excretion becomes clotted. (**C**) The bloody excretion is usually small in amount and not profuse, ie, no major blood loss occurs. (**D**) The site of cups application and scarifications after finishing Al-hijamah.

hijamatologist (a physician therapist) who did superficial scarifications using 10 large sucking cups (8 cups at the upper back and 2 cups at the right hypochondrium, and subcostal region). Two weeks later, third blood samples (after ledipasvir + Al-hijamah) indicated that his hepatitis viral load became 1,200,000 copies/mL and his AIDS viral load became 500,000 copies/mL. His CD4 count was 396 cells/mm^3 (normal range: 500–1500 cells/mm^3). A nutritional cocktail containing grinded nigella sativa (2 grams/dose), grinded costus (0.5 gram/dose), grinded fennel (3 grams/dose), natural honey (15 mL/dose), Ajwa date fruit (7 dates/day) and camel milk (200 mL/day) was added three times/day to the nutritional regimen. Two weeks later, fourth blood samples (after ledipasvir + Al-hijamah + other prophetic medicine remedies) indicated that his hepatitis viral load was 5000 copies/mL and his AIDS viral load was 500 copies/mL. His CD4 count was 550 cells/mm^3 (normal range: 500–1500 cells/mm^3). The adjuvant treatment was recommended for another 4 months. Dosage was based on our previous reports.[34,95–97]

How can Al-hijamah benefits be evaluated in the first 2 weeks?

Answers: Using Al-hijamah indices, therapeutic benefits of Al-hijamah can be quantitated.[18,93]

1* Excretion index for hepatitis C particles = (initial concentration of viral particles in serum before Al-hijamah) – (their concentration after Al-hijamah).

= 3,200,200–1,200,000 = 2,000,000 copies/mL, ie, about 2 million copies/mL were excreted in the bloody excretion during Al-hijamah.

- Excretion index for HIV particles = 1,500,000–500,000 = 1,000,000 copies/mL, ie, about 1 million HIV copies/mL were excreted in the bloody excretion during Al-hijamah.

2* Plasma purification index (from hepatitis C viral content) = 100 × ([initial concentration of viral particles in serum before Al-hijamah – concentration of the same viral particles in serum after Al-hijamah]/their initial concentration before Al-hijamah).

= 100 × (3,200,000–1,200,000)/3,200,000 = 62.5%, ie, a single session of Al-hijamah cleared blood plasma from 62.5% of the hepatitis C viral content.

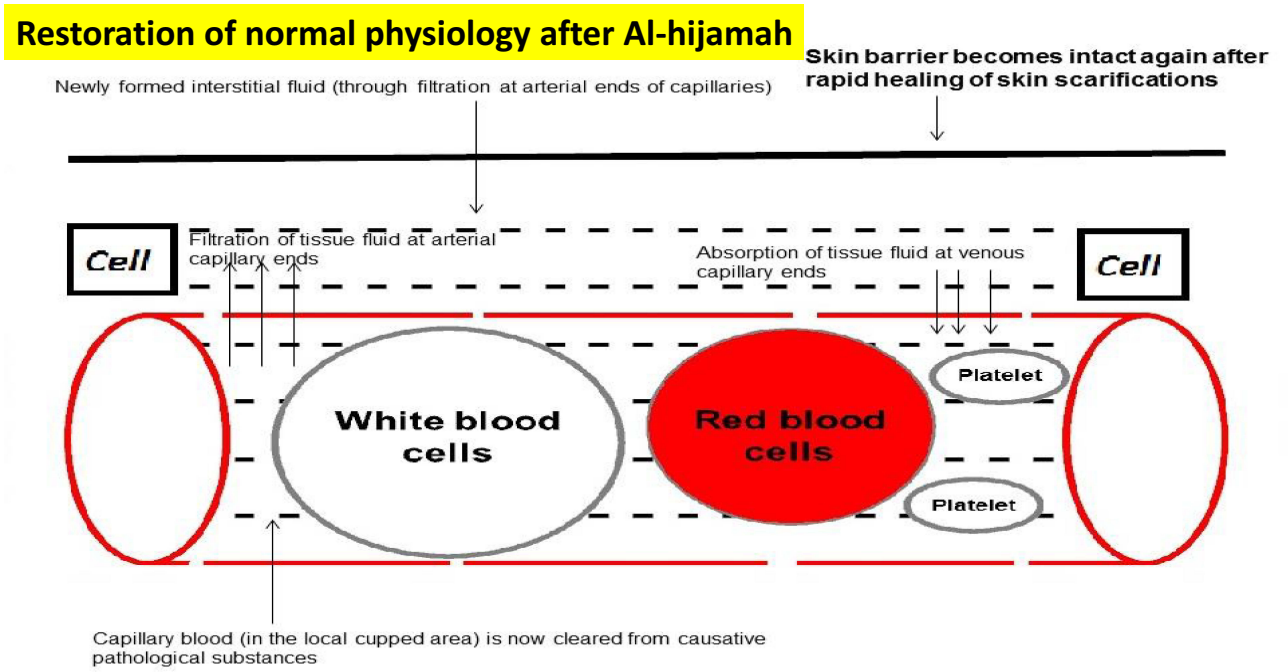

Figure 7 Restoration of homeostasis (through excretion of the causative pathological substances).
Notes: This decreases the virus load and allows the immune system to overcome hepatitis infection and potentiates the therapeutic effects of pharmacological treatments (in agreement with Taibah theory).

Figure 8 Natural prophetic medicine remedies.
Notes: (**A**) Medicinal plants. (**B**) Prophetic medicine drinks. Prophetic medicine foods.

Box 3 Nigella Sativa Benefits to Viral Hepatitis and HCC Patients

Hepatoprotective

- Ameliorates acute endotoxemia-induced liver dysfunction in rats.[43]
- Improves diabetic control, weight gain in streptozotocin-induced experimental diabetes.[44]
- Protects viability and architecture of the hepatocytes and islet cells in streptozotocin-induced experimental diabetes.[44]
- Exerts hepato-protective activity (protects against ischemia-reperfusion injury).[45]
- Behaves as an agonist of PPAR-gamma receptors and is suitable as a treatment for diabetes, obesity and metabolic syndrome.
- Protects against liver damage induced by Schistosoma mansoni (reduces worm number, ova deposition, potentiates praziquantel anti-schistosomiasis effect and protects the liver functions during bilharzisis).[45]
- Exerts hepatoprotective effects against hypervitaminosis A and enhances the immunological functions (potent inducer of IgG and IgM).[46]
- Protected the liver cells against injury in cholestatic jaundice (during bile duct ligation).[47]
- Exerts therapeutic and anti-oxidant effects against lipopolysaccharides-induced inflammation in diabetic patients.[48]

Antifibrotic effect

- Attenuates hepatic fibrosis.[49]

Nutritional supplement

- Nigella sativa improves malnutrition associated with metabolic diseases, eg, Refsum's disease.[50]
- Induces significant hyperfibrinogenemia, significant transient prothrombin time prolongation and thrombin time reduction.[51]

Antioxidant

- Prevents loss of hepatic GSH in toluene-induced oxidative stress.[52]
- Improves greatly (especially thymoquinone-rich fraction) the plasma antioxidant capacity and expression of antioxidant genes in hypercholesterolemic animals.[53]
- Thymoquinone induces hepatic quinone reductase and glutathione transferase and plays a possible role in protection against chemical carcinogenesis and toxicity.[54]
- Protects maternal liver and embryos against free radical-induced damage in diabetic animals.[55]

Antimicrobial

- Exerted protective effects against murine cytomegalovirus infection.[56]
- Exerts in vivo antifungal effects.[57]
- Exerts strong biocidal effects against all stages of Schistosoma parasite (miracidia, cercaria and adult worm).[45]
- Decreases hepatitis viral load, improves response to oxidative stress and improves the clinical condition and glycemic control in hepatitis patients.[42]

Anticancer effects

- Protects against DNA damage, colon carcinogenesis and liver damage induced by azoxymethane.[58]
- Inhibits benzo(a)pyrene-induced forestomach carcinogenesis in mice.[59]

Immunopotentiation

- Exerts hypoglycemic and immunopotentiation effects in streptozotocin-induced diabetic hamsters.[60]

Antitoxic

- Protects against cisplatin-induced toxicity in rats.[61]
- Inhibits effects of 20-methylcholanthrene-induced fibrosarcoma tumorigenesis.[62]
- Protects against aflatoxin-induced hepatotoxicity.[63]
- Exert antimutagenic activity.[64]
- Helps in resolution of hepato-renal toxicity induced by bromobenzene.[65]
- Induces hepatoprotective effects against isoniazide-induced hepatotoxicity in rabbits.[66]
- Protects against hepatotoxic metals, eg, lead, CCL4 and cadmium.[45]

Anticancer

- Has a chemo-preventive effect against the progression to liver cancer.[67]
- Attenuates diethyl nitrosamine-induced hepatic carcinogenesis (through antioxidant mechanisms).[54]
- Protects liver and tissues against chemotherapy (cyclophosphamide)-induced hepatotoxicity.[55]
- Exerts antineoplastic effects on hepatocellular carcinoma cells.[62]

Miscellaneous

- Enhances memory, attention and cognition while preserving the normal cardiac, liver and kidney functions.[68]
- Thymoquinone is safe with no harmful effects.[69]
- Has no or minimal side effects (at high doses) as regards liver functions.[70]

Box 4 Natural Honey Benefits to Viral Hepatitis and HCC Patients

Hepato-tonic effects
- Honey protected the ultrastructure of hepatocytes during experimental obstructive jaundice.[71]
- Exerts significant antibacterial activity (against staphylococcus aureus).[72]
- Honey is a prebiotic food that re-engineers the gut microbiome towards a healthy state & decreases significantly gut bacterial colonization.[73]
- Exerts antimicrobial properties and bifidogenic effects.[74]
- Improves intestinal microflora.[74]

Antitoxic effects
- Hepatoprotective effects, eg, honey protects against carbon tetrachloride-induced hepatonephrotoxicity
- Protects against toxicity of mycotoxins (of Aspergillus parasiticus and Aspergillus ochraceus) and ochratoxins.[74]
- Protects against cadmium-induced hepatotoxicity.[75]
- Decreases side effects and toxic effects of concomitantly administered therapeutics, eg, toxic effects of pentylenetetrazole.[76]

Antioxidant
- Contains active ingredients, eg, chrysin that possesses potent anti-oxidant and cancer chemopreventive activities.[77]
- Propolis decreases hepatocytes apoptosis, protects hepatocytes against oxidative stress and improves hepatic histomorphology in experimental obstructive jaundice.[78]

Box 5 Costus Benefits to Viral Hepatitis and HCC Patients

Anti-hepatitis
- Suppress hepatitis B virus surface antigen and envelop antigen gene expression in human hepatoma cells.[79]
- A related herb (Saussurea grandifolia) is used in Korea for treating hepatitis and hematuria.[80]

Hepatoprotective
- Protects the liver cells against D-galactosamine and lipopolysaccharide-induced hepatitis.[81]
- Exhibits hepatoprotective, anti-inflammatory, anti-ulcer and anticancer activities.[82]

Anticancer
- Dehydrocostuslactone (an extract of saussurea lappa) induces apoptosis in liver cancer cells (via an endoplasmic reticulum stress mechanism).[83]
- Cynaropicrin (in Saussurea lappa extract) suppressed the viability of cancer cells with minimal toxicity to hepatocytes.[84]

Antioxidant
- Potent antioxidant effects (scavenges DPPH, nitric oxide, superoxide radicals along with its ability to inhibit lipid peroxidation and glutathione oxidation).[79,82]

Box 6 Ajwa Benefits to Viral Hepatitis and HCC Patients

Antitoxic
- Protects hepatic functions and hepatocyte structure against aflatoxin-induced hepatotoxicity (together with nigella sativa).[89]
- Protects hepatocytes against lead-induced hepatotoxicity.[90]
- Proved to treat tissue damage due to toxin exposure through many mechanisms.[88]
- Exerts potent antitoxic mechanisms.[88]

Exerts potent antioxidant effects
- Contain large amounts of antioxidants, eg, melatonin and vitamin E.
- Protects against oxidative damage and hepatotoxicity induced by subchronic exposure to dimethoate.[91]
- Boosted up the antioxidant enzymes that stabilize biological molecules in the liver tissue.

Antiatherogenic nutrient
- Exerted a significant decrease in serum triacylglycerol and oxidative stress and did not worsen serum glucose and lipid/lipoprotein patterns.
- Exerted antimutagenic, anti-inflammatory, gastroprotective, hepatoprotective, nephroprotective, anticancer and immunostimulant activities.

Nutritional supplement
- Is a potent safe nutritional supplement (main chemical components include carbohydrates, dietary fiber, enzymes, protein, fat, minerals, vitamins, phenolic acids and carotenoids).[92]
- Protein content in dates may treat hypoproteinemia of liver diseases.

Table 1 Comparison Between Al-Hijamah (Wet Cupping Therapy) and Phlebotomy (Venesection)

	Phlebotomy (Venesection)	**Al-Hijamah (Wet Cupping Therapy of Prophetic Medicine)**
Definition	Venesection, a hematological treatment that involves cutting (or puncturing) a vein to cause it to bleed, reduces the quantity of noxious substances in blood or blood-related chemicals inside the vessel wall.	A minor therapeutic percutaneous treatment in which blood is filtered at the fenestrated dermal skin capillaries under the influence of the suction pressure in the sucking cups. The excretory function is carried out by clearing blood and interstitial fluids of pathogenic agents that, depending on the etiology and pathogeneses of the various diseases, cause those diseases.
Worldwide practice	Practiced worldwide	Very minimal. Not receiving enough attention worldwide despite its marvelous therapeutic benefits in all medical specialties.
Therapeutic indications	To reduce the quantity or concentration of an element or component of the blood, such as the red cell mass and hematocrit value in polycythemia and the iron overload in thalassemia and hemochromatosis.	Treats all disease indications that benefit from blood and tissues clearance from causative pathological substances including: 1. Musculoskeletal pain conditions 2. Hematological conditions as hemolysis and iron overload 3. Cardiovascular diseases as hypertension 4. Inborn metabolic errors as galactosemia 5. Dermatological conditions as urticaria. 6. Neuropsychiatric conditions as headache. 7. Malignancy 8. Metabolic conditions as gout infections 9. Viral conditions as hepatitis and AIDS 10. Respiratory and ENT conditions
How to perform?	Venesection and bloodletting (donation) in a donation bag.	6 Ss: 1. Selecting the appropriate anatomical areas for the application of sucking cups 2. Strict skin sterilization (at the beginning) 3. Skin suction (1st time using sucking cups) 4. Skin scarifications 5. Skin suction (2nd time using sucking cups) 6. Strict skin sterilization (at the end).
Side effects	Rare. Anemia, phlebitis, bleeding.	Rare. Skin blebs (Taibah sign),[93] transient post-cupping marks, transient skin bruises.
Nature of excretion	Whole blood.	A mixture of components forming a bloody fluid that contains some blood cells, hemolyzed blood cells, filtered fluids (at the fenestrated dermal capillaries), interstitial fluids, and a significant proportion of the causative pathological substances.
Quantity of excreted causative pathological substances	A proportionate amount of the causative pathological substances ie, removal of 500 cc whole blood (out of 5 Liters) decreases 10% of substances concentration.	Maximal (a filtrate at the dermal capillaries) and not related to the blood component in the bloody excretion. In a previous report, removal of about 20 cc of the bloody excretion during Al-hijamah clears the circulation from about 25% of the excess ferritin and 69% of malondialdehyde.[18]

(*Continued*)

Table 1 (Continued).

	Phlebotomy (Venesection)	Al-Hijamah (Wet Cupping Therapy of Prophetic Medicine)
The need for subsequent blood transfusion	None if phlebotomy was done properly.	No need as the amount of blood loss is minimal.
Can it be done for certain anemias as thalassemia?	No. To avoid exaggerating the anemic condition.	Yes. It is recommended (minimal blood loss) to excrete the excess iron overload, free radicals and other causative pathological substances. It did not increase the anemic condition.
Repeatability	Repeatable according to patient's condition and indications.	Repeatable according to patient's condition and indications.
Other names	Venesection, phlebotomy, fasd (in Arabic medicine).	Triple S technique.
A plenty of therapeutic benefits eg, analgesic effect	None.	Present.

- Plasma purification index (from HIV viral content) = 100 × ([initial concentration of viral particles in serum before Al-hijamah – concentration of the same viral particles in serum after Al-hijamah]/their initial concentration before Al-hijamah).

= 100 × (1,500,000–500,000)/1,500,000 = 66.7%, ie, a single session of Al-hijamah cleared blood plasma from 66.7% of the HIV viral content.

3* Pharmacological potentiation index for treating viral hepatitis = 100 × (therapeutic effects of Al-hijamah + conventional pharmacological treatments)/(therapeutic effects of conventional pharmacological treatments only).

= 100 × (viral load decrease due to ledipasvir + Al-hijamah)/(viral load decrease due to ledipasvir only).

= 100 × (2,000,000)/400,000 = 500%, ie, Al-hijamah potentiated ledipasvir effects about 5 times.

Pharmacological potentiation index for treating AIDS particles = 100 × (viral load decrease due to HAART + Al-hijamah)/(viral load decrease due to HAART only).

= 100 × (1,000,000)/500,000 = 200%, ie, Al-hijamah potentiated HAART effects 2 times.

4* Immunological index: [100 × (Immunological response after Al-hijamah)/(Immunological response before Al-hijamah)]

= 100 * 396/198 = 200%, ie, Al-hijamah increased cell-mediated immunity by twice the original value.

5* Clinical therapeutic index: is the percentage improvement of a tested clinical parameter after Al-hijamah (as a combined treatment here) measured at different time points.

Practical Example 2: Pharmacotherapy Combined with Al-Hijamah and Other Prophetic Medicine Remedies for Treating HCC (for Continuous Medical Education)

Mr YYYY was receiving Sorafenib for treating HCC but he cannot tolerate the side effects. His serum lactate level (Warburg effect, cancer cell's products) was 4 mmol/L (normal range: <2 mmol/L).[98] α-fetoprotein level was initially 400 (normal range: 5 −10 ng/mL).[99] Al-hijamah was done for him by an expert hijamatologist (a physician therapist) who did superficial scarifications using 10 large sucking cups (8 cups at the upper back and 2 cups at the right hypochondrium, subcostal region). Two weeks later, his serum lactate level became 1.5 mmol/L (normal range: <2 mmol/L) and α-fetoprotein level became 150 (normal range: 5 −10 ng/mL). A nutritional cocktail containing grinded nigella sativa (2 grams/dose), grinded costus (0.5 gram/dose), grinded fennel (3 grams/dose), natural honey (15 mL/dose), Ajwa date fruit (7 dates/day) and camel milk

(200 mL/day) was added three times/day to the nutritional regimen. Two weeks later, his serum lactate level became 1 mmol/L (normal range: <2 mmol/L) and α-fetoprotein level became 75 (normal range: 5 −10 ng/mL). The adjuvant treatment was recommended for another 4 months.

How can Al-hijamah benefits be evaluated in the first 2 weeks?

Answers: Using Al-hijamah indices, therapeutic benefits of Al-hijamah can be quantitated.

1* Excretion index for serum lactate = (initial concentration of lactate in serum before Al-hijamah) – (concentration after Al-hijamah).

= 4–1.5 = 2.5 mmol/L, ie, about 2.5 mmol/L of lactate were excreted in the bloody excretion during Al-hijamah.

- Excretion index for α-fetoprotein = 400–150 = 250 ng/mL, ie, about 250 ng/mL of α-fetoprotein were excreted in the bloody excretion during Al-hijamah.

2* Plasma purification index (for serum lactate) = 100 × ([initial concentration of lactate of serum before Al-hijamah – concentration of lactate in serum after Al-hijamah]/their initial concentration before Al-hijamah).

= 100 × (4–1.5)/4 = 62.5%, ie, a single session of Al-hijamah cleared blood plasma from 62.5% of lactate content.

- Plasma purification index (from α-fetoprotein) = 100 × ([initial concentration of α-fetoprotein in serum before Al-hijamah – concentration of α-fetoprotein in serum after Al-hijamah]/their initial concentration before Al-hijamah).

= 100 × (400–150)/400 = 62.5%, ie, a single session of Al-hijamah cleared blood plasma from 62.5% of its α-fetoprotein content.

Anti-Inflammatory and Immunological Benefits of Al-Hijamah Were Confirmed by Chinese Cupping Therapy

Al-hijamah is totally different from phlebotomy therapy (Table 1). Al-hijamah is better when it is needed to clear the blood and tissues from disease-causing substances. Zhang et al reported that in asthmatic patients, Chinese cupping therapy (equals only one step of Al-hijamah) caused a significant increase of immune stimulating cytokines and a significant decrease in immune inhibition. Cupping therapy caused elevated levels of CD4+ (T-helper cells), CD4+/CD8+ (elevated T-helper to T-cytotoxic ratio), IL-2, IFN-gamma, C3, C4, IgA, IgG and IgM. There was a significant corresponding decrease in immune inhibitory cytokines, eg, IgE, IL-4, IL-10 and CD8 cells.[100] The authors concluded that the improvements were better in the treated group than that in the control group.[100]

Factors Affecting the Effectiveness of Al-Hijamah in Treating Viral Hepatitis

1. The hand skills of the hijamatologist (therapist).
2. The superficial nature of skin scarifications: to preserve the subepidermal capillaries networks (acting as blood filters during Al-hijamah).
3. The duration of applying the sucking cups (optimal is 4–5 minutes).
4. The size of the sucking cups (largest are the best).
5. The number of sucking cups (the more cups the better).
6. Number of sessions of Al-hijamah (the more sessions the better).
7. Time interval between sessions (the fewer the better): optimal is 3–4 weeks.
8. The amount of the bloody excretion of Al-hijamah (cupped bloody excretion): the more the better.
9. Combination with other prophetic medicine remedies: the more the better.
10. Combination with given drugs: better to combine.

Conclusion

Al-hijamah is a strongly recommended adjuvant to current pharmacological treatments to viral hepatitis. Al-hijamah (wet cupping therapy of prophetic medicine) may be a promising treatment for increasing the immunity of the human body, decreasing free radicals and their damaging effects and clearing the blood from the pathological substances causing and related to pathogenesis of viral hepatitis. Other viral diseases like AIDS can benefit from the same treatment advantages. Al-hijamah is

absolutely necessary for the excretion and removal of CPS that promote cancer, such as lactate (the Warburg effect), growth factors, metalloproteinases, and others. Even if HCC has developed, patients with HCC benefit from the immune potentiation brought on by Al-hijamah. The therapeutic effects of al-hijamah will be maximized by combining it with other natural antioxidant remedies of prophetic medicine, such as nigella sativa, costus, natural honey, Zamzam water, and others. Al-hijamah is a strongly suggested supplement to the pharmacological treatments now available for viral hepatitis and HCC, along with other cures from prophetic medicine.

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Disclosure

The author declares that there are no conflicts of interest in this work.

References

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1. Gurtsevitch V. Human oncogenic viruses: hepatitis B and hepatitis C viruses and their role in hepatocarcinogenesis. *Biochemistry*. 2008;73:504–513.
2. Traore KA, Rouamba H, Nebie Y, et al. Seroprevalence of fecal-oral transmitted hepatitis A and E virus antibodies in Burkina Faso. *PLoS One*. 2012;7(10):e48125. doi:10.1371/journal.pone.0048125
3. But DY-K, Lai C-L, Yuen M-F. Natural history of hepatitis-related hepatocellular carcinoma. *World J Gastroenterol*. 2008;14:1652. doi:10.3748/wjg.14.1652
4. Stanciu C, Muzica CM, Girleanu I, et al. An update on direct antiviral agents for the treatment of hepatitis C. *Expert Opin Pharmacother*. 2021;22(13):1729–1741. doi:10.1080/14656566.2021.1921737
5. Fadnes LT, Aas CF, Vold JH, et al. Integrated treatment of hepatitis C virus infection among people who inject drugs: a multicenter randomized controlled trial (INTRO-HCV. *PLoS Med*. 2021;18(6):e1003653. doi:10.1371/journal.pmed.1003653
6. Ali M, Idrees M, Ali L, et al. Hepatitis B virus in Pakistan: a systematic review of prevalence, risk factors, awareness status and genotypes. *Virol J*. 2011;8(1):1–9. doi:10.1186/1743-422X-8-102
7. Kulikov SM, Mikhaylova EA, Gemdzhyan EG, et al. Long-term results of HBV and HCV infection in patients with blood diseases. *Ter Arkh*. 2011;83:17–26.
8. Mukhtarov D. [Clinical picture, course and therapeutic efficiency of pulmonary tuberculosis in patients with organochlorine pesticides and hepatitis B markers]. *Probl Tuberk*. 1998;5:23–24. Russian.
9. Guidotti LG, Chisari FV. Immunobiology and pathogenesis of viral hepatitis. *Annu Rev Pathol Mech Dis*. 2006;1:23–61. doi:10.1146/annurev.pathol.1.110304.100230
10. Lim HK, Jeffrey GP, Ramm GA, Soekmadji C. Pathogenesis of viral hepatitis-induced chronic liver disease: role of extracellular vesicles. *Front Cell Infect Microbiol*. 2020;10:587628. doi:10.3389/fcimb.2020.587628
11. Schaff Z, Lotz G, Schulte-Herman R. Pathomorphological characteristics and pathogenesis of viral hepatitis. *Pathol Oncol Res*. 1996;2(3):132–143. doi:10.1007/BF02903516
12. El Sayed SM. Biochemical origin of the Warburg effect in light of 15 years of research experience: a novel evidence-based view (an expert opinion article. *Onco Targets Ther*. 2023;Volume 16:143–155. doi:10.2147/OTT.S397593
13. El Sayed SM, Mahmoud AA, El Sawy SA, et al. Warburg effect increases steady-state ROS condition in cancer cells through decreasing their antioxidant capacities (anticancer effects of 3-bromopyruvate through antagonizing Warburg effect. *Med Hypotheses*. 2013;81:866–870. doi:10.1016/j.mehy.2013.08.024
14. Xu L, Yang H, Yan M, Li W. Matrix metalloproteinase 1 is a poor prognostic biomarker for patients with hepatocellular carcinoma. *Clin Exp Med*. 2022:1–19. doi:10.1007/s10238-022-00897-y
15. El Sayed SM. Natural remedies of prophetic medicine are promising in the management of viral hepatitis: towards better preventive and therapeutic outcomes (A review article). *Am J Clin Med Res*. 2023;11(1):14–21. doi:10.12691/ajcmr-11-1-3
16. El Sayed SM, Mahmoud HS, Nabo MMH. Methods of wet cupping therapy (Al-Hijamah): in light of modern medicine and prophetic medicine. *Altern Integr Med*. 2013;2:1–16.
17. Takada M, Hattori S. Presence of fenestrated capillaries in the skin. *Anat Rec*. 1972;173(2):213–219. doi:10.1002/ar.1091730210
18. El-Shanshory M, Hablas NM, Shebl Y, et al. Al-hijamah (wet cupping therapy of prophetic medicine) significantly and safely reduces iron overload and oxidative stress in thalassemic children: a novel pilot study. *J Blood Med*. 2018;9:241. doi:10.2147/JBM.S170523

19. Grammatikos G, Lange C, Susser S, et al. Vitamin D levels vary during antiviral treatment but are unable to predict treatment outcome in HCV genotype 1 infected patients. *PLoS One*. 2014;9(2):e87974. doi:10.1371/journal.pone.0087974
20. Borges SC, Cheinquer H, Wolff FH, Cheinquer N, Krug L, Prolla PA. Effect of hfe gene polymorphism on sustained virological response in patients with chronic hepatitis c and elevated serum ferritin. *Arq Gastroenterol*. 2012;49(1):9–13. doi:10.1590/S0004-28032012000100003
21. Hayashi H, Piperno A, Tomosugi N, et al. Patients with chronic hepatitis C may be more sensitive to iron hepatotoxicity than patients with HFE-hemochromatosis. *Intern Med*. 2010;49(22):2371–2377. doi:10.2169/internalmedicine.49.4088
22. Sumida Y, Nakashima T, Yoh T, et al. Serum thioredoxin elucidates the significance of serum ferritin as a marker of oxidative stress in chronic liver diseases. *Liver*. 2001;21(5):295–299. doi:10.1034/j.1600-0676.2001.210501.x
23. Sebastiani G, Tempesta D, Alberti A. Hepatic iron overload is common in chronic hepatitis B and is more severe in patients coinfected with hepatitis D virus. *J Viral Hepat*. 2012;19(2):e170–e176. doi:10.1111/j.1365-2893.2011.01508.x
24. Vagu C, Sultana C, Ruta S. Serum iron markers in patients with chronic hepatitis C infection. *Hepat Mon*. 2013;13:e13136.
25. Elalfy MS, Esmat G, Matter RM, Aziz HEA, Massoud WA. Liver fibrosis in young Egyptian beta-thalassemia major patients: relation to hepatitis C virus and compliance with chelation. *Ann Hepatol*. 2013;12(1):54–61. doi:10.1016/S1665-2681(19)31385-7
26. Abergel A, Ruivard M, Bonny C. Iron overload and chronic liver diseases. *Rev Prat*. 2006;56(19):2130–2134.
27. Nahon P, Ganne-Carrié N, Trinchet J-C, Beaugrand M. Hepatic iron overload and risk of hepatocellular carcinoma in cirrhosis. *Gastroenterol Clin Biol*. 2010;34:1–7. doi:10.1016/j.gcb.2009.07.032
28. Desai TK, Jamil LH, Balasubramaniam M, Koff R, Bonkovsky HL. Phlebotomy improves therapeutic response to interferon in patients with chronic hepatitis C: a meta-analysis of six prospective randomized controlled trials. *Dig Dis Sci*. 2008;53(3):815–822. doi:10.1007/s10620-007-9945-7
29. Alexander J, Tung BY, Croghan A, Kowdley KV. Effect of iron depletion on serum markers of fibrogenesis, oxidative stress and serum liver enzymes in chronic hepatitis C: results of a pilot study. *Liver Int*. 2007;27(2):268–273. doi:10.1111/j.1478-3231.2007.01449.x
30. Carlo C, Daniela P, Giancarlo C. Iron depletion and response to interferon in chronic hepatitis C. *Hepato-Gastroenterology*. 2003;50 (53):1467–1471.
31. El-Shanshory M, Hablas NM, El-Tahlawi R, et al. Al-hijamah (the triple S treatment of prophetic medicine) significantly increases CD4/CD8 ratio in thalassemic patients via increasing TAC/MDA ratio: a clinical trial. *Am J Blood Res*. 2022;12:125.
32. El-Shanshory M, Hablas NM, Aboonq MS, et al. Nigella sativa improves anemia, enhances immunity and relieves iron overload-induced oxidative stress as a novel promising treatment in children having beta-thalassemia major. *J Herb Med*. 2019;16:100245.
33. El Sayed SM, Abou-Taleb A, Mahmoud HS, et al. Percutaneous excretion of iron and ferritin (through Al-hijamah) as a novel treatment for iron overload in beta-thalassemia major, hemochromatosis and sideroblastic anemia. *Med Hypotheses*. 2014;83:238–246. doi:10.1016/j.mehy.2014.04.001
34. El Sayed SM, Almaramhy HH, Aljehani YT, et al. The evidence-based taibUVID nutritional treatment for minimizing COVID-19 fatalities and morbidity and eradicating COVID-19 pandemic: a novel approach for better outcomes (A treatment protocol). *Am J Public Health Res*. 2020;8:54–60.
35. Harrington PR, Fleischer R, Connelly SM, Lewis LL, Murray J. Ribavirin reduces absolute lymphocyte counts in hepatitis C virus–infected patients treated with interferon-free, direct-acting antiviral regimens: figure 1. *Clin Infect Dis*. 2015;61(6):974–977. doi:10.1093/cid/civ419
36. El-Shanshory M, Hablas NM, Shebel Y, et al. Al-hijamah (the triple S treatment of prophetic medicine) exerts cardioprotective, tissue-protective and immune potentiating effects in thalassemic children: a pilot clinical trial. *Am J Blood Res*. 2020;10:447.
37. El Sayed SM, Baghdadi H, Abou-Taleb A, et al. Al-hijamah and oral honey for treating thalassemia, conditions of iron overload, and hyperferremia: toward improving the therapeutic outcomes. *J Blood Med*. 2014;5:219. doi:10.2147/JBM.S65042
38. Baghdadi H, Abdel-Aziz N, Ahmed NS, et al. Ameliorating role exerted by Al-Hijamah in autoimmune diseases: effect on serum autoantibodies and inflammatory mediators. *Int J Health Sci*. 2015;9:207. doi:10.12816/0024129
39. Mahmoud HS, Abou-El-Naga M, Omar NAA, et al. Anatomical sites for practicing wet cupping therapy (Al-Hijamah): in light of modern medicine and prophetic medicine. *Altern Integ Med*. 2013;2:1–30.
40. Sayed E, Mahmoud H, Nabo M. Medical and scientific bases of wet cupping therapy (Al-hijamah): in light of modern medicine and prophetic medicine. *Altern Integr Med*. 2013;2:1–16.
41. Xu Y, Hao X, Ren Y, et al. Research progress of abnormal lactate metabolism and lactate modification in immunotherapy of hepatocellular carcinoma. *Front Oncol*. 2023;12:1063423.
42. Barakat EMF, El Wakeel LM, Hagag RS. Effects of Nigella sativa on outcome of hepatitis C in Egypt. *World J Gastroenterol*. 2013;19:2529. doi:10.3748/wjg.v19.i16.2529
43. Helal GK. Thymoquinone supplementation ameliorates acute endotoxemia-induced liver dysfunction in rats. *Pak J Pharm Sci*. 2010;23:131–137.
44. Alimohammadi S, Hobbenaghi R, Javanbakht J, et al. Retracted article: protective and antidiabetic effects of extract from Nigella sativa on blood glucose concentrations against streptozotocin (STZ)-induced diabetic in rats: an experimental study with histopathological evaluation. *Diagn Pathol*. 2013;8:1–7. doi:10.1186/1746-1596-8-137
45. Ahmad A, Husain A, Mujeeb M, et al. A review on therapeutic potential of Nigella sativa: a miracle herb. *Asian Pac J Trop Biomed*. 2013;3 (5):337–352. doi:10.1016/S2221-1691(13)60075-1
46. Al-Suhaimi EA. Hepatoprotective and immunological functions of Nigella sativa seed oil against hypervitaminosis A in adult male rats. *Int J Vitamin Nutr Res*. 2012;82(4):288–297. doi:10.1024/0300-9831/a000121
47. Coban S, Yildiz F, Terzi A, et al. The effects of Nigella sativa on bile duct ligation induced-liver injury in rats. *Cell Biochem Funct*. 2010;28 (1):83–88. doi:10.1002/cbf.1624
48. Beheshti F, Norouzi F, Abareshi A, et al. Nigella sativa prevented liver and renal tissue damage in lipopolysaccharide-treated rats. *Saudi J Kidney Dis Transpl*. 2018;29(3):554–566. doi:10.4103/1319-2442.235184
49. Bai T, Lian L-H, Wu Y-L, Wan Y, Nan J-X. Thymoquinone attenuates liver fibrosis via PI3K and TLR4 signaling pathways in activated hepatic stellate cells. *Int Immunopharmacol*. 2013;15(2):275–281. doi:10.1016/j.intimp.2012.12.020
50. Straube R, Gäckler D, Thiele A, Muselmann L, Kingreen H, Klingel R. Membrane differential filtration is safe and effective for the long-term treatment of Refsum syndrome—an update of treatment modalities and pathophysiological cognition. *Transfus Apher Sci*. 2003;29(1):85–91. doi:10.1016/S1473-0502(03)00102-2

51. Al-Jishi S, Hozaifa BA. Effect of Nigella sativa on blood hemostatic function in rats. *J Ethnopharmacol*. 2003;85(1):7–14. doi:10.1016/S0378-8741(02)00356-2
52. Ashraf SS, Rao MV, Kaneez FS, et al. Nigella sativa extract as a potent antioxidant for petrochemical-induced oxidative stress. *J Chromatogr Sci*. 2011;49(4):321–326. doi:10.1093/chrsci/49.4.321
53. Ismail M, Al-Naqeep G, Chan KW. Nigella sativa thymoquinone-rich fraction greatly improves plasma antioxidant capacity and expression of antioxidant genes in hypercholesterolemic rats. *Free Radic Biol Med*. 2010;48(5):664–672. doi:10.1016/j.freeradbiomed.2009.12.002
54. Sayed-Ahmed MM, Aleisa AM, Al-Rejaie SS, et al. Thymoquinone attenuates diethylnitrosamine induction of hepatic carcinogenesis through antioxidant signaling. *Oxid Med Cell Longev*. 2010;3:254–261.
55. Al-Enazi MM. Effect of thymoquinone on malformations and oxidative stress-induced diabetic mice. *Pak J Biol Sci*. 2007;10(18):3115–3119. doi:10.3923/pjbs.2007.3115.3119
56. Salem ML, Hossain MS. Protective effect of black seed oil from Nigella sativa against murine cytomegalovirus infection. *Int J Immunopharmacol*. 2000;22(9):729–740. doi:10.1016/S0192-0561(00)00036-9
57. Khan M, Ashfaq M, Zuberi H, Mahmood M, Gilani A. The in vivo antifungal activity of the aqueous extract from Nigella sativa seeds. *Phytother Res*. 2003;17(2):183–186. doi:10.1002/ptr.1146
58. Al-Johar D, Shinwari N, Arif J, et al. Role of Nigella sativa and a number of its antioxidant constituents towards azoxymethane-induced genotoxic effects and colon cancer in rats. *Phytother Res*. 2008;22:1311–1323. doi:10.1002/ptr.2487
59. Badary OA, Ai-shabanah O, Nagi M, AI-Rikabi A, Elmazar M. Inhibition of benzo (a) pyrene-induced forestomach carcinogenesis in mice by thymoquinone. *Eur J Cancer Prev*. 1999;8(5):435–440. doi:10.1097/00008469-199910000-00009
60. Fararh K, Atoji Y, Shimizu Y, Shiina T, Nikami H, Takewaki T. Mechanisms of the hypoglycaemic and immunopotentiating effects of Nigella sativa L. oil in streptozotocin-induced diabetic hamsters. *Res Vet Sci*. 2004;77(2):123–129. doi:10.1016/j.rvsc.2004.03.002
61. El Daly ES. Protective effect of cysteine and vitamin E, Crocus sativus and Nigella sativa extracts on cisplatin-induced toxicity in rats. *J Islamic Acad Sci*. 1996;9:105–118.
62. Badary OA, AM GE-D. Inhibitory effects of thymoquinone against 20-methylcholanthrene-induced fibrosarcoma tumorigenesis. *Cancer Detect Prev*. 2001;25:362–368.
63. Nili-Ahmadabadi A, Tavakoli F, Hasanzadeh G, Rahimi H, Sabzevari O. Protective effect of pretreatment with thymoquinone against Aflatoxin B1 induced liver toxicity in mice. *Daru*. 2011;19(4):282.
64. Khader M, Bresgen N, Eckl P. Antimutagenic effects of ethanolic extracts from selected Palestinian medicinal plants. *J Ethnopharmacol*. 2010;127(2):319–324. doi:10.1016/j.jep.2009.11.001
65. Hamed M, El-Rigal N, Ali S. Effects of black seed oil on resolution of hepato-renal toxicity induced by bromobenzene in rats. *Eur Rev Med Pharmacol Sci*. 2013;17:569–581.
66. Hassan AS, Ahmed JH, Al-Haroon SS. A study of the effect of Nigella sativa (Black seeds) in isoniazid (INH)-induced hepatotoxicity in rabbits. *Indian J Pharmacol*. 2012;44:678. doi:10.4103/0253-7613.103239
67. Abdel-Hamid N, Abdel-Ghany M, Nazmy M, Amgad S. Can methanolic extract of Nigella sativa seed affect glyco-regulatory enzymes in experimental hepatocellular carcinoma? *Environ Health Prev Med*. 2013;18(1):49–56. doi:10.1007/s12199-012-0292-8
68. Sayeed MSB, Asaduzzaman M, Morshed H, Hossain MM, Kadir MF, Rahman MR. The effect of Nigella sativa Linn. seed on memory, attention and cognition in healthy human volunteers. *J Ethnopharmacol*. 2013;148(3):780–786. doi:10.1016/j.jep.2013.05.004
69. Al-Ali A, Alkhawajah AA, Randhawa MA, Shaikh NA. Oral and intraperitoneal LD50 of thymoquinone, an active principle of Nigella sativa, in mice and rats. *J Ayub Med Coll Abbottabad*. 2008;20:25–27.
70. Dollah MA, Parhizkar S, Latiff LA, Hassan MHB. Toxicity effect of Nigella sativa on the liver function of rats. *Adv Pharm Bull*. 2013;3:97. doi:10.5681/apb.2013.016
71. Kılıcoglu B, Gencay C, Kısmet K, et al. The ultrastructural research of liver in experimental obstructive jaundice and effect of honey. *Am J Surg*. 2008;195:249–256. doi:10.1016/j.amjsurg.2007.04.011
72. Miorin PL, Levy Junior N, Custodio A, Bretz W, Marcucci M. Antibacterial activity of honey and propolis from Apis mellifera and Tetragonisca angustula against Staphylococcus aureus. *J Appl Microbiol*. 2003;95:913–920. doi:10.1046/j.1365-2672.2003.02050.x
73. Schell KR, Fernandes KE, Shanahan E, et al. The potential of honey as a prebiotic food to re-engineer the gut microbiome toward a healthy state. *Front Nutr*. 2022;9:957932. doi:10.3389/fnut.2022.957932
74. Ezz El-Arab AM, Girgis SM, Hegazy EM, Abd El-Khalek AB. Effect of dietary honey on intestinal microflora and toxicity of mycotoxins in mice. *BMC Complement Altern Med*. 2006;6:1–13. doi:10.1186/1472-6882-6-6
75. Çavuşoğlu K, Yapar K, Yalçin E. Royal jelly (honey bee) is a potential antioxidant against cadmium-induced genotoxicity and oxidative stress in albino mice. *J Med Food*. 2009;12:1286–1292. doi:10.1089/jmf.2008.0203
76. Mussulini BHM, Leite CE, Zenki KC, et al. Seizures induced by pentylenetetrazole in the adult zebrafish: a detailed behavioral characterization. *PLoS One*. 2013;8:e54515. doi:10.1371/journal.pone.0054515
77. Khan MS, Devaraj H, Devaraj N. Chrysin abrogates early hepatocarcinogenesis and induces apoptosis in N-nitrosodiethylamine-induced preneoplastic nodules in rats. *Toxicol Appl Pharmacol*. 2011;251:85–94. doi:10.1016/j.taap.2010.12.004
78. Kismet K, Sabuncuoglu M, Kilicoglu S, et al. Effect of propolis on oxidative stress and histomorphology of liver tissue in experimental obstructive jaundice. *Eur Surg Res*. 2008;41(2):231–237. doi:10.1159/000136479
79. Chen H-C, Chou C-K, Lee S-D, Wang J-C, Yeh S-F. Active compounds from Saussurea lappa Clarks that suppress hepatitis B virus surface antigen gene expression in human hepatoma cells. *Antiviral Res*. 1995;27(1–2):99–109. doi:10.1016/0166-3542(94)00083-K
80. Nugroho A, Lim S-C, Lee CM, Choi JS, Park H-J. Simultaneous quantitative determination and validation of quercetin glycosides with peroxynitrite-scavenging effects from Saussurea grandifolia. *J Pharm Biomed Anal*. 2012;61:247–251. doi:10.1016/j.jpba.2011.11.016
81. Yaeesh S, Jamal Q, Shah AJ, Gilani AH. Antihepatotoxic activity of Saussurea lappa extract on D-galactosamine and lipopolysaccharide-induced hepatitis in mice. *Phytother Res*. 2010;24(S2):S229–S232. doi:10.1002/ptr.3089
82. Pandey MM, Rastogi S, Rawat AKS. Saussurea costus: botanical, chemical and pharmacological review of an ayurvedic medicinal plant. *J Ethnopharmacol*. 2007;110:379–390. doi:10.1016/j.jep.2006.12.033
83. Hsu Y-L, Wu L-Y, Kuo P-L. Dehydrocostuslactone, a medicinal plant-derived sesquiterpene lactone, induces apoptosis coupled to endoplasmic reticulum stress in liver cancer cells. *J Pharmacol Exp Ther*. 2009;329(2):808–819. doi:10.1124/jpet.108.148395

84. Cho JY, Kim AR, Jung JH, Chun T, Rhee MH, Yoo ES. Cytotoxic and pro-apoptotic activities of cynaropicrin, a sesquiterpene lactone, on the viability of leukocyte cancer cell lines. *Eur J Pharmacol*. 2004;492(2–3):85–94. doi:10.1016/j.ejphar.2004.03.027
85. Selim S, Al Jaouni S. Anticancer and apoptotic effects on cell proliferation of diosgenin isolated from Costus speciosus (Koen.) Sm. *BMC Complement Altern Med*. 2015;15(1):1–7. doi:10.1186/s12906-015-0836-8
86. El-Fakharany EM, El-Baky NA, Linjawi MH. Influence of camel milk on the hepatitis C virus burden of infected patients. *Exp Ther Med*. 2017;13(4):1313–1320. doi:10.3892/etm.2017.4159
87. Khan F, Khan TJ, Kalamegam G, et al. Anti-cancer effects of Ajwa dates (Phoenix dactylifera L.) in diethylnitrosamine induced hepatocellular carcinoma in Wistar rats. *BMC Complement Altern Med*. 2017;17(1):1–10. doi:10.1186/s12906-017-1926-6
88. Hassan SMA, Aboonq MS, Albadawi EA, et al. The preventive and therapeutic effects of Ajwa date fruit extract against acute diclofenac toxicity-induced colopathy: an Experimental Study. *Drug Des Devel Ther*. 2022;2601–2616. doi:10.2147/DDDT.S344247
89. Al-Ghasham A, Ata HS, El-Deep S, Meki A-R, Shehada S. Study of protective effect of date and Nigella sativa on aflatoxin B1 toxicity. *Int J Health Sci*. 2008;2(2):26.
90. Ragab AR, Elkablawy MA, Sheik BY, Baraka HN. Antioxidant and tissue-protective studies on Ajwa extract: dates from Al Madinah Al-Monwarah, Saudia Arabia. *J Environ Anal Toxicol*. 2013;3:2161.
91. Saafi EB, Louedi M, Elfeki A, et al. Protective effect of date palm fruit extract (Phoenix dactylifera L.) on dimethoate induced-oxidative stress in rat liver. *Exp Toxicol Pathol*. 2011;63(5):433–441. doi:10.1016/j.etp.2010.03.002
92. Tang ZX, Shi LE, Aleid SM. Date fruit: chemical composition, nutritional and medicinal values, products. *J Sci Food Agric*. 2013;93:2351–2361. doi:10.1002/jsfa.6154
93. El Sayed SM, Al-quliti A-S, Mahmoud HS, et al. Therapeutic benefits of Al-hijamah: in light of modern medicine and prophetic medicine. *Am J Med Biol Res*. 2014;2(2):46–71. doi:10.12691/ajmbr-2-2-3
94. Camus G, Han B, Asselah T, et al. Resistance characterization of ledipasvir and velpatasvir in hepatitis C virus genotype 4. *J Viral Hepat*. 2018;25:134–143. doi:10.1111/jvh.12795
95. El Sayed SM, Aboonq MS, Aljehani YT, et al. TaibUVID nutritional supplements help rapid cure of COVID-19 infection and rapid reversion to negative nasopharyngeal swab PCR: for better public prophylaxis and treatment of COVID-19 pandemic. *Am J Blood Res*. 2020;10:397.
96. El Sayed SM, Almaramhy HH, Aljehani YT, Ahmed MO, Okashah A. TaibUVID for minimizing COVID-19 fatalities and morbidity: an evidence-based approach for better outcomes (a treatment protocol. *Am J Public Health Res*. 2020;8:54–60.
97. El Sayed SM, Aboonq MS, El Rashedy AG, et al. Promising preventive and therapeutic effects of TaibUVID nutritional supplements for COVID-19 pandemic: towards better public prophylaxis and treatment (A retrospective study. *Am J Blood Res*. 2020;10:266.
98. Foucher CD, Tubben RE. Lactic acidosis. In: *StatPearls [Internet]*. StatPearls Publishing; 2022.
99. Lee C-W, Tsai H-I, Lee W-C, et al. Normal alpha-fetoprotein hepatocellular carcinoma: are they really normal? *J Clin Med*. 2019;8(10):1736. doi:10.3390/jcm8101736
100. Zhang C, Liang T, Zhang W. Effects of drug cupping therapy on immune function in chronic asthmatic bronchitis patients during protracted period. *Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi*. 2006;26(11):984–987.