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MINISTRY OF HIGHER EDUCATION AND SCIENTIFIC RESEARCH

Dr. MOULAY TAHAR UNIVERSITY OF SAIDA

FACULTY OF SCIENCES

DEPARTMENT OF BIOLOGY

Dissertation

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SUBMITTED FOR THE MASTER'S DEGREE IN: PLANT BIOTECHNOLOGY

THEME

"Ethno botanical survey on medicinal plants used in liver diseases".

Defended in front of the members of the jury:

The jury will be chaired by	**Mrs.** SARMOUM radhia	**MAB**	**Saida University**
Under the supervision of	**Mr.** AMMAM Abdelkader	**Prof**	**Saida University**
Member of the jury	**Mrs**. RABİE Fatma	**MAB**	**Saida University**

Academic year 2023/2024

Dedications

This work was made in honor of my mother, who inspired me to choose this topic because she is one of the people who suffer from liver diseases, especially hepatocelluar carcinoma.

I hope you get well soon inchallah

To my dear father who was always by my side to support and encourage me

To all my brothers Yacine and Feth-allah

To all my loved ones

To all my friends especially Hamami Amine

I dedicate the fruit of my 22 years of studies.

With thanks

First of all, I would like to thank Almighty Allah for giving me the courage and health to carry out this Work.

The presentation of this modest work gives me the opportunity to express my deep gratitude to Mr. (Ammam-Abdelkader), Professor at the University of Saida, who agreed to accompany me in the realisation of this work and kindly directed it throughout the experimentation and the formatting of the final document.

His many pieces of advice never failed me. I am pleased to express my respectful gratitude to him.

I would also like to thank Professors at the Saida University the biotechnology department, for all the facilities they provided and for agreeing to chair the thesis jury.

We cannot thank them enough for the great honor they have conferred on us by judging this work.

I send my best wishes to my friends at the Saida university biotechnology department

Summary:

An ethnobotanical survey was carried out in the city of Saida, to initiate a floristic and ethnobotanical study of medicinal plants used by the local population in the treatment of liver diseases using a questionnaire form collecting information on the medicinal plant, the disease and the person surveyed. This ethnobotanical study was carried out on a sample of people spread over different areas of the city, especially Saida hospital, during four weeks in April. The results enabled us to draw up a catalogue of 0 medicinal species used in indigenous therapeutic recipes and to analyze the plant-based therapeutic treatments used by the population concerned. The aim of the study is to help scientific research to produce plant-based medicines to treat.

ملخص :

تم إجراء مسح عرقي نباتي في مدينة سعيدة، لبدء دراسة نباتية وعرقية نباتية للنباتات الطبية التي يستخدمها السكان المحليون في علاج أمراض الكبد باستخدام استمارة استبيان تجمع معلومات عن النبات الطبي والمرض والشخص الذي شملته الدراسة. أُجريت هذه الدراسة النباتية العرقية على عينة من السكان موزعة على مناطق مختلفة من المدينة، وخاصة مستشفى سعيدة، خلال أربعة أسابيع في شهر أبريل. وقد مكنتنا النتائج التي تم الحصول عليها من وضع فهرس لـ 0 نوع من الأنواع الطبية المستخدمة في الوصفات العلاجية المحلية وتحليل العلاجات النباتية التي يستخدمها السكان المعنيون. الهدف من هذه الدراسة هي المساعدة في البحث العلمي لإنتاج أدوية نباتية لعلاج أمراض الكبد.

Résumé :

Une enquête ethnobotanique a été menée dans la Ville de Saida, pour entamer une étude floristique et ethnobotanique des plantes médicinales utilisées par la population locale dans le traitement des les maladies hépatique à l'aide d'une fiche questionnaire collectant des informations sur les plante médicinale, la maladie et sur la personne enquêtée.

Cette étude ethnobotanique a été effectuée sur un échantillon de personnes réparties sur les différentes zones de la ville et spécialement l'hôpital de Saida pendant quatre semaines du mois avril. Les résultats obtenus nous ont permis de dresser un catalogue de 0 espèces médicinales employées dans des recettes thérapeutiques autochtones et d'analyser le traitement thérapeutique à base de plante employée par la population concernée. Cette étude a pour but d'aider la recherche scientifique à produire des médicaments à base des plantes médicinales contre les maladies hépatique.

Key words: ethnobotanical, medicinal plants, liver, indigenous therapeutic recipes, liver diseases

Listes des figures

List of abbreviations

Abbreviations	significance
ALD	Alcoholics liver disease
SFE	Supercritical Fluid Extraction
PLE	Pressurized Liquid Extraction
UAE	Ultrasound-Assisted Extraction
MAE	Microwave-Assisted Extraction
EAE	Enzyme-Assisted Extraction
NASH	
NAFLD	Non-alcoholic fatty liver disease
NK	(Natural Killer).
HAV	hepatitis A virus
HBV	hepatitis B virus
OMS	Organisation Mondiale de la Santé
INPES	Institut national de prévention de la santé
HCV	hepatitis C virus
WHO	World Health Organization
MSM	men who have sex with men
HIV	Human Immunodeficiency Virus
CDCP	Centers for Disease Control and Prevention
DAA	direct-acting antiviral
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
HEV	hepatitis E virus
GLP_1	Glucagon-like peptide-1

FXR	farnesoid X receptor
PPAR	Peroxisome Proliferator-Activated Receptors
LAH	Livsooth authentic herbal formula
FDA	Food and Drug Administration
HSC	hepatic stellate cells
ECM	extracellular matrix
HELLP	*Hemolysis Elevated Liver enzymes Low Platelet count*
MELD	Model for End-Stage Liver Disease
RYR	Red yeast rice
AIH	Auto immune hepatitis
PBC	primary biliary cholangitis
PSC	primary sclerosing cholangitis
MMF	mycophenolate mofetil
PD	Programmed cell death 1
HCC	hepatocellular carcinoma
TME	The tumor microenvironment
AFP	Alpha-Foetoprotéine
TGF	Le tranforming growth factor-β
KNEIPP	La méthode Kneipp consiste à marcher dans l'eau froide:
MMPs	Les métalloprotéases matricielles (MMP) sont des protéases.

Table of contents

General introduction

General introduction

One of the most health burden worldwide is liver diseases contributes to the development of several problems on a key organ called the liver who plays a significant role in metabolism, detoxification, and storage, leaving it susceptible to Liver diseases which involve complex mechanisms, with matrix metalloproteinase's (MMPs) playing a crucial role in their pathogenesis by influencing cellular activities like proliferation, survival, gene expression, and inflammation (1) this non stable situation lead to numerous disorders that pose a global health concern such as alcoholic liver disease, nonalcoholic fatty liver disease, cirrhosis, and hepatitis, that can lead even to a liver cancer which are on the increase worldwide. (2) (3) .

Despite advancements in modern medicine, there is growing interest in exploring alternative treatment options for liver diseases. One area of interest is the use of medicinal plants, which have been used for centuries in traditional medicine systems. Traditional herbal medicine, also known as phytotherapy, has received attention for its hepatoprotective and regenerative properties, making it a promising therapeutic option for liver illness. Turmeric, Guduchi, Amla, Milk Thistle, Madder, are plants with antioxidant and anti-inflammatory characteristics that have been demonstrated to preserve and restore liver function. these plants contain bioactive compounds like flavonoids, alkaloids, and polyphenolics that exhibit antioxidant properties, protecting the liver from oxidative stress and chemical damage Theses natural medicines have been utilized for centuries and continue to be investigated for their pharmacological effects in addressing liver problems, emphasizing the need of integrating traditional herbal medicine into current healthcare procedures for liver health management (5).Currently, this plant-based medicine is regaining popularity, thanks to scientific studies based on analytical methods and new experiments, as the medical world discovers the benefits of empirical prescriptions of medicinal plants (6).

The main objective of this study is to get to know how does "Ethnobotanical" practices with medicinal plants can be used to deal with liver diseases and extract herbal compounds that help to treat liver disorders also studying their therapeutic effects and properties mentioning different methods of preparation. In order to contribute in the pharmacological industry to produce medicine based on plants compounds helping cure liver illnesses.

Our memory is divided into four large chapters:

The first chapter focuses on the bibliographic analysis, which includes: Gaining knowledge about the liver's architecture, function, and major diseases, including hepatic diseases, nonalcoholic fatty liver disease (NAFLD), fibrosis, cirrhosis, alcoholic liver disease (ALD), autoimmune liver illnesses, and liver cancer.
The second chapter presents a General overview of the medicinal plants. Ethnobotany, Phytotherapy involves the use of plants for healthcare and the treatment of common disorders. Medicinal plant qualities and biological activity, the various types of herbal medicine Methods and Preparations.
The third chapter addresses the Presentation of the Study Area materials and working methodology with study objectives.
The fourth chapter and the last illustrates the materials and methods used to complete this Survey and its Results and Analysis

This work ends with a conclusion and some perspectives.

Bibliographical summary

Chapter I: LIVER

1. The liver

1.1. Definition and general information

The biggest organ and gland in the human body, is positioned in the right upper quadrant of the belly and weighs between 1 and 2 kg (7). It is responsible for metabolism, cleansing, and storage, and it receives blood from both the portal vein and the hepatic artery (8). Embryologically, the liver develops from the hepatic diverticulum and shrinks in size postnatally, leaving four anatomical lobes. This organ has a high metabolic, synthetic, hematopoietic, and immunological activity, as well as a remarkable ability to regenerate (9). The liver functions as a blood filter reservoir, metabolizing nutrients and medicines and responding to damage via a variety of mechanisms (10). Overall, the liver's varied functions and structural characteristics make it an essential organ for maintaining overall health and balance in the body.

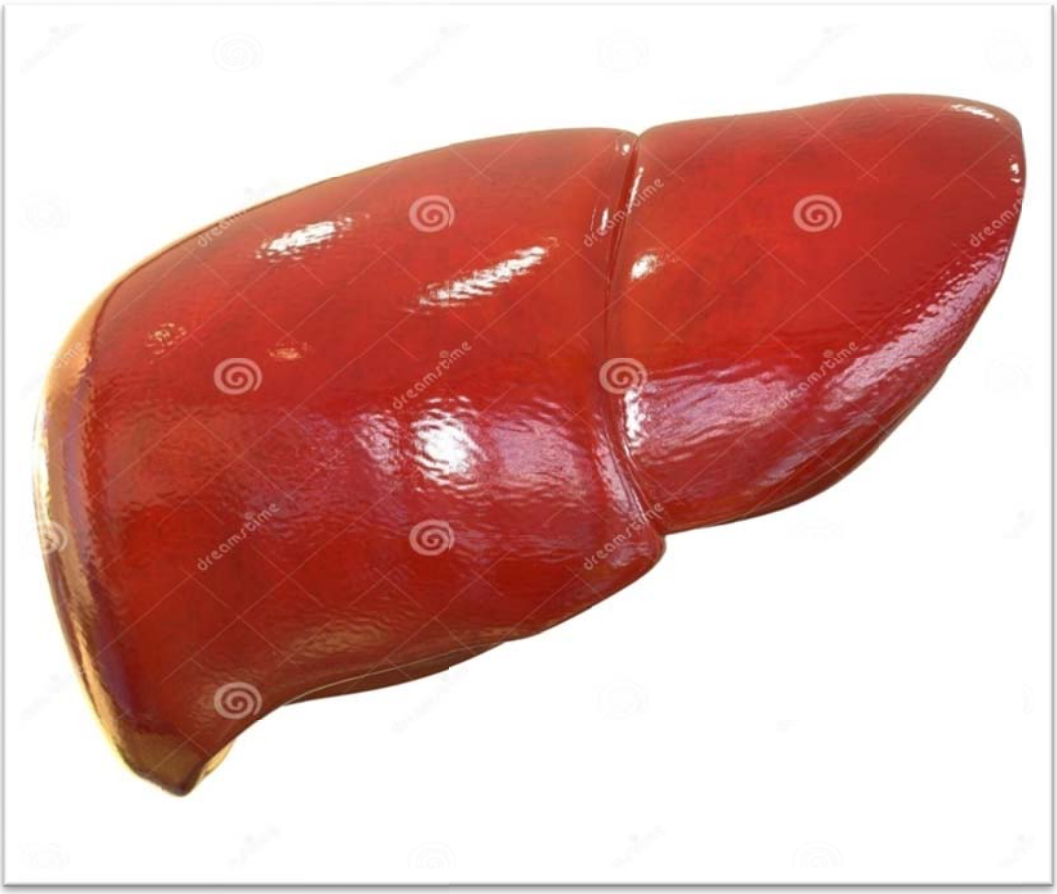


Figure 1: Realistic picture for Human Body Organs (liver) (11)

1.2 Liver anatomy

The liver is the largest internal organ, accounting for approximately 2-3% of body weight, and has distinct physical features. It is made up of four lobes: right, left, caudate, and quadrate, separated by ligaments such as the falciform ligament (12) (13).Anatomical abnormalities in hepatic arteries, portal veins, and bile ducts are prevalent, accounting for approximately 45%, 14%, and 43% of cases, respectively (10). Liver morphological abnormalities, such as accessory lobes, might mimic malignancies and cause clinical problems such as gastric volvulus or portal hypertension (14). Understanding liver anatomy is critical for successful hepatic procedures, and while contemporary imaging tools can aid in preoperative planning, not all defects are evident(15). The liver's notable anatomical features include its complex circulatory and ductal systems, regeneration potential, and broad metabolic functions.

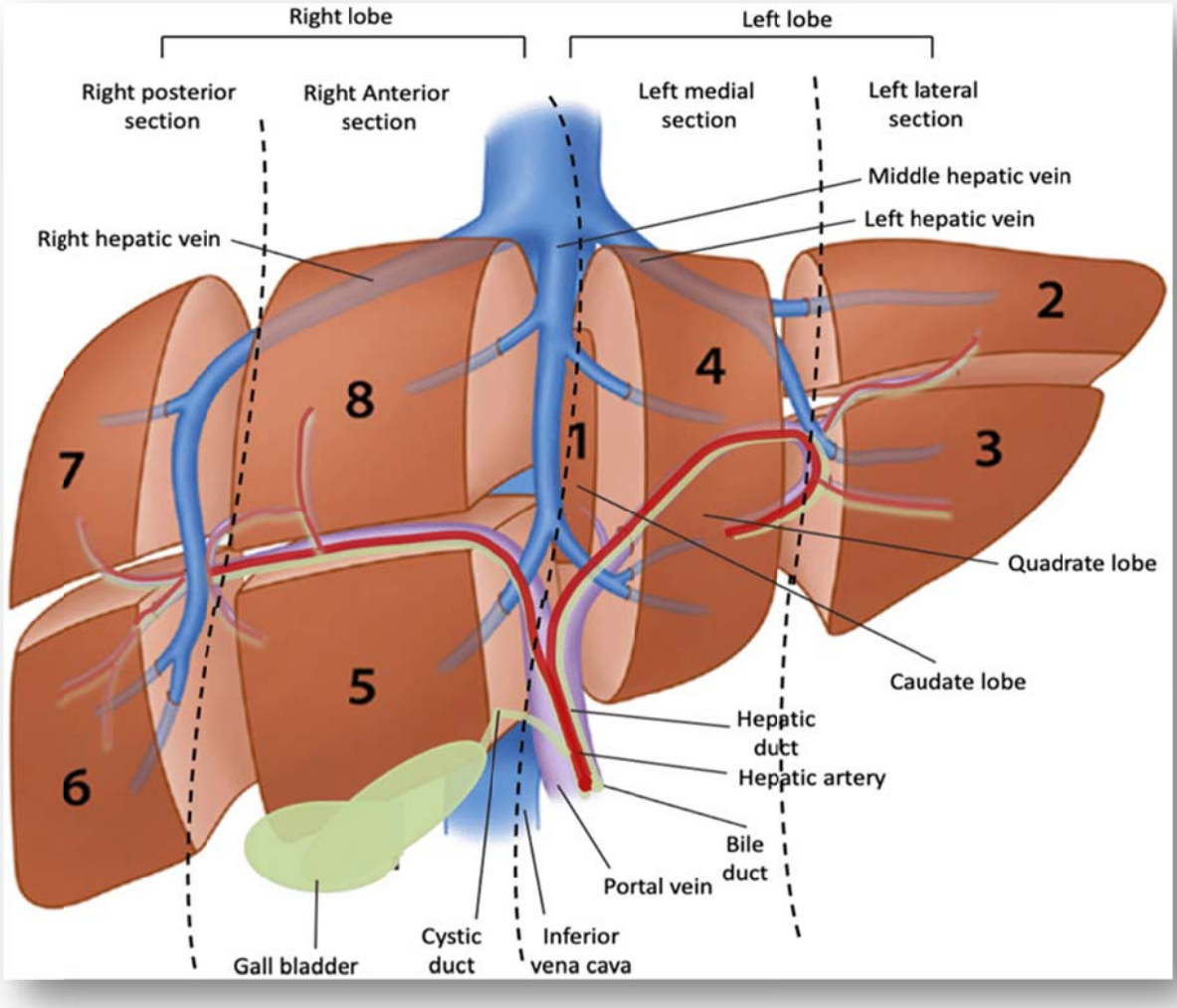


Figure 2: Schematic illustration for (Anatomy of liver); (16)

1. The functions of the liver :

a) Purification:

The liver is the central detoxification organ enabling the body to eliminate endogenous or exogenous substances (known as xenobiotics).

While water soluble can be eliminated directly by the kidneys, lipophilic substances must first be must first be transformed by the liver. Classically, this transformation is divided into three main phases and takes place in the hepatocytes:

- Phase I: hydroxylation of the compound to be eliminated,
- Phase II: conjugation of the compound with a protein. These two stages transform the compound, which is often very hydrophobic, into a water-soluble molecule that is easier to eliminate.
- Phase III: consists of the active excretion of the compound, using transmembrane transporters, either into the body or into the environment.

Transmembrane transporters, either into the bloodstream for renal elimination, or into the bile to be eliminated via the faces, after secretion of the bile from the intestine (17)

b) Immune system function

As described above, two-thirds of the blood flow to the liver comes from the portal vein after passing through numerous organs, including the intestine.

The blood therefore carries many antigens, particularly from nutrients.

The liver contains many innate immune system cells, Kupffer cells, dendritic cells, and NK (Natural Killer).

The liver is therefore one of the first lines of immune defense after the intestine against various pathogens and toxins. It also helps to establish a tolerance threshold against antigens from food.(18)

c) storage and production function

The liver stores numerous compounds such as iron and vitamins.

The compounds stored by the liver are then released into the circulation according to the body's needs.

The liver is also an organ in which a large number of proteins useful to the body as a whole are synthesized.

Most of the proteins circulating in the bloodstream are produced and secreted by the liver.

By the liver these include various plasma 'cargo' proteins such as albumin, transferrin, and lipoproteins, as well as proteins linked to the immune system such as complement, and most of the factors involved in regulating coagulation (19)

Because of its storage and synthesis capacities, the liver plays a key role in regulating the body's energy metabolism.

It adapts its action according to the body's nutritional status and is the hub connecting different tissues such as skeletal muscle and adipose tissue (20).

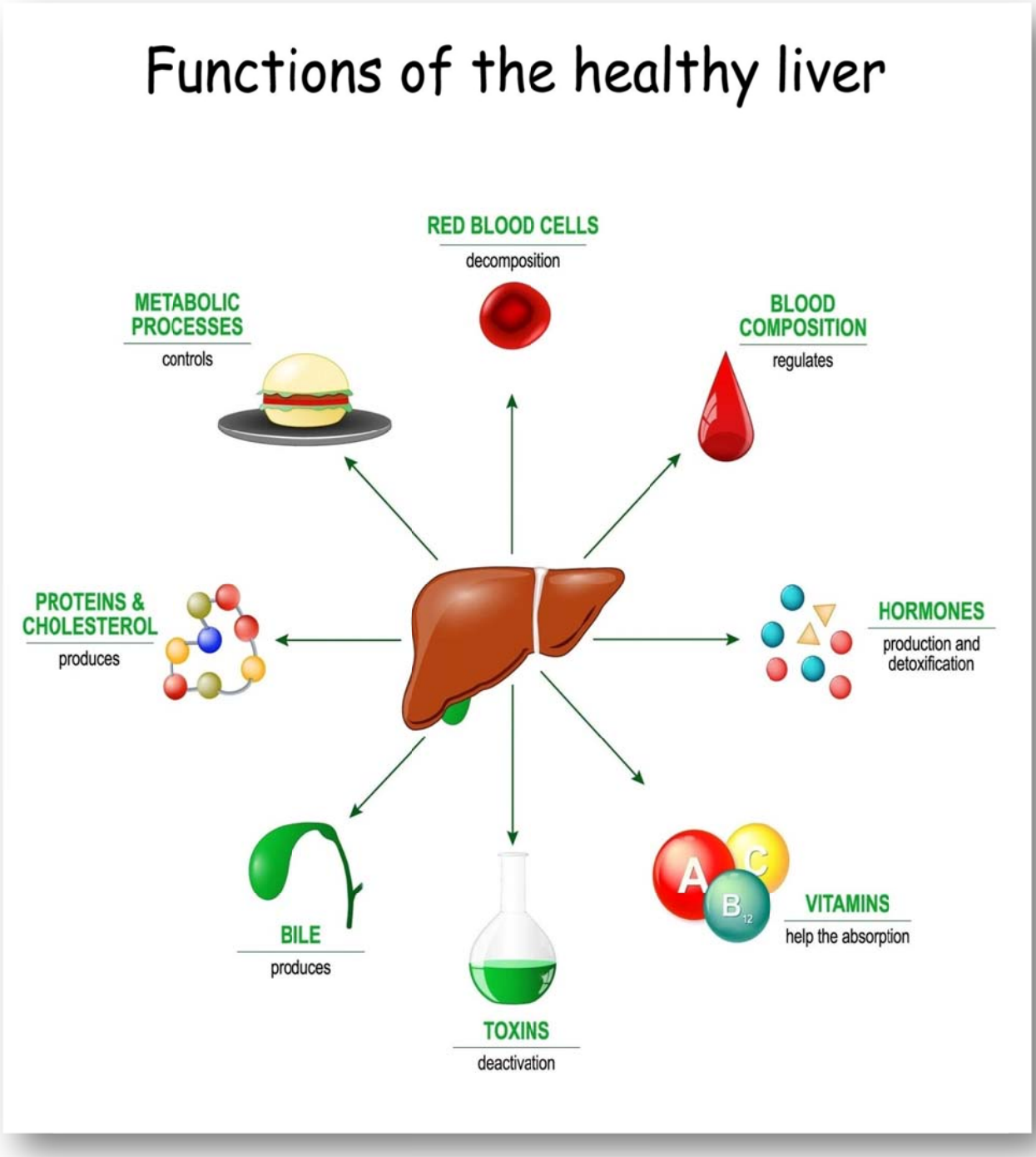


Figure 3: Functions of the liver; (21)

2. Liver diseases

"All conditions affecting the liver, an essential organ for metabolism, digestion and detoxification of the body".

This definition highlights the three main functions of the liver:

- Metabolic function: The liver is responsible for synthesizing many proteins, converting carbohydrates into energy and storing fat-soluble vitamins.

- Digestive function: The liver produces bile, which is needed to digest fats.

- Detoxification function: The liver filters the blood and eliminates toxins from the body.

Liver disease can affect one or more of these functions. They can be acute or chronic, and their severity can vary considerably...(22).

3. Liver diseases dangers

They can impair the liver's ability to perform its essential functions, leading to serious health complications. Here's a breakdown of the dangers:

- **Liver Failure:** The liver acts as the body's filter, removing toxins and waste products from your blood. When liver disease strikes, this filtration process gets disrupted. In severe cases, the liver can fail altogether, leading to coma and even death. (23)
- **Increased Risk of Cancer:** Scarring from chronic liver disease (cirrhosis) is a major risk factor for developing liver cancer. Liver cancer is aggressive and often has a poor prognosis. (23)
- **Internal Bleeding:** The liver plays a crucial role in blood clotting. Damaged livers can struggle to produce clotting factors, increasing the risk of internal bleeding.(24)
- **Malnutrition:** The liver plays a key role in processing nutrients from food. Liver disease can disrupt this process, leading to malnutrition and deficiencies in essential vitamins and minerals.(25)
- **Brain Dysfunction:** In severe liver disease, toxins can build up in the bloodstream and affect the brain, leading to confusion, disorientation, and even coma.(26)
- **Weakened Immune System:** The liver helps fight infections. When the liver is diseased, it becomes less effective, making you more susceptible to infections. (27).

5. Main liver disease

o Hepatic diseases:

The main hepatic diseases responsible for the highest levels of morbidity and mortality are viral hepatitis (chronic hepatitis B and C), alcoholic liver disease, non-alcoholic fatty liver, cirrhosis, and hepatocellular carcinoma.

These diseases are responsible for more than 95% of all deaths from liver disease (28)

• Hepatitis A

Is an acute infectious disease of the liver caused by the hepatitis A virus (HAV) the liver is a vital organ which plays an important function in digestion, filtering toxins and storing nutrients. When the hepatitis A virus attacks the liver, it can cause inflammation and impaired function.(29).

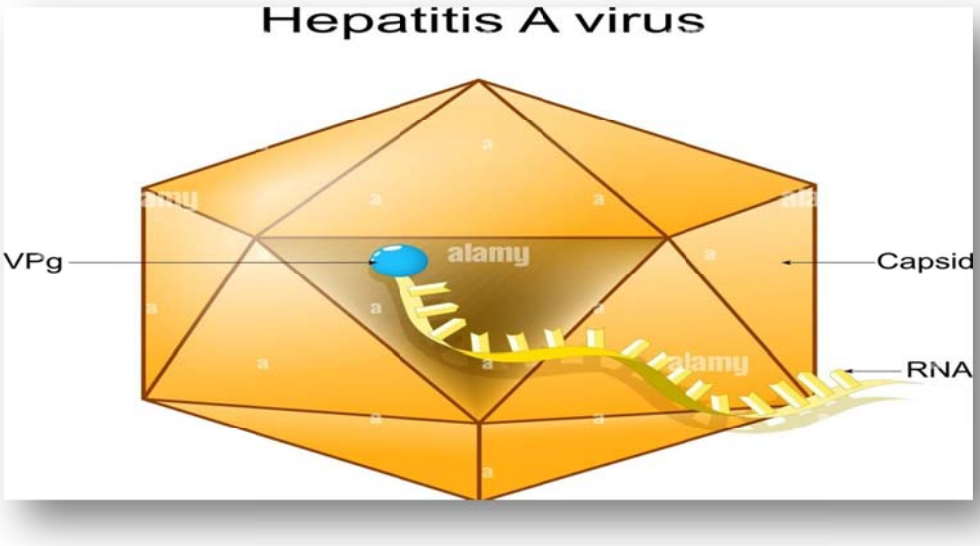


Figure 4: Structure of hepatitis A virus; (30)

Causes

The hepatitis A virus is generally transmitted via the faeco-oral route, i.e. by contact with the faeces of an infected person. This can happen in several ways:

- Consumption of contaminated food or water: The virus can be found in food or water contaminated by the faeces of an infected person. This can happen if the food is not properly cooked or the water is not safe to drink.

- Direct contact with an infected person: The virus can also be transmitted by direct contact with the faeces of an infected person, for example during sexual intercourse or when changing a baby's nappy. (29)

Symptoms

Symptoms of hepatitis A may appear 15 to 50 days after exposure to the virus. They may include

- Tiredness, Loss of appetite

- Nausea and vomiting

- Abdominal pain

- Diarrhea

- Jaundice (yellowing of the skin and whites of the eyes)

- Dark urine

In some cases, hepatitis A can be serious, even fatal, particularly in the elderly or people with chronic liver disease.(31)

Treatment

There is no specific treatment for hepatitis A. Treatment aims to relieve symptoms and allow the liver to heal naturally. Most people recover completely from hepatitis A within a few weeks or months and then develop lifelong immunity to the virus. (31)

Prevention

The best way to prevent hepatitis A is through vaccination. The hepatitis A vaccine is safe and effective and can protect against the disease by more than 90%. The following people are recommended to be vaccinated:

- Travelers to countries where hepatitis A is common

- People living with someone infected with hepatitis A

- Men who have sex with men

- Injecting drug users

- People who work in the food or wastewater sectors

In addition to vaccination, other measures can help prevent the transmission of hepatitis A:

- Wash your hands frequently with soap and water, especially before eating and after using the toilet

- Avoid consuming food or water that could be contaminated

- Practice safe sex.

- Do not share personal items such as razors or toothbrushes with an infected person.

In Algeria, the hepatitis A vaccine is available at public and private health centers. It is advisable to consult your doctor to find out if you are at risk. (32)

- **Hepatitis B**

Hepatitis B is a liver disease caused by the hepatitis B virus (HBV). This virus can attack the liver, causing serious damage and even death in severe cases. HBV infection can be acute or chronic.(33) In the Figure **(5)** we can see how HBV virus looks alike**.**

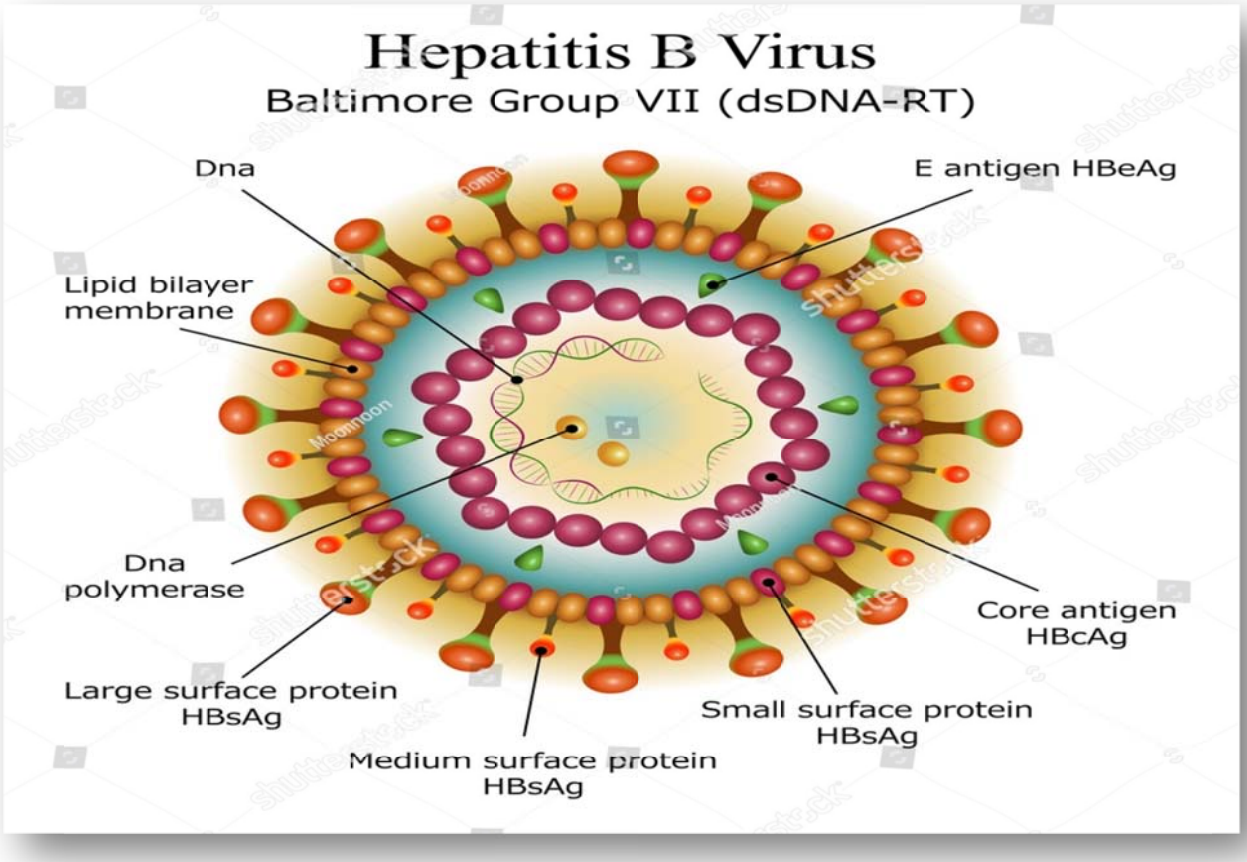


Figure 5 : Hepatitis B virus particle structure **;** (34)

1. **Transmission of the virus**

HBV is transmitted mainly through contact with infected body fluids, such as:

Blood: The virus can be transmitted by contact with infected blood, for example during a needle stick or blood transfusion.

Sexual fluids: HBV can also be transmitted by sexual contact with an infected person.

Mother-to-child transmission: A pregnant woman infected with HBV can transmit the virus to her baby during pregnancy or childbirth.(35)

2. Symptoms

The symptoms of hepatitis B can vary from person to person and according to the stage of infection.(36)

Acute hepatitis B:

Tiredness, Fever, Loss of appetite, Nausea and vomiting, abdominal pain, Jaundice (yellowing of the skin and eyes), Dark urine

Chronic hepatitis B:

Fatigue, Loss of appetite, abdominal pain, Enlargement of the liver, Jaundice

Signs of cirrhosis of the liver (advanced stage of liver scarring)

3. Complications

Chronic hepatitis B can lead to serious complications, such as:

Cirrhosis of the liver: Cirrhosis is irreversible scarring of the liver, which can impair its function and lead to liver failure.

Liver cancer: Chronic hepatitis B increases the risk of developing liver cancer.

Liver failure: Liver failure is a life-threatening medical emergency if not treated promptly.(37)

4. Treatment

Treatment of hepatitis B depends on the stage of infection. (37)

Acute hepatitis B:

Most cases of acute hepatitis B heal on their own without treatment.

Rest, Abundant fluids, Medication to relieve symptoms

Chronic hepatitis B:

Antiviral drugs can help control the virus and reduce the risk of complications.

In some cases, a liver transplant may be necessary.

5. Prevention

The best way to prevent hepatitis B is through vaccination. The hepatitis B vaccine is safe and effective and can protect against HBV infection.(38)

Other preventive measures:

Safe sexual practices: Use condoms during all sexual intercourse.

Avoid sharing injection equipment: Never use shared needles or other sharp objects.

Hygiene: Wash your hands frequently with soap and water, especially after contact with blood or other body fluids.(39)

- **Hepatitis C**

Is a viral infection that attacks the liver. It can cause acute and chronic inflammation of the liver and can lead to serious complications such as cirrhosis, liver cancer and liver failure.

The hepatitis C virus (HCV) is transmitted mainly through contact with contaminated blood, usually by injecting drugs, unprotected sex or vertical transmission from mother to child.(40)

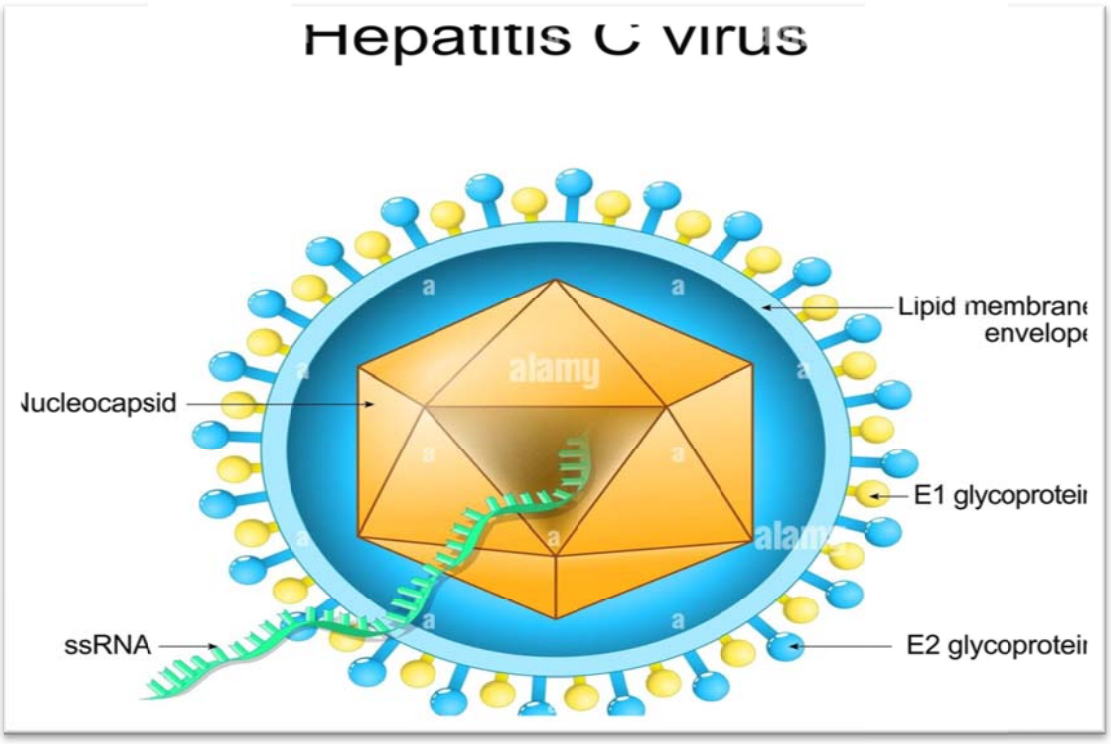


Figure 6: Structure of the hepatitis C virus; (30)

Causes

Contact with contaminated blood: The most common mode of transmission of HCV is contact with contaminated blood.

This can occur through sharing syringes or other contaminated needles, accidental pricks with contaminated needles, blood transfusions or organ transplants before 1987 (when HCV screening was not yet systematic), or unsterile medical or dental procedures.

Sexual transmission: HCV can also be transmitted by sexual contact, particularly among men who have sex with men (MSM).

The risk of sexual transmission is higher for people who have several sexual partners, who have unprotected sex or who have sexually transmitted infections (STIs) such as HIV.

Vertical transmission: HCV can be transmitted from mother to child during pregnancy or childbirth. The risk of transmission is higher in women with a high viral load. (41)

Symptoms

Acute infection: Most people infected with HCV have no symptoms during acute infection. However, some people may experience symptoms such as fatigue, nausea, vomiting, abdominal pain, jaundice (yellowing of the skin and eyes) and dark urine.

Chronic infection: Most people infected with HCV develop a chronic infection. In most cases, chronic infection presents no symptoms for many years. However, over time, chronic infection can cause serious liver damage such as cirrhosis, liver cancer and liver failure. (40)

Treatment

Hepatitis C is now curable thanks to direct antiviral treatments (DAAs). These drugs are highly effective in eliminating the virus from the body and preventing liver damage. DAA treatment generally lasts 12 to 24 weeks and is taken orally in pill form. Most people recover from hepatitis C with DAA treatment. (40)

Prevention

Avoid contact with contaminated blood: The best way to prevent hepatitis C is to avoid all contact with contaminated blood. This means not sharing syringes or other needles, using condoms during sex and getting tattoos and piercings in sterile establishments.

Screening: It's important to get tested for hepatitis C, especially if you think you've been exposed to the virus. Screening can be done by a simple blood test. If you are diagnosed with hepatitis C, you can be treated and cured of the infection.

Vaccination: A vaccine against hepatitis C was approved in 2019. The vaccine is 95% effective in preventing HCV infection. The vaccine is recommended for people at risk of HCV infection, such as people who inject drugs, people with multiple sexual partners and people who have been exposed to contaminated blood. (41)

Hepatitis C is a serious infection, but it is curable. It is important to get tested and treated if you are diagnosed with hepatitis C. Preventing infection is also important, by avoiding contact with contaminated blood and getting vaccinated.

- **Hepatitis D**

Virus is unusual because it can only infect you when you also have a hepatitis B virus infection. In this way, hepatitis D is a double infection. You can protect yourself from hepatitis D by protecting yourself from hepatitis B by getting the hepatitis B vaccine. (42)

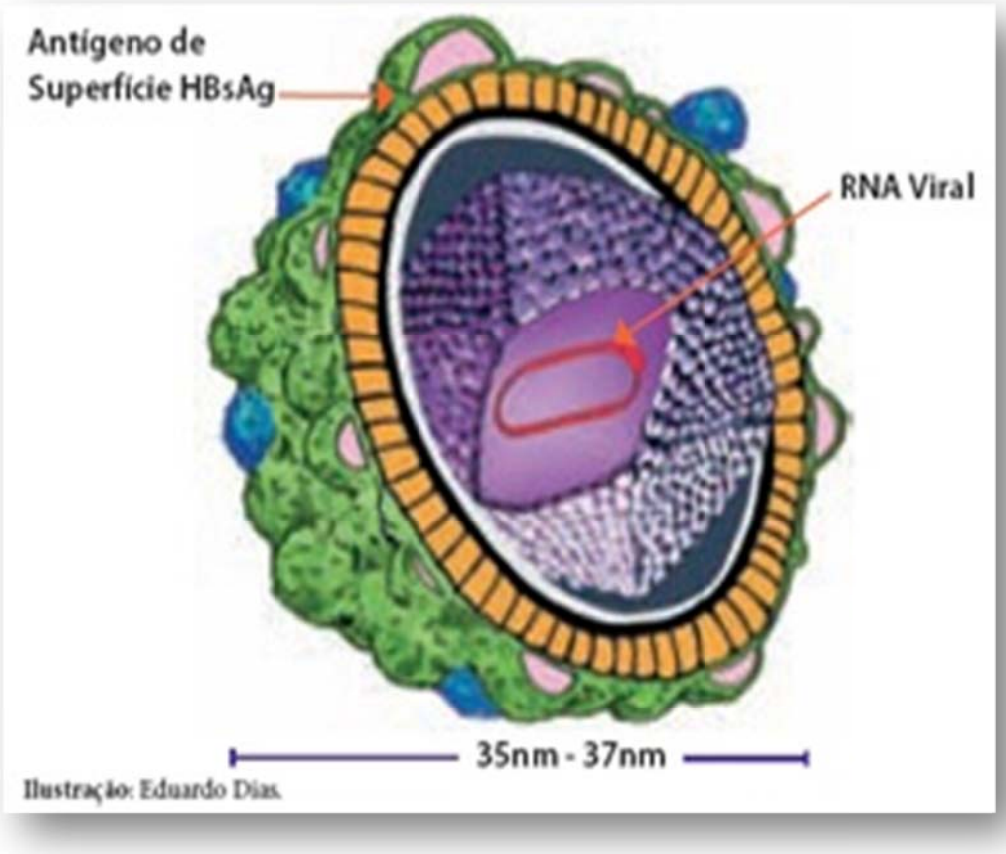


Figure 7: Structure of the hepatitis D virus; (43)

Hepatitis D spreads the same way that hepatitis B spreads, through contact with an infected person's blood or other body fluids. The hepatitis D virus can cause an acute or chronic infection, or both.

Acute hepatitis D

Acute hepatitis D is a short-term infection. The symptoms of acute hepatitis D are the same as the symptoms of any type of hepatitis and are often more severe.(44) Sometimes your body is able to fight off the infection and the virus goes away. (42)

Chronic hepatitis D

Chronic hepatitis D is a long-lasting infection. Chronic hepatitis D occurs when your body is not able to fight off the virus and the virus does not go away. People who have chronic hepatitis B and D develop complications more often and more quickly than people who have chronic hepatitis B alone.(42)

Causes

The hepatitis D virus causes hepatitis D. The hepatitis D virus spreads through contact with an infected person's blood or other body fluids. Contact Can occur by

- sharing drug needles or other drug materials with an infected person
- having unprotected sex with an infected person
- getting an accidental stick with a needle that was used on an infected person

The hepatitis D virus rarely spreads from mother to child during birth.

You can't get hepatitis D from

- being coughed on or sneezed on by an infected person
- drinking water or eating food
- hugging an infected person
- shaking hands or holding hands with an infected person
- sharing spoons, forks, and other eating utensils
- Sitting next to an infected person.(45)

The symptoms of hepatitis D

Most people with acute hepatitis D have symptoms, which may include

- feeling tired ,
- nausea and vomiting
- poor appetite pain over the liver
- in the upper part of the abdomen
- darkening of the color of urine
- lightening of the color of stool
- yellowish tint to the whites of the eyes and skin, called jaundice

In contrast, most people with chronic hepatitis D have few symptoms until complications develop, which could be several years after they were infected. Some symptoms of cirrhosis include:

- weakness and feeling tired
- weight loss
- swelling of the abdomen
- swelling of the ankles
- called edema
- itching skin
- Jaundice. (45)

Treatment

Doctors may treat chronic hepatitis D with medicines called interferons, such as peginterferon alfa-2a *external link* (Pegasys). Researchers are studying new treatments for hepatitis D. In addition, medicines for hepatitis B may be needed. These are usually medicines taken once daily by mouth. (46)

Prevention

Prevent hepatitis B infection, such as getting the hepatitis B vaccine. If you do not get hepatitis B, you cannot get hepatitis D.

If you already have hepatitis B, you can take steps to prevent hepatitis D infection by

- not sharing drug needles or other drug materials
- wearing gloves if you have to touch another person's blood or open sores
- not sharing personal items such as toothbrushes, razors, or nail clippers

Prevent spreading hepatitis D to others

If you have hepatitis D, follow the steps above to avoid spreading the infection. Your sex partners should get a hepatitis B test and, if they aren't infected, get the hepatitis B vaccine.

Preventing hepatitis B will also prevent hepatitis D.You can protect others from getting infected by telling your doctor, dentist, and other health care professionals that you have hepatitis D. don't donate blood or blood products, semen, organs, or tissue. (46)

Hepatitis E

Is a viral infection that attacks the liver it is caused by the hepatitis E virus (HEV), which is generally transmitted through contaminated water or food. Hepatitis E is more common in regions of the world where hygiene and sanitation conditions are precarious (47) .

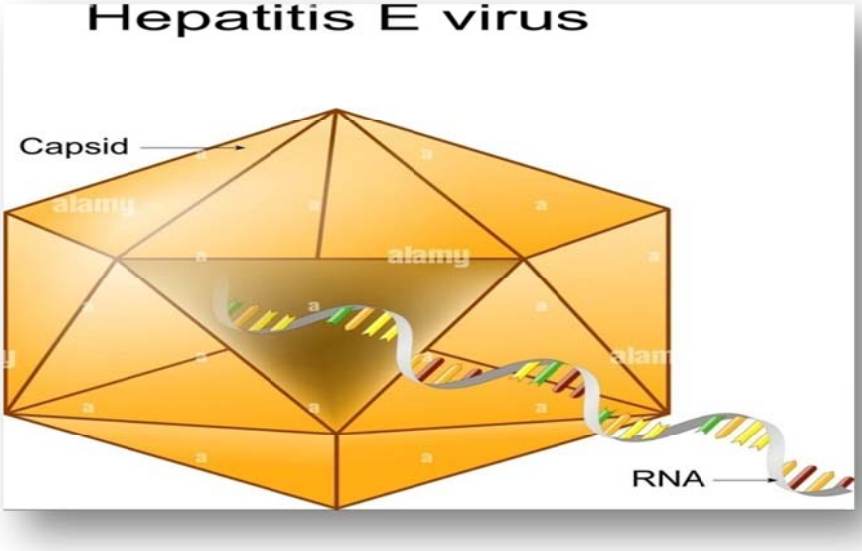


Figure 8 Structure of the hepatitis E virus**;** (48)

Causes

HEV is transmitted by ingesting water or food contaminated with the faeces of an infected person. The most common foods responsible for the transmission of hepatitis E are:

Raw or undercooked pork, Seafood, Raw vegetables, contaminated water (49)

Symptoms

Symptoms of hepatitis E may appear 15 to 60 days after exposure to the virus. The most

Jaundice (yellowing of the skin and eyes), Tiredness, Nausea and vomiting, abdominal pain, Diarrhea, loss of appetite, Fever

In some cases, hepatitis E can be serious, even fatal. This is more common in pregnant women and people with weakened immune systems. (50)

Treatment

There is no specific treatment for the hepatitis E virus. Most people recover on their own within a few weeks or months. Treatment is aimed at relieving symptoms and supporting the liver. This may include:

Rest, Fluids, Medication for nausea and vomiting, Pain medication

In some severe cases, hospitalization may be necessary. (47)

Prevention

Wash your hands often with soap and water , Drink drinking water or bottled water, Eat well-cooked food ,Avoid raw foods of animal origin , Practice safe sex Pregnant women and people with weakened immune systems should take special precautions to avoid hepatitis E. They should talk to their doctor about the possibility of being vaccinated against hepatitis E.(50)

- **Nonalcoholic fatty liver disease (NAFLD)**

Is a condition in which excess fat builds up in your liver. This buildup of fat is not caused by heavy alcohol use as we see in **Figure (9).** When heavy alcohol use causes fat to build up in the liver, this condition is called alcohol-associated liver disease. (51)

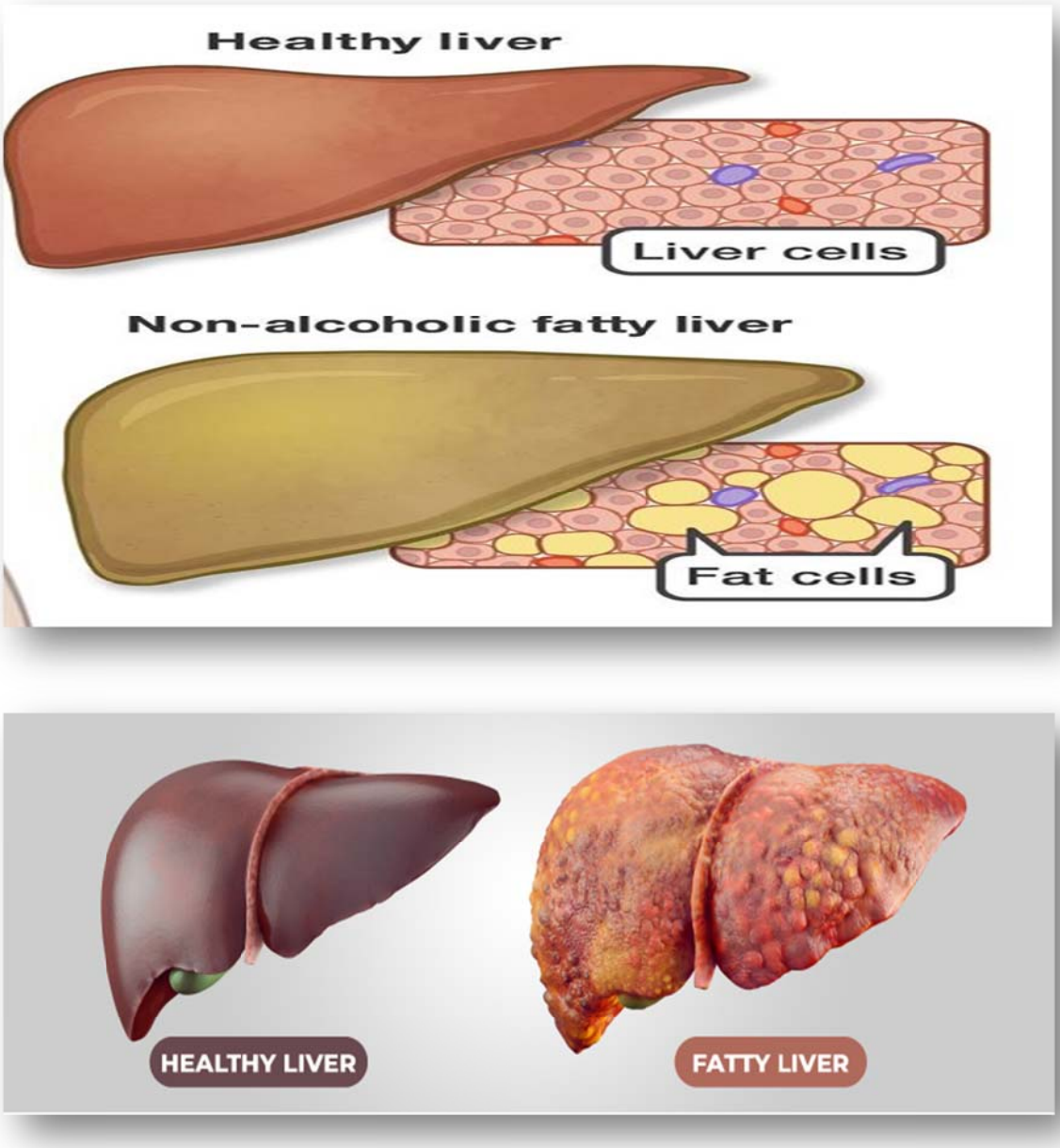


Figure 9; Schematic illustration and realistic picture of a healthy and fatty liver (52)

Two types of NAFLD are nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH). People typically develop one type of NAFLD or the other, although sometimes people with one form are later diagnosed with the other form of NAFLD.

NAFL

NAFL is a form of NAFLD in which you have fat in your liver but little or no inflammation or liver damage. NAFL typically does not progress to cause liver damage or complications. However, NAFL can cause pain from enlargement of the liver.

NASH

NASH is the form of NAFLD in which you have inflammation of the liver and liver damage, in addition to fat in your liver. The inflammation and liver damage of NASH can cause fibrosis, or scarring, of the liver. NASH may lead to cirrhosis, in which the liver is scarred and permanently damaged. Cirrhosis can lead to liver cancer .(51)

Causes

Non-alcoholic fatty liver disease (NAFLD) causes various adverse outcomes and complications. NAFLD is closely linked to metabolic syndrome, obesity, type 2 diabetes mellitus, insulin resistance, and dyslipidemia, all of which are crucial risk factors for the development and progression of the disease (53). NAFLD can progress to non-alcoholic steatohepatitis (NASH), cirrhosis, and even liver cancer (54). Factors contributing to NAFLD include genetic, environmental, and metabolic elements (55). Additionally, NAFLD can lead to anemia and erythropoietin hypo responsiveness in chronic kidney disease patients, possibly due to iron deficiency and inflammation (56). NAFLD is also associated with liver inflammation, which can increase the risk of atherosclerotic cardiovascular disease and liver cancer (57). Overall, NAFLD poses significant health risks and requires comprehensive management to prevent severe complications.

Symptoms

Depending on the degree of liver damage, nonalcoholic fatty liver disease (NAFLD) symptoms can change (58)Although NAFLD is frequently asymptomatic in its early stages, people may have general symptoms including malaise, exhaustion, or slight discomfort in the upper right abdomen (59)The symptoms of non-alcoholic steatohepatitis (NASH), which develops from non-alcoholic fatty liver disease (NAFLD), may worsen and eventually result in cirrhosis or liver cancer (60). Furthermore, extrahepatic symptoms and comorbidities, such as chronic renal disease, sleep apnea, and cardiovascular diseases, might exacerbate the clinical presentation in patients with non-alcoholic fatty liver disease (NAFLD) ((61). (62). It's critical to keep an eye out for these related disorders for the full management of NAFLD and its possible effect on the results of general health.

Treatment

The complicated pathophysiology of nonalcoholic fatty liver disease (NAFLD) necessitates a multimodal approach to treatment. Exercise and dietary changes are important lifestyle changes (58)(59), and drugs that target inflammation, liver protection, glucose, and lipid metabolism are frequently used (60)(61). For the resolution of NASH, vitamin E and pioglitazone are being used in pharmacotherapy. Research is also being done on GLP-1 agonists and substances that target bile acid signaling, insulin resistance, and lipid metabolism (62). New therapy approaches for NAFLD appear promising, including FXR and PPAR ligands, GLP-1 agonists, and other medicines. Furthermore, it's critical to address the cardiovascular risks linked with NAFLD/NASH. Drugs like metformin, aspirin, and statins can improve liver function and reduce inflammation. In general, management requires an all-encompassing strategy that combines targeted medicines and lifestyle modifications.

Prevention

Due to the absence of efficacious traditional pharmacological interventions, phytotherapy has attracted substantial interest in the prevention of nonalcoholic fatty liver disease (NAFLD) (63)(64). Because of their great efficacy and minimal chance of adverse effects, herbal medications have gained attention as promising therapeutic agents for NAFLD (65). Tea, flaxseed, cinnamon, silybin, soy, ginger, licorice, and flaxseed oil are a few plant-derived compounds that have demonstrated potential in the treatment and prevention of NAFLD (66). Additionally, network pharmacology analyses have predicted mechanisms of action for botanical drug formulas like Livsooth authentic herbal formula (LAH), and subsequent experimental validation has demonstrated efficacy in ameliorating hepatocyte steatosis and improving oxidative stress markers in NAFLD models. These studies have explored the potential of botanical drug formulas in the treatment of nonalcoholic fatty liver disease (NAFLD) (67). These results demonstrate the potential of plant-derived substances and herbal medications for the management and prevention of NAFLD.

- **Fibrosis**

Develops when the liver is damaged repeatedly or continuously. After a single episode of damage, even if severe (as in acute hepatitis), the liver often repairs itself by producing new liver cells and attaching them to the connective tissue matrix (internal structure) left by the liver cells when they die. However, if the damage is repeated or continuous (as occurs in chronic hepatitis), the liver cells attempt to repair the damage, but these attempts result in the formation of scar tissue (fibrosis). Fibrosis can develop more rapidly when it is due to obstruction of the bile ducts.

Scar tissue replaces liver cells and, unlike them, does not perform any function. Scar tissue can deform the internal structure of the liver and interfere with blood flow to and within the liver, limiting the blood supply to the liver cells. Without a sufficient blood supply, these cells die and more scar tissue is formed. In addition, blood pressure increases in the vein that carries blood from the intestines to the liver (portal vein), a condition known as portal hypertension.(68)

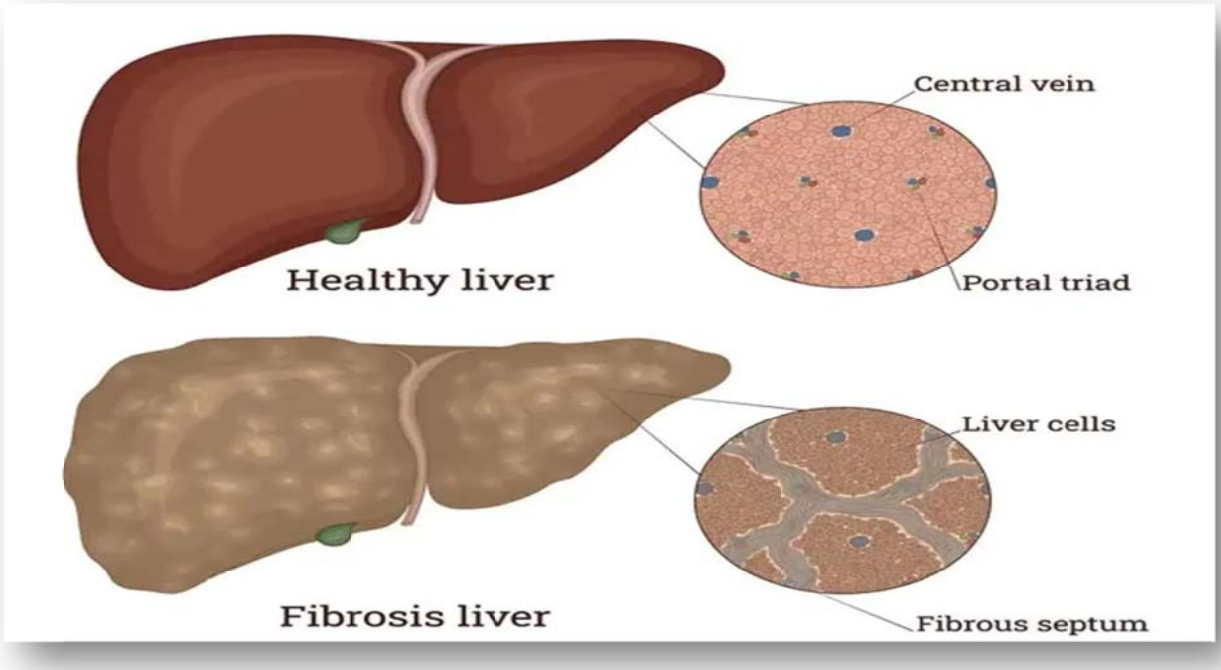


Figure 10: schematic illustration for Liver Fibrosis; (69)

Causes

Liver fibrosis is primarily caused by chronic liver injuries from various factors like hepatitis B and C, fatty liver, alcohol consumption, and rare diseases such as hemochromatosis (70). Factors contributing to advanced liver fibrosis include cadmium exposure, smoking, excessive alcohol use, poverty, and susceptibility to lead exposure, with variations among racial/ethnic groups [71]. The process of liver fibrosis involves abnormal wound repair responses due to chronic liver injuries, leading to over-deposition of the extracellular matrix and connective

tissue hyperplasia (72). Liver cell damage, especially by diseases like Hepatitis B, C, and fatty liver disease, triggers fibrosis progression, significantly impacting patient morbidity and mortality, with fibrosis being a key step towards cirrhosis and hepatocellular carcinoma development (73).

Symptoms

Liver fibrosis, a common consequence of various liver diseases including cirrhosis, presents with a range of symptoms. These symptoms can include fatigue, muscle cramps, anxiety, insomnia, lack of appetite, and pain (74)(75). Additionally, liver fibrosis can lead to complications such as ascites, hepatic encephalopathy, variceal bleeding, and spontaneous bacterial peritonitis [(76)]. Alcohol consumption is a significant contributor to liver fibrosis, exacerbating scar tissue deposition and leading to severe liver damage (77) (78). The progression of liver fibrosis is crucial in determining the prognosis and treatment strategies for patients with liver diseases, emphasizing the importance of early detection and management of symptoms associated with fibrosis.

Treatment

Various approaches have been explored, including dietary supplements, biological treatments, drugs, genetic regulation, and stem cell transplantation, yet none have gained FDA approval (79). Targeting hepatic stellate cells (HSCs) and related signaling pathways is crucial for reversing fibrosis (80). Anti-fibrotic strategies involve inhibiting inflammation, protecting the liver, controlling HSC activation, reducing extracellular matrix (ECM) production, and promoting ECM degradation [(81)]. Novel therapies are being researched, emphasizing the need for effective anti-fibrotic drugs to prevent liver fibrosis progression and its severe complications. And there are some researchers have proven the effectiveness of medicinal plants in treating hepatic fibrosis.

Prevention

Prevention of liver fibrosis can be achieved through various strategies based on the research findings. Deferasirox, an iron chelation drug, has shown effectiveness in reducing liver fibrosis caused by iron overload in mice, highlighting its potential preventive role (82). Germacrone, found in zedoary turmeric, has demonstrated the ability to inhibit hepatic fibrosis by regulating multiple signaling pathways, protecting hepatocytes, and inducing apoptosis of activated hepatic stellate cells (83). Lifestyle modifications, along with potential antifibrotic drug candidates like obeticholic acid, lanifibranor, and cenicriviroc, offer hope for effective pharmacological therapy against liver fibrosis, particularly in non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) (84). Furthermore, herbal medicines such as silymarin, curcumin, and ginseng have been found to have beneficial effects on cirrhosis, a condition often preceding liver fibrosis [(85)]. The bioactive compounds in plants can help attenuate the complex pathophysiological processes involved in chronic inflammation and liver cirrhosis, offering a potential alternative for preventing and treating liver fibrosis(86)(87).

- **Cirrhosis**

An irreversible liver disease, cirrhosis is characterized by chronic inflammation. This leads to the destruction of liver cells and their uncontrolled regeneration in the form of nodules. The disease leads to the loss of the organ's functions and is accompanied by multiple complications. As cirrhosis gets worse, your liver begins to fail.(88).

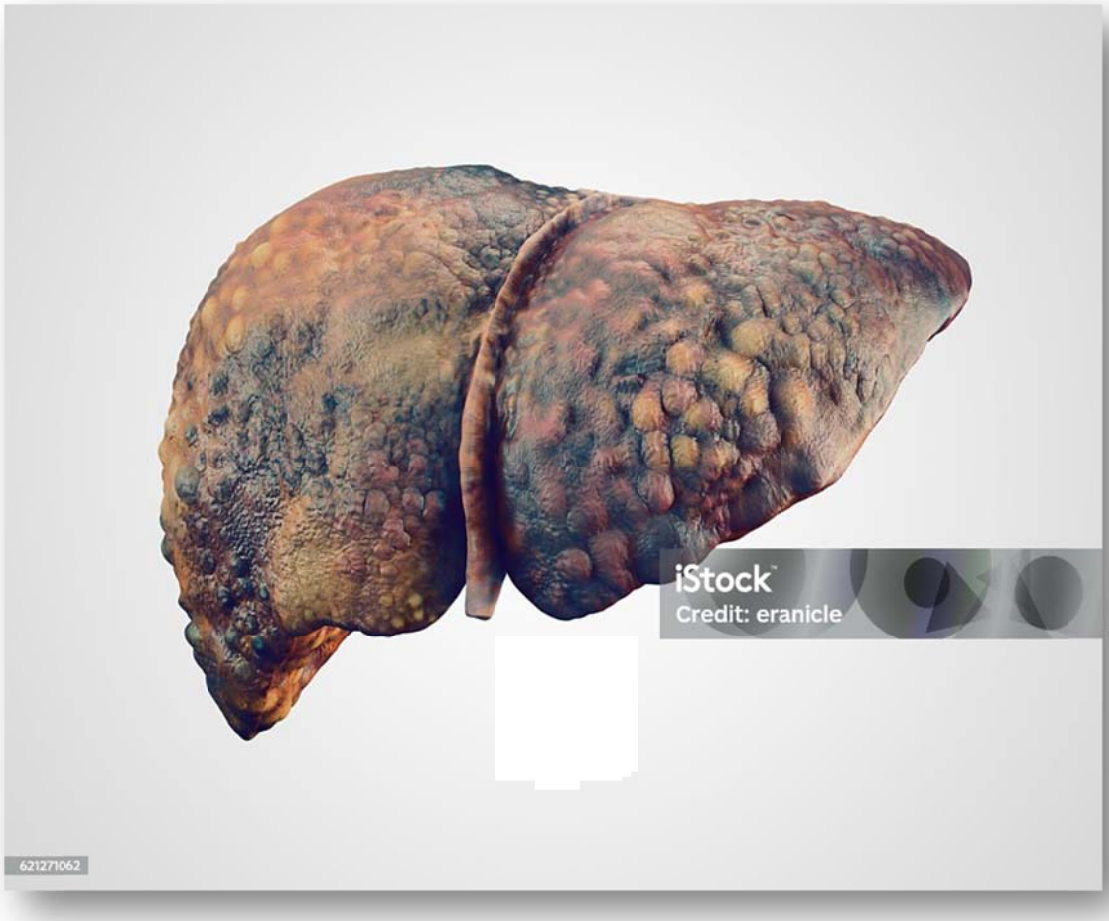


Figure 11: Realistic illustration of cirrhosis of human liver (89)

Causes

- Liver cirrhosis can be caused by various factors such as alcohol intake, biliary obstruction, chronic hepatitis B or C, and hemochromatosis.
- Chronic hepatitis C virus infection is a significant cause of liver disease globally, leading to cirrhosis or hepatocellular carcinoma in a percentage of infected individuals.
- Studies in India show that alcohol-related liver disease, NASH, and HBV-related cirrhosis are common etiologies of cirrhosis, with a higher prevalence in males.

- Non-alcoholic fatty liver disease (NAFLD) is becoming a major public health concern in India due to factors like a sedentary lifestyle, obesity, and diabetes, leading to cirrhosis, hepatocellular carcinoma, and liver transplants.(90)

Symptoms

- Early symptoms of cirrhosis include fatigue, poor appetite, weight loss, nausea, abdominal discomfort, bruising, confusion, swelling, ascites, itchy skin, dark urine, blood in vomiting, and jaundice.
- Cirrhosis can progress to end-stage liver scarring with symptoms like jaundice, fatigue, easy bleeding, nausea, swelling, and confusion. Patients may also experience multiple nutrient deficiencies leading to various signs and symptoms. (90)

Treatment

There is no cure for cirrhosis, but treatment can halt or slow its progress and prevent complications. Treatment is devised by a multidisciplinary medical team in coordination with the treating physician.

Treating the cause of cirrhosis and aggravating factors

It is vital to act on the cause of cirrhosis and any factors that weaken the liver:

Alcohol must be stopped.

If viral hepatitis B or viral hepatitis C has become chronic, antiviral treatment is prescribed to prevent progression to cirrhosis. Regular tests are carried out to monitor the progress of the disease.

In cases of metabolic syndrome or non-alcoholic steatosis, control of diabetes, overweight and blood fat abnormalities (cholesterol, triglycerides) is essential,

Specific treatment is given for other causes of cirrhosis (haemochromatosis, metabolic disease, autoimmune disease, etc.).

It is essential to eliminate factors that aggravate cirrhosis:

Stopping drug use;

Eliminating drugs that are toxic to the liver

Elimination of sedative drugs that encourage the onset of neurological disorders (encephalopathy);

Stop all tobacco use, etc. (91)

PREVENTING AND TREATING THE COMPLICATIONS OF CIRRHOSIS

It is important to prevent the complications that make cirrhosis so serious. When they do occur, hospitalisation is often necessary.

To prevent the bacterial or viral infections that are more frequent and more serious in cirrhosis, certain measures are essential:

Good oral and dental hygiene.

Prompt skin care in the event of a skin wound.

Vaccination against certain diseases, such as hepatitis A and B, influenza, pneumococcal infections and Covid.

Antibiotics are essential when a bacterial infection occurs.

Oesophageal varices are a source of haemorrhagic complications.

Medication with beta blockers or ligation of oesophageal varices can reduce the risk of bleeding.

In the presence of ascites, a low-salt diet and diuretics are prescribed. Evacuation of the ascites is sometimes necessary.

If the patient is suffering from encephalopathy, treatment with a laxative (lactulose) can reduce the production of ammonia by digestive bacteria.

Liver transplantation may be considered in cases of:

Decompensate cirrhosis beyond the reach of any medical treatment

Liver cancer. (91).

Fibrosis and cirrhosis are not specific disorders. Rather, they are the result of other causes of liver damage.

- **Jaundice**

Or ictreus is a yellow discoloration of the skin and sclerae caused by excessive bilirubin levels in the blood, which can be caused by a variety of factors including hemolysis, liver illness, and bile duct obstruction (92). It is critical to treat jaundice as soon as possible since it might suggest dangerous illnesses such as acute liver failure, which requires immediate examination and intervention. (93) (94)

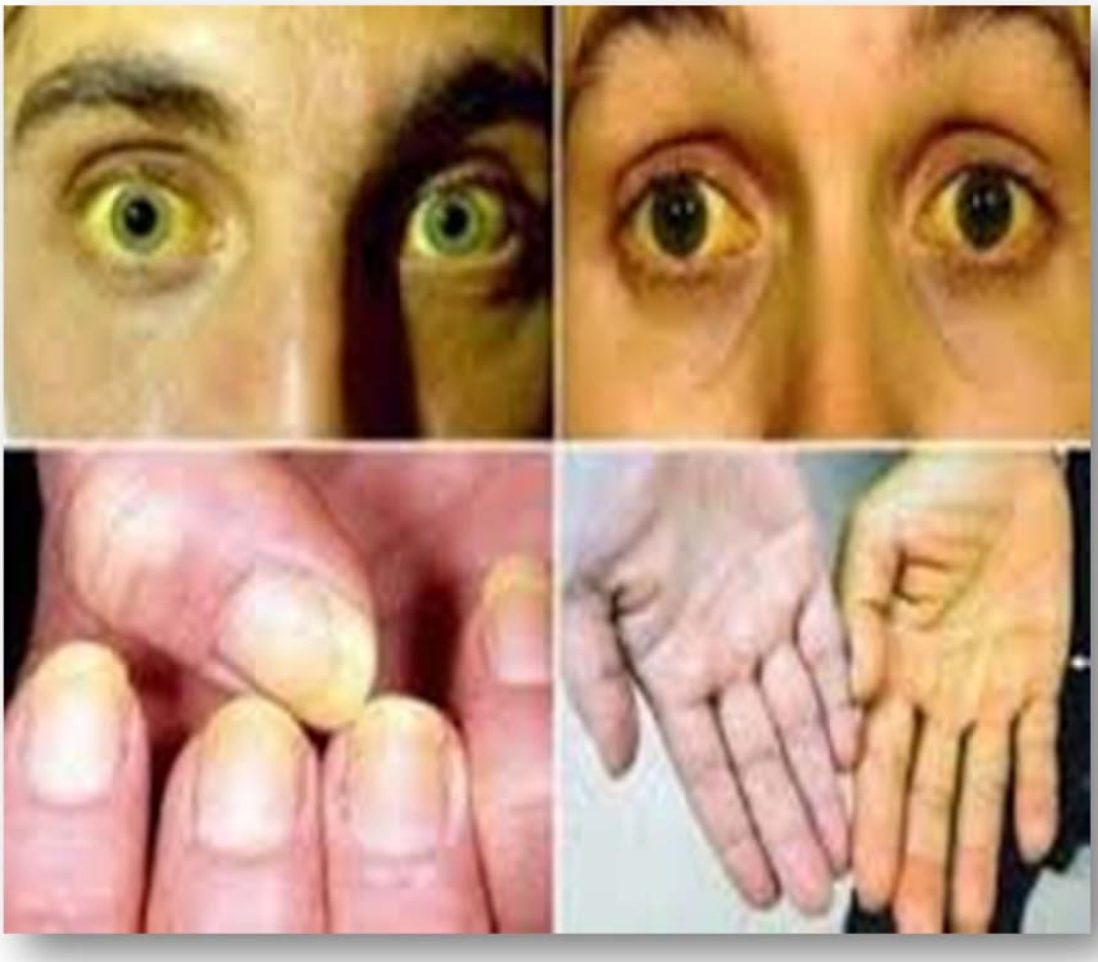


Figure 12: Icterus disease signs; (95)

Causes

Jaundice can be induced by a variety of reasons including viral hepatitis infection, acute fatty liver of pregnancy, hyperemesis gravidarum, HELLP syndrome, intrahepatic cholestasis of pregnancy, hemolysis, liver illness, bile duct obstruction, and immature liver function in newborns (96) (97) (98). The condition results from an imbalance between bilirubin synthesis and clearance, which causes hyperbilirubinemia (99). Birth weight, gestational age, hypoxia, infection, labor length, and sex can all contribute to jaundice in newborns, however primiparous women may not be a significant cause (100). Choledocholithiasis, pancreatic ductal adenocarcinoma, cholangiocarcinoma, and biliary atresia are all potential causes of

obstructive jaundice. To avoid problems and ensure better outcomes, jaundice must be diagnosed early and managed appropriately.

Symptoms

Jaundice symptoms include yellowing of the skin, eyes, and body fluids caused by the buildup of bilirubin in the blood, a pigment generated when red blood cells break down (101) (102) (103). Other symptoms may include dark or reddish urine, lack of appetite, bitter taste in the mouth, pale skin, nausea, itching, and a sluggish heart rate (104). Furthermore, symptoms can range from moderate to severe, with many forms of jaundice detected, including normal jaundice in infants, hepatic jaundice, and post-hepatic jaundice (105). Patients with obstructive jaundice may also have pruritus, pale stools, dark urine, and stomach pain. Traditional Chinese medicine has therapies for jaundice, which address symptoms such as fever, exhaustion, nausea, abdominal pain, yellow skin, and thirst.

Treatment

Jaundice treatment frequently includes phytotherapy, which uses medicinal plants to treat liver disorders (106) (107). Several studies have shown that medicinal herbs can reduce bilirubin levels and normalize liver enzymes, hence benefiting from jaundice therapy (108). Plants such as Cotoneaster discolor and Ziziphus jujube Miller is frequently used in Iranian traditional medicine to cure infant jaundice, albeit as a supplemental rehabilitation (109). Clinical experiments using H. vulgare seed flour have shown good effects in lowering indirect bilirubin levels, indicating that it could be used as a supplemental treatment for jaundice (110). The use of medicinal plants in drug development for jaundice treatment is gaining popularity, with a particular emphasis on identifying active components in plants. Phytotherapy is a natural and possibly beneficial way to manage jaundice of several plant-derived chemicals.

Prevention

Jaundice can be prevented using a variety of techniques, depending on the stage and condition. Probiotics such as L. rhamnosus, L. reuteri, and B. animalis substantially decrease the occurrence and duration of neonatal jaundice in full-term babies, with B. animalis having the strongest effect(111). Oral zinc sulfate delivery to healthy term neonates has been demonstrated to lower transcutaneous bilirubin levels, suggesting a preventative impact (112). Early detection and prevention of pregnancy-related jaundice are critical to avoiding serious consequences such as liver dysfunction, maternal mortality, and neonatal morbidity (113). Zinc sulfate injection in neonates did not delay jaundice onset, but it did shorten hospitalizations and phototherapy duration, highlighting its potential preventative role (114). Preventive treatments for thrombohemorrhagic consequences in patients with obstructive jaundice should be individualized.

- **Alcoholic liver disease (ALD)**

Refers to a variety of liver injuries induced by excessive alcohol intake, ranging from simple steatosis to more serious disorders such as alcoholic hepatitis, fibrosis, cirrhosis, and even hepatocellular cancer.(115)(116)(117). ALD is a major global health concern, accounting for a large proportion of liver-related deaths globally. (118)(119)

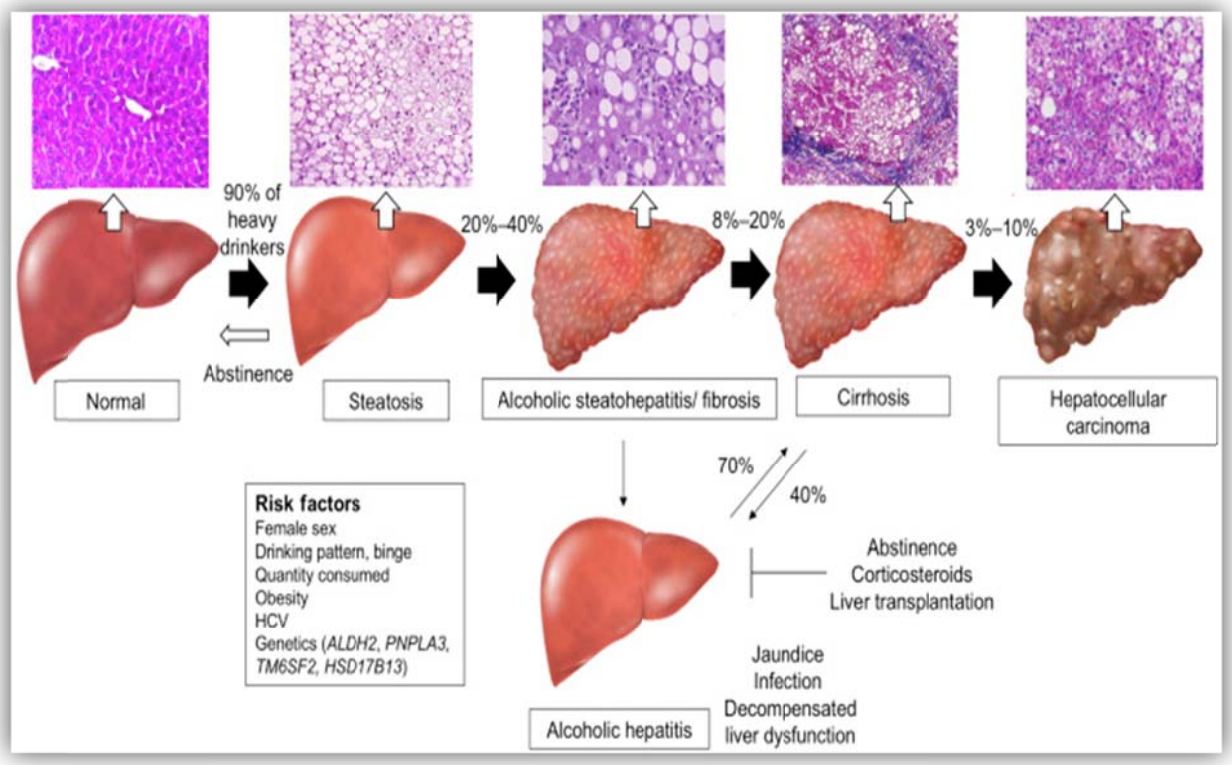


Figure 13: Schematic illustration for the progression of ALD**;** (120)

Causes

Alcoholic liver disease (ALD) typically occurs by continuous alcohol intake, which results in a series of liver damage ranging from steatosis to cirrhosis and hepatocellular cancer. ALD is caused by a variety of causes, including genetic and epigenetic abnormalities, oxidative stress, acetaldehyde toxicity, inflammation, metabolic changes, immunological damage, and gut microbiota dysbiosis (121), (122). Risk factors for ALD include the amount and duration of alcohol intake, the kind of alcohol drank, gender, genetic susceptibility, nutritional condition, hepatotoxic medications, smoking, viral hepatitis, and environmental variables (123). Individual vulnerability to ALD progression is determined by behavioral, environmental, genetic, and epigenetic variables (124). ALD is related with abnormalities in bile acid communication and metabolism, which affect disease development and severity (125). Effective treatments for ALD care emphasize alcohol abstinence and symptom control, with continuing research aimed at identifying novel therapeutic targets.

Symptoms

The symptoms of Alcoholic Liver Disease (ALD) vary depending on the stage of the disease. The most frequent signs include jaundice, ascites, lack of appetite, nausea, vomiting, hepatic encephalopathy, and esophageal varices (126). Patients with ALD may also develop extrahepatic symptoms affecting other organ systems, including the gastrointestinal tract, neurological system, cardiovascular system, musculoskeletal system, and endocrine problems (127). These symptoms are frequently missed, resulting in delayed diagnosis and therapy commencement. ALD can range from fatty liver to more serious diseases such as alcoholic hepatitis, fibrosis, cirrhosis, and even hepatocellular cancer (128)(129). Early identification and therapy are critical, as some forms, such as delirium tremens and Wernicke's encephalopathy, necessitate immediate treatment to avoid fatal results (130). Regular screening, clinical assessment, and knowledge of both hepatic and extrahepatic

Treatment

ALD treatment consists of several critical measures. Abstinence from alcohol is essential (131), as it is the foundation of treatment and aids in the reversal of fatty liver diseases. Corticosteroids may be administered in severe cases of Alcoholic Hepatitis (AH), particularly in patients with a high Model for End-Stage Liver Disease (MELD) score (132). Furthermore, support measures such as dietary supplementation and treating alcohol withdrawal syndrome are critical (133). For patients with ALD, therapeutic options include psychotherapy, group therapy, inpatient addiction treatment, and relapse prevention drugs. New medicines aimed at the innate immune response, gut dysbiosis, and liver damage pathways are being explored, indicating hope for the future of AH treatment. Integrated care approaches between addiction clinicians and hepatologists are essential to improve care for this group.(134)

Prevention

A variety of dietary strategies can be used to prevent alcoholic liver disease (ALD). Studies have emphasized the potential of bioactive components contained in foods such as milk, fermented milk, whey, and camel milk (135) (136). Furthermore, edible dietary plants and their bioactive substances have been found to protect the liver from ALD through mechanisms such as anti-oxidation, anti-inflammation, and gut microbiota composition regulation (137). Red yeast rice (RYR), which is well-known for its cholesterol-lowering properties, has also been shown to help prevent ALD by reducing oxidative stress, inflammation, and liver damage (138). These data imply that adding bioactive-rich dietary ingredients may be useful in avoiding the onset and progression of ALD, opening up new pathways for novel preventative interventions.

- **Autoimmune liver illnesses**

Are a group of inflammatory conditions that affect the liver, including autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC) (139)(140)(141). These disorders are distinguished by histological features such mononuclear cell infiltrates, bile duct lesions, and periductal fibrosis (142)(143). AIH, for example, is an autoimmune reaction to hepatocytes caused by genetic predisposition and environmental circumstances.

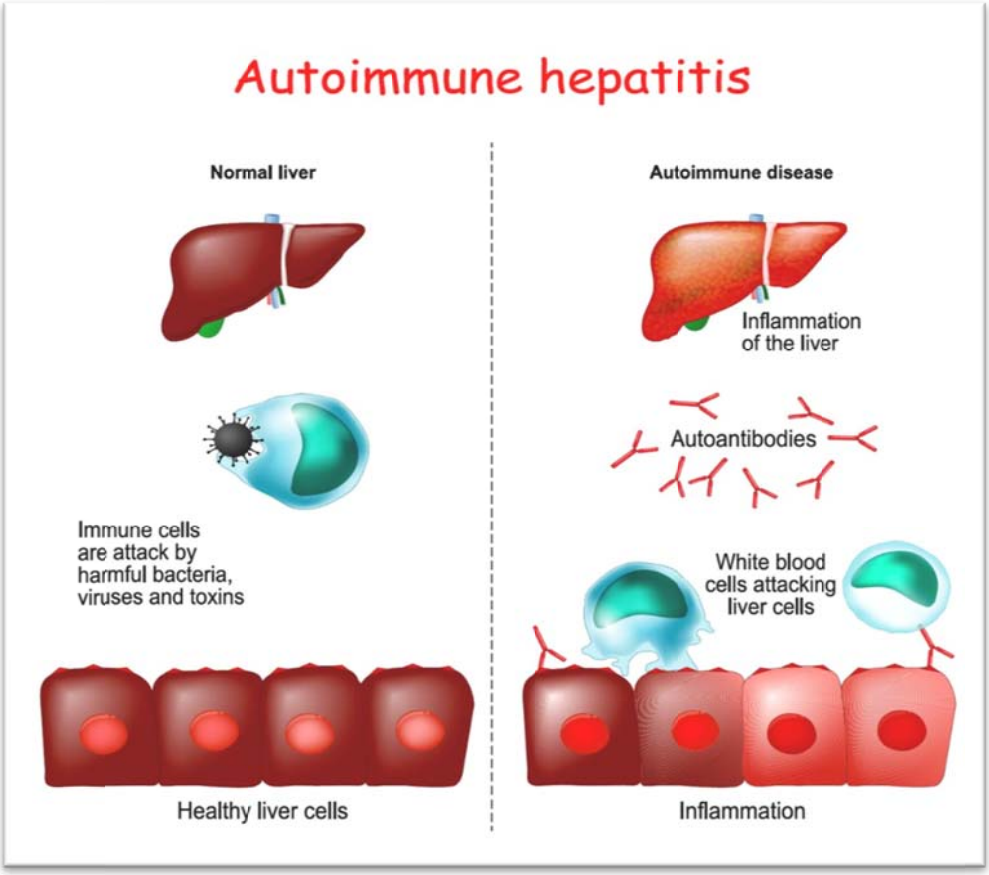


Figure 14: Autoimmune Hepatitis; (144)

Causes

Autoimmune liver disorders (ALDs) are the outcome of autoimmune responses that target liver tissue, causing inflammation and damage. ALDs include illnesses such as autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, and IgG4-related sclerosing cholangitis (145)(146)(147). Genetic susceptibility, environmental variables, and immune response dysregulation all play a role in ALDs (148). The interaction of immunometabolism, epigenetics, and inflammasome-mediated pyroptosis is critical in the pathogenesis of ALD. Infections, inflammatory illnesses, and changes in the gut microbiota are all associated to the development and progression of ALD. Understanding these intricate connections is critical for identifying disease processes and creating effective treatments for autoimmune liver disorders. (149)

Symptoms

Autoimmune liver illnesses, including autoimmune hepatitis (AIH), primary sclerosing cholangitis (PSC), and primary biliary cirrhosis, cause tiredness, arthralgia, abdominal discomfort, jaundice, and changing disease activity(150)(151). Patients with AIH may also develop mild to severe depression or anxiety symptoms, which can have an impact on their quality of life (152). Furthermore, these disorders are distinguished by necrotic-inflammatory hepatocyte lesions, hypergammaglobulinemia, and positive autoantibodies such as antinuclear and anti-smooth muscle antibodies (153). The clinical symptoms can differ, with jaundice being a typical presenting feature and some individuals advancing to cirrhosis at the time of diagnosis (154). Overall, autoimmune liver diseases cause a variety of symptoms that influence both physical and emotional well-being, highlighting the importance of comprehensive therapeutic measures.

Treatment

Autoimmune liver diseases, such as autoimmune hepatitis (AIH), primary biliary cholangitis (PBC), and primary sclerosing cholangitis (PSC), require long-term treatment. AIH treatment often includes glucocorticoids and azathioprine as first-line choices, with alternatives such as budesonide or mycophenolate mofetil (MMF)(155) (156). Ursodeoxycholic acid is critical for PBC patients to avoid recurrence and improve survival after liver transplantation (157). There are no specific immunosuppressive drugs for PSC, but colectomy and regular colonoscopies are required after transplant (158). Treg immunotherapy is being investigated as a potential treatment for autoimmune liver disorders, to maintain immunological tolerance and control hepatic inflammation (159). Overall, effective management of autoimmune liver disorders requires a tailored treatment approach that includes immunosuppressive medicines and constant monitoring.

Prevention

Depending on the condition, autoimmune liver disorders can be prevented using a variety of measures. The focus of post-liver transplant care for autoimmune hepatitis is on proper immunosuppressive therapy (160). In primary biliary cholangitis, starting ursodeoxycholic acid post-transplant is critical for preventing recurrence and improving patient survival (161). Meanwhile, primary sclerosing cholangitis lacks particular immunosuppressive medications, necessitating colectomy and routine colonoscopies after transplantation (162). Investigating immune checkpoint molecules such as PD-1 and 4-1BB in autoimmune hepatitis patients can provide novel treatment targets (163). Furthermore, investigating the protective properties of artesunate in autoimmune liver injury may provide novel intervention options (164). Overall, early detection, appropriate therapy, and thorough monitoring post-transplant are critical for preventing autoimmune liver disorders and improving patient outcomes.

- **Liver cancer**

Also known as hepatocellular carcinoma (HCC) is a serious global health concern with a high mortality rate (165)(166). Chronic hepatitis B and C virus infections, aflatoxin exposure, alcohol intake, and smoking all increase the risk of developing liver cancer. HCC treatment options are limited, with a 5-year survival rate of about 15%, necessitating research beyond typical cytotoxic chemotherapy to target the epigenetic makeup of malignant hepatocytes(167)(168). The tumor microenvironment (TME) in HCC is important for disease progression and therapy resistance, as it contains both cellular and noncellular components that affect signaling pathways and promote metastasis.(169)

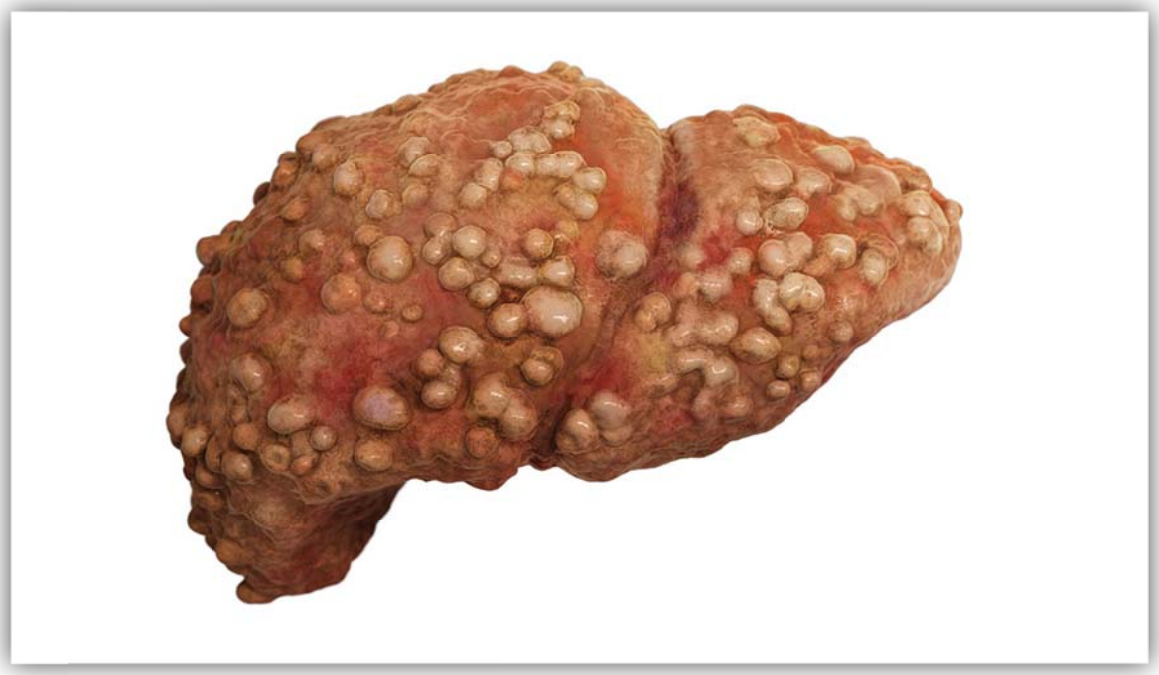


Figure 15: Liver Hepatocellular carcinoma illustration;(170)

Causes

Liver cancer, particularly hepatocellular carcinoma (HCC), is mainly caused by chronic hepatitis B and C infections, alcoholism, obesity, diabetes, aflatoxin exposure, and metabolic disorders. (171) (172).These risk factors lead to liver cancer development through pathways such as chronic inflammation, gut microbiome dysbiosis, genetic and epigenetic changes, oxidative stress, and immune system dysregulation(173) (174) . In addition, environmental variables such as vinyl chloride, arsenic, cadmium, organic solvents, and N-nitrosamines contribute to hepatocarcinogenesis. Understanding the various etiological factors and their interactions is critical for understanding the pathophysiology of liver cancer and creating effective targeted therapeutics to battle this aggressive disease.(175)

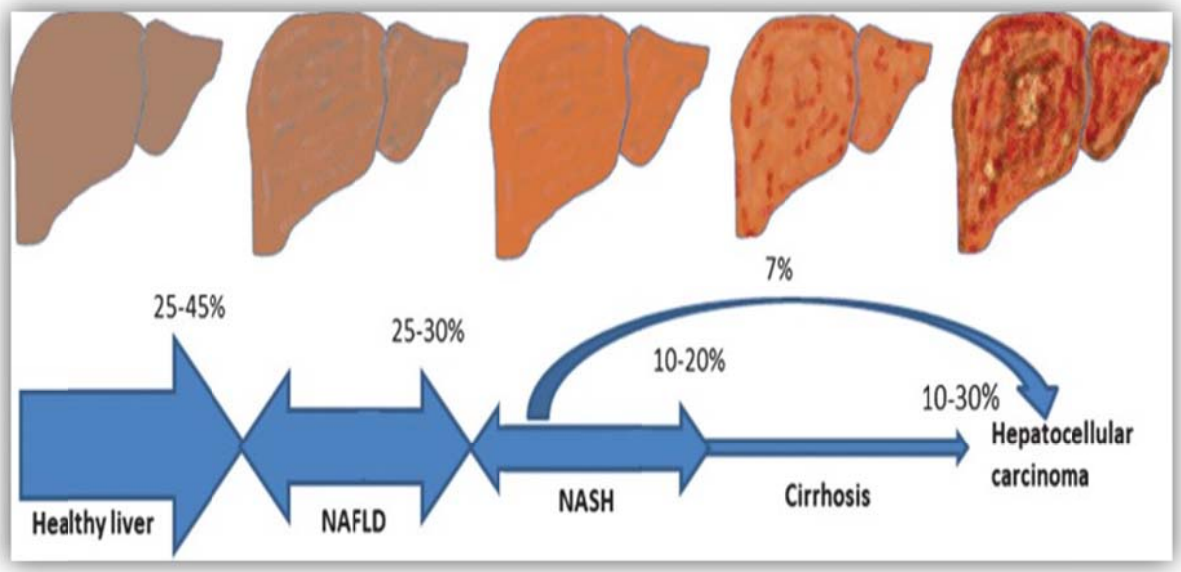


Figure 16: Potential routes of progression from fatty liver to hepatocellular carcinoma; (176)

Symptoms

Liver cancer, specifically hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC) causes a variety of symptoms and indications. HCC symptoms include fatigue, weight loss, stomach pain, pruritus, and jaundice (177). Patients with HCC may also be asymptomatic until late stages, with 90% of cases linked to risk factors that necessitate surveillance (178). CC symptoms, on the other hand, include jaundice, dark urine, clay-colored feces, and pruritus as a result of tumor-induced bile duct obstruction (179). Furthermore, individuals with HCC who arrive with fluid retention or jaundice have considerably shorter overall survival, highlighting the predictive importance of early symptoms. Liver cancer symptoms similar to pyogenic liver abscess include fever, abdominal discomfort, weight loss, and jaundice, with increased AFP or CA19-9 assisting in differentiation (180). Early detection through screening programs is crucial since clinical indications frequently present late in HCC cases, limiting curative treatment options.

Treatment

Liver cancer, particularly hepatocellular carcinoma (HCC), is a major worldwide health concern due to its high death rate when diagnosed at an advanced stage. Current treatments include liver resection, transplantation, sorafenib, immunotherapy, and chemotherapy (181)(182). Novel techniques for treating primary and secondary hepatic malignancies have been proposed, including the combination of talimogene laherparepvec with pembrolizumab (183). Furthermore, the use of adhatoda ventricosa extracts has shown promising inhibition of liver cancer cell proliferation, indicating a possible therapeutic avenue (184). Combining chemotherapy and radiation therapy has proven effective in several malignancies, but its use in liver cancer is limited due to increased toxicity to normal tissues (185). Future directions include customized and interdisciplinary therapies, emphasizing more evidence-based radiation treatments for liver cancer. Overall, phytotherapy presents a promising avenue for liver cancer treatment, emphasizing the significance of natural compounds in enhancing

therapeutic outcomes. Utilizing plant-derived natural products shows promise in treating liver cancer. These natural compounds exhibit various mechanisms beneficial in combating hepatocellular carcinoma (HCC), such as anti-inflammatory effects, inhibition of tumor growth, induction of apoptosis, and sensitizing cells to chemotherapy(186) (187)(188).

Prevention

There are three levels of preventative techniques for liver cancer. Primary prevention focuses on reducing risk factors such as viral hepatitis through immunization and lifestyle changes (189) (190). Secondary prevention consists of long-term treatment with nucleoside analogues to lower the risk of HBV-related HCC and regular screening for early identification (191). Tertiary prevention tries to lower the chance of HCC recurrence after treatment by providing lifelong antiviral therapy (192). Furthermore, therapies such as safranal injection have demonstrated potential in preventing liver cancer by lowering oxidative stress and inflammation (193). Public health policies and initiatives are also important in preventing liver cancer, particularly hepatitis B and C in high-risk groups. Combining these measures can considerably contribute to reducing the prevalence of liver cancer and improving patient outcomes.

Chapter II: General overview of medicinal plants

I.1 General Overview of medicinal plants

Medicinal plants

Are a broad category of plants used for their therapeutic properties (194)(195). These plants have historically played an important role in many medical practices around the world, notably traditional Asian medicine (196). They are important resources for producing medications to treat a variety of ailments, including infections. India has a long history of herbal medicine, notably in the Western Ghats region, and has served as a hub for medicinal herbs. The usage of medicinal plants extends back to antiquity, demonstrating their continued importance in healthcare systems. Innovative technologies, such as employing convolutional neural networks to detect medicinal flora species, are being used to better research and utilize the potential of these plants for therapy. (197)(198)

In Algeria

Medicinal plants have an important part in Algerian traditional medicine. Globularia alypum, Dittrichia viscosa, Juniperus oxycedrus, and Retama sphaerocarpa have all been shown in studies to exhibit antioxidant and antibacterial properties (199). Local people in areas such as El Bayad and Ain Sefra use medicinal plants to heal diseases, with a concentration on gastrointestinal and skin problems (200) . Chemical investigations of aromatic and medicinal plants native to Algeria highlight the necessity of knowing chemical diversity and arguing for standardized methods of employing essential oils produced from wild plants (201). Overall, Algerian medicinal plants show a rich biodiversity linked with the cultural past, providing a natural supply of bioactive chemicals with a variety of health advantages.(202)

Phytotherapy

Is the study and use of extracts from natural origin as medicines or health-promoting agents. Moreover, it traditionally aligns with herbal medicine practices that focus on the use of plants and their extracts for therapeutic purposes. Modern phytotherapy integrates traditional knowledge with scientific research to understand the medicinal properties of plants and how they can be used to treat various health conditions (203)((204).

In Algeria

Research conducted in Algeria has demonstrated the extensive application of herbal medicines in veterinary care, with private vets endorsing phytotherapy as a substitute for traditional medications (205).studies carried out in various parts of northern Algeria have shown that a significant section of the populace makes use of medicinal plants; 22 species from 12 families are used to treat ailments such as Covid-19, demonstrating the possibility of integrating phytotherapy with traditional medicine in the future (206). The Aures region's ethnobotanical surveys revealed 112 medicinal plant species that the locals employed, highlighting the profoundly ingrained traditional knowledge of phytotherapy among some

demographics—information that might be lost without adequate documentation, but (207). The Guerbes-Sanhadja wetland complex study revealed that 102 plant species were used by indigenous plants for a range of therapeutic uses, underscoring the significance of developing management strategies to safeguard and encourage the responsible use of these plants (208) .

Ethnobotany

is the study of the relationships between people and plants, encompassing the ways in which different cultures perceive, utilize, and manage plant species. The field requires a combination of botanical knowledge for plant identification and preservation, anthropological insights to understand cultural notions about plants, and linguistic competency to accurately record and understand local plant names and uses ((209).

Using plants for healthcare and treating everyday ailments

Each plant has unique qualities and benefits determined by its chemical and nutritional composition. This includes the nutrients it contains (vitamins, minerals, trace elements, proteins, fatty acids, carbs, and so on) as well as its active components, which include antioxidants like flavonoids, tannins, alkaloids, and plant sterols. Plants and their effects are effective in a wide range of locations due to the combination of these various factors.

Cardiovascular health includes managing high blood pressure, preventing vascular diseases and accidents, and so forth.

Inflammation: anti-inflammatory properties, inflammatory joint pain, intestinal inflammation, etc.

Respiratory problems include asthma and allergies.

Digestive issues include digestive support, common gastrointestinal illnesses, gastric and intestinal disease symptoms, diuretic qualities, and so on.

Pain: headaches, muscle and joint pain.

Neurological Disorders: Prevention Using plants to care for oneself and heal common ailments.

Each plant has unique qualities and benefits determined by its chemical and nutritional composition. This includes the nutrients it contains (vitamins, minerals, trace elements, proteins, fatty acids, carbs, etc.) as well as its active compounds, such as antioxidants (flavonoids, tannins, alkaloids, neurodegenerative disease plant, cognitive function support, etc.).

Hormonal problems include menopausal symptoms, menstrual issues, endometriosis, and testosterone.

Sports performance enhancements include increased endurance and physical performance.(210)

Medicinal plants properties and biological activities

Medicinal plants properties and biological activities that possess various benefit human health. These properties are often attributed to the presence of bioactive compounds known as secondary metabolites. Here are some common properties and activities of medicinal plants:

1. **Antioxidant:** They combat oxidative stress by neutralizing free radicals in the body, which can prevent cellular damage and contribute to the prevention of diseases such as cancer and heart disease ((211)

2. **Anti-inflammatory**: Some plants have the ability to reduce inflammation, which is beneficial in treating conditions like arthritis and other inflammatory disorders (212)

3. **Antimicrobial:** They can inhibit the growth of bacteria, fungi, and viruses, thereby acting as natural antibiotics to treat infections (213)

4. **Antidiabetic:** Certain medicinal plants have the ability to modulate blood sugar levels, making them helpful in the management of diabetes (212)

5. **Anticancer:** Some bioactive substances in medicinal plants have been investigated for their potential use as cancer chemotherapeutic agents or chemopreventives (214)

6. **Cardiovascular effects**: Flavonoids and other compounds in medicinal plants can have beneficial effects on the cardiovascular system, including improving heart health (211)

These beneficial effects make medicinal plants a vital resource for developing new therapeutics and enhancing health care. However, the efficacy and safety of medicinal plants and their extracts must be scientifically assessed through rigorous pharmacological and toxicological studies (212) (215).

Collecting and Using Medicinal Plants for Their Medicinal properties

These plants can be harvested and used in various forms, such as dried herbs, herbal drinks, tinctures, and creams. Before you start collecting medicinal herbs, it is important to have precise information on the plants and their use. This information can be gained from trusted sources such as ethnobotanical studies, traditional medicine practitioners, and recognized herbal medicine books and websites. Once you've obtained the essential information, you can start collecting therapeutic plants using the guidelines below :((216)

1. Determine which medicinal plants you intend to harvest based on their therapeutic characteristics and availability in your area. . (217)
2. Learn the right harvesting techniques for each plant to guarantee that you collect the most potent and effective components (216)

3. Treating the plants with care to prevent harm and loss of medicinal characteristics.(217)

4. Dry the harvested plants properly to preserve their medicinal compounds. (218)

5. Store the dried plants in a cool, dry place in airtight containers to maintain their potency.

6. Consult with a healthcare professional or herbalist to ensure safe and appropriate use of the collected medicinal plants (216)

7. Keeping the track of plants collected, including their common and scientific names, as well as any specific instructions for their use. (217)

8. Constantly update your understanding of medicinal plants and their applications through continuing research and learning opportunities. (218)

Applying these recommendations allows you to securely harvest and use medicinal herbs to harness their therapeutic and beneficial properties for your health and well-being. always keep in consedriation to emphasize sustainable approaches when harvesting medicinal herbs and respecting natural habitat in which they thrive. In today's quickly changing world, the importance of correct information about medicinal plants and their applications cannot be stressed. Individuals can efficiently harvest and use medicinal plants to enjoy their myriad health advantages in a sustainable manner by using trusted sources and according to appropriate standards. Ethnobotanists, anthropologists, pharmacists, and physicians can work together to analyze and validate the use of traditional medicinal plants using current scientific methods, assuring efficacy and safety. (216)

The different forms of herbal medicine

i. Aromatherapy

Is a practice that uses plant-derived essential oils to improve overall health and well-being (219)(220)(221). These oils, derived through procedures such as steam distillation, have long been utilized in numerous cultures for therapeutic purposes, including the treatment of fever, headaches, and infections (222). Aromatherapy can be taken in a variety of ways, including inhalation and topical administration, and each essential oil has a unique chemical composition that determines absorption and effects (223). Aromatherapy has a wide range of applications, including cosmetics, physiotherapy, and healthcare, demonstrating its adaptability and effectiveness. Aromatherapy, which uses the therapeutic characteristics of essential oils, provides a natural and comprehensive approach to promoting health and wellness.

ii. Gemmotherapy

Also known as phytoembryotherapy is a new homeopathic technique for biotherapeutic drainage that employs extracts from various trees and plants (224). One gemmotherapy extract under investigation is the bud extract of Corylus avellana, which has been demonstrated to have hepatoprotective properties in a diabetic mouse model of liver fibrosis. This extract contains flavonoids, including hyperoside and chlorogenic acids, which inhibit hepatic stellate cells, reduce oxidative stress, and modulate the TGF-β1/Smad signaling pathway(225). Similarly, a standardized black currant gemmotherapy extract was discovered to have anti-neuroinflammatory and neuroprotective properties due to its unique composition of approximately 133 phytonutrients, including flavonoids such as luteolin, quercetin, apigenin, and kaempferol, making it a promising complementary therapeutic approach for neuroinflammatory conditions (226) (227).

iii. Herboristerie

Is the most prevalent and most traditional kind of phytotherapy

Herbal therapy makes use of fresh or dried plants, either whole or in part (bark, fruit, or flowers). Decoction, infusion, and maceration are common ways of preparation, all of which use water. These treatments are also available in a more modern form, such as a capsule containing dried plant powder that the patient can swallow.(228)

iv. Homeopathy

Is another type of alternative medicine that employs alcoholates composed of typically 75% fresh plant strains macerated in alcohol and 25% strains of mineral and/or animal origin. The granulates, either alone or in combination, are then thoroughly diluted before being used to soak the granules supplied in pharmacies and parapharmacies. In cases of low energy, a homeopathic medicine to control liver processes might be extremely beneficial. Homeopathy is an excellent way to treat a cold, particularly in young children and pregnant or breastfeeding mothers.(229)

v. Phytobalneotherapy

the KNEIPP therapy, which was created over a century ago, involves pouring botanical additions into hot baths (230).

Methods and preparations

Methods for using medicinal plants

Plants are used in a variety of ways, depending on whether they are prescribed:

- **Internal usage**

Infusion: The simplest and most frequent approach is to make herbal tea by steeping the dried components of the plant in hot water.
Decoction: For the plant's tougher portions, such as the roots or bark, a decoction is prepared by boiling the plant in water for several minutes.
Tincture: A tincture can also be made by macerating plant materials in an alcoholic solvent (often brandy).
Capsules: Dried extracts from medicinal plants can be put as capsules for easier usage.
Powder: Some plants can be crushed into a fine powder and consumed alone or combined with food or drink. (Oral absorption, gargle, mouthwash)(231)

- **Local usage**

Skin application: Creams, ointments, gels, or compresses containing medicinal plant extracts can be used to treat skin disorders, joint or muscle discomfort, and so on.
Baths: Some plants can be added to bath water to provide relaxation, soothing, or anti-inflammatory effects. Inhalations:
To cleanse the respiratory system or alleviate a cold, inhale steam from an infusion of certain herbs.
Herbal mouthwashes can help cure sore throats, oral ulcers, and gingivitis. (231)(232)
Oral and local use Some plants can be utilized both inside and externally.
Chamomile, for example, can be consumed as an herbal tea to promote digestion and sleep, or used as a compress to relieve skin irritation.

- **External usage**

To treat with cataplasm, apply plant slurry to the affected region. Secure with a bandage. Cataplasms are used to treat pain, inflammation, and infection.
Herbal poultice. Compress: Soak a compress in a plant infusion or decoction and apply to the affected region. Compresses are used to reduce pain, inflammation, and irritation. Herbal compress. Bath: Mix an herbal infusion or decoction into the bath water. Herbal baths promote relaxation and help alleviate muscular and joint discomfort.
Bathe with therapeutic herbs. Inhalation: Inhale steam from a plant infusion or decoction. Inhalations are used to clear the respiratory tract and alleviate coughing.
The inhalation of medicinal herbs Essential oil: Dilute a few drops of essential oil with vegetable oil before applying to the skin. Essential oils are extremely potent and should be used with caution. Always dilute essential oils before applying them to the skin.

(Poultice, lotion, gargle, mouthwash, bath, natural cavity injection, fumigation). (232)

A. Conventional preparation methods forms

They are techniques used to isolate desired substances from a mixture by using a solvent. These methods have been around for centuries and are still widely used in various industries today, especially due to their relative simplicity and affordability.(233) Here are some of the most common conventional extraction methods:

Maceration

it obtain plant extracts, immerse coarse or ground plant materials in a closed stoppered container in a solvent and allow it stand at room temperature for 2-3 days with frequent stirring. A sealed extractor is used to prevent solvent evaporation under atmospheric pressure. The technique is designed to soften and shatter the plant's cell walls in order to release the soluble phytoconstituents. After a predetermined amount of time, the mixture is squeezed or strained via filtration or decantation (234), (235). Maceration is the simplest and most commonly utilized process. The extraction approach in this stationary process is based on the molecular diffusion principle and is time-consuming. Maceration disperses the concentrated solution buildup around the particles' surface and delivers fresh solvent to the particle surface for subsequent extraction (236).

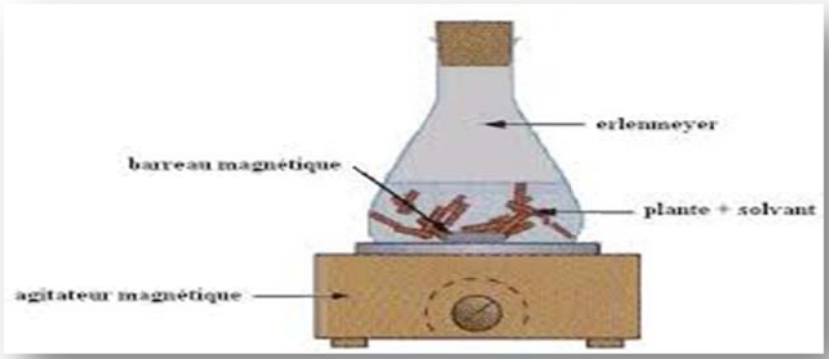


Figure 17 : Schematic diagram of the extraction with Maceration (237)

Infusion

This is an extraction method as maceration. The medication material is ground into fine powder and stored in a clean container. The extraction solvent, hot or cold, is then poured over the drug substance, soaked, and stored for a brief length of time. This approach is appropriate for extracting bioactive components that are readily soluble. Furthermore, it is a good procedure for preparing fresh extract for application. The solvent-to-sample ratio is typically 4:1 or 16:1, depending on the desired application.(238)

Digestion

This is an extraction method that uses moderate heat throughout the extraction process. The extraction solvent is placed into a clean container, and then the powdered drug material is added. The mixture is placed over a water bath or in an oven at around 50 degrees Celsius. Heat was applied throughout the extraction process to reduce the viscosity of the extraction solvent and improve the removal of secondary metabolites. This approach is appropriate for plant components that are readily soluble.(239)

Decoction

The present method includes boiling plant material in water to obtain plant extracts. Heat is transported via convection and conduction, and the solvents used dictate the type of substance recovered from the plant material (240). The sample is cooked in a given volume of water for a predetermined time (15 to 60 minutes). It is then chilled, strained, and filtered before passing enough water through the medicine to get the necessary volume. This process is appropriate for extracting thermostable (temperature-insensitive) and water-soluble chemicals, as well as hard plant materials, and typically yields more oil-soluble compounds than maceration.(241)

Figure 18: Schematic diagram of the extraction with decoction; (242)

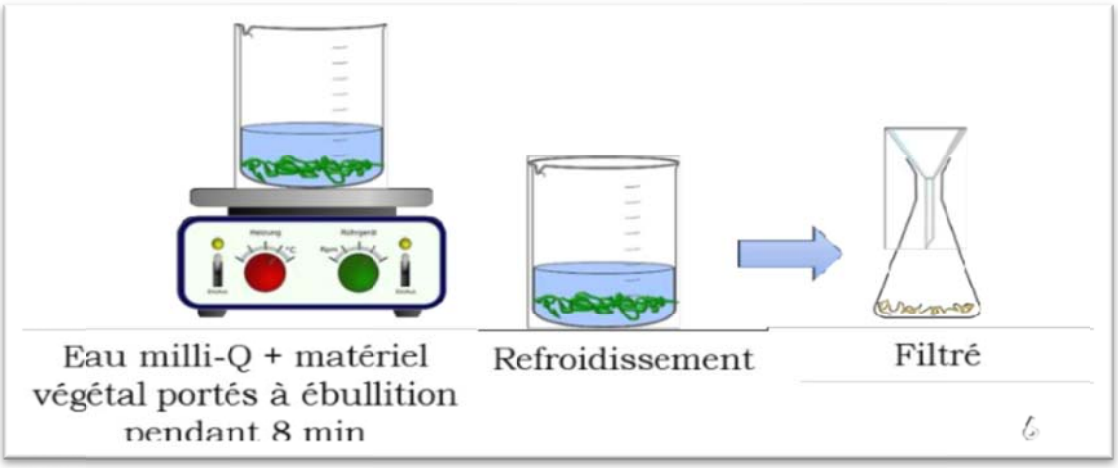
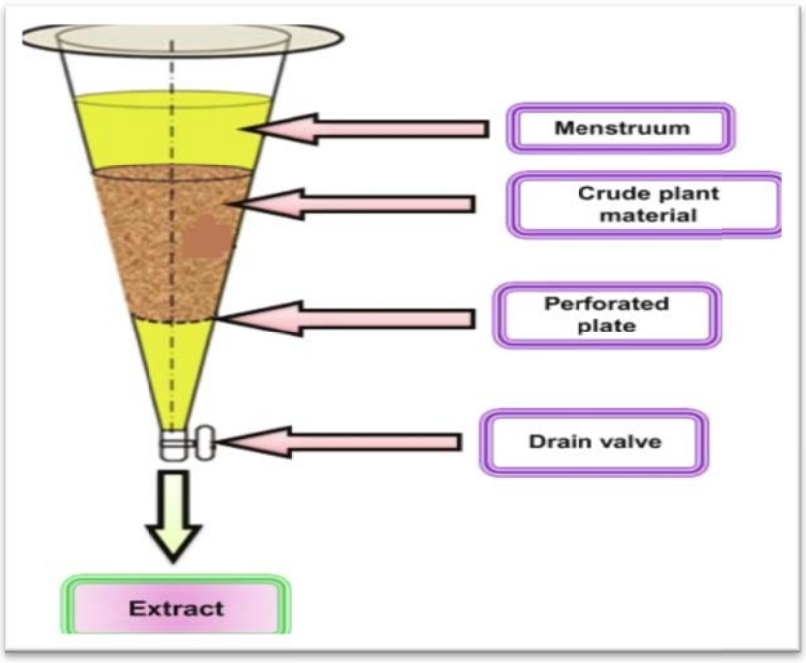


Figure 19: Schematic diagram of the extraction of a crude drug using percolation; (243)



Percolations

this process, sometimes known as leaching, is similar to that used in the same-named coffee makers. A solvent is used to cover finely ground plant powder for nearly a full day. The solvent drips off gently, a few drops per minute, and the grounds are then squeezed. Although this type of extraction is successful, it is becoming increasingly rare.(244)

Herbal poultices

Plant preparations applied to the skin, poultices soothe muscular pain and neuralgia, relieve sprains and fractures, and extract pus from infected wounds, ulcers and boils. The plant is heated for 2 minutes, and then squeezed to extract the liquid, before applying oil to the affected area, covering with the still-warm plant and bandaging. Leave on for a maximum of 3 hours.(245)

The tincture

Is formed by macerating the plants in 95° alcohol (ethanol) for three weeks, then decanting, pressing, and filtering. Given the plants' water content, the alcoholic strength is decreased to approximately 70°. The final maceration ratio is (1:10), which means that 10 g of mother tincture equals 1 g of dried plant. Children should avoid alcohol, and the suggested dosage is one drop per kilogram per day.
The amount of alcohol consumed in 100 drops per day is similar to 2 mL of 70° alcohol or 10 mL of 14° alcohol.
In some situations, wine (gentian wine) or oil (wild thyme oil) can replace alcohol.
Homeopathic dilutions of plants are created by diluting the mother tincture.(246)

Soxhlet extraction:

This is a more advanced process that uses a Soxhlet extractor to continually cycle hot solvent through the substance being extracted. This process is extremely efficient and produces a high yield of the required chemical. However, it necessitates more sophisticated equipment and can be time demanding.(247)

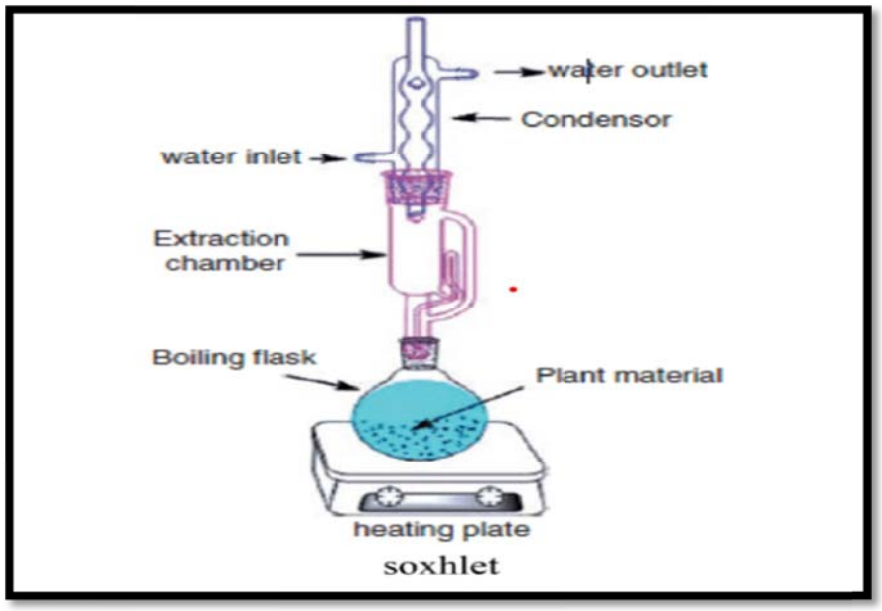


Figure 20: The pictorial representation of soxhlet extraction;(248)

Conventional fluid extracts or glycerin extracts are made by extracting the active components in consecutive mixes with increasing alcohol concentrations and then reintroducing them or not into a neutral glycerin solution. .(246)

B. Other forms of preparations

Powder

Dried medications are frequently utilized in powder form. In general, finer powders are of higher quality. Plants powdered can be used internally (swallowed or absorbed through the oral mucosa) and topically (as a foundation for poultices and combined with ointments).(249)

Syrup

Honey and unrefined sugar are excellent preservatives that may be used with infusions and decoctions to create syrups and cordials. They also have calming effects, making them effective cures for sore throats.
The sweet flavors of syrups can conceal the unpleasant taste of some plants, allowing youngsters to absorb them more freely.(250)

Ointments

Ointments are creamy solutions produced from oils or other fats in which plants' active components are dissolved. They are used to treat wounds and prevent inflammation. Ointments are good against hemorrhoids and chapped yeast. (249)

Creams

Creams are emulsions made from ingredients (oils, fats, etc.) and plant extracts (infusions, decoctions, tinctures, essences, powders).
Creams, unlike ointments, can penetrate the skin. They soften the skin while yet enabling it to breathe and perspire normally. However, they degrade fast and should be stored away from light in sealed jars in the refrigerator. (249)

Lotions and Compresses

Lotions are water-based plant preparations (infusions, decoctions, or diluted tinctures) that are applied to the skin of irritated or inflamed regions. Compresses can assist decrease swelling, bruising, and discomfort, as well as soothe inflammation and headaches and lower temperature (251)

Inhalations

Inhalations reduce nasal congestion and clean the respiratory system. They are effective against catarrh, colds, and bronchitis, and can occasionally ease asthma episodes.
Aromatic plants can add balsamic and antiseptic properties to steam. To use, add finely chopped aromatic plants or essential oils to a large Pyrex glass or enameled container filled with boiling water.(252)

Medical oils

Infusing a plant in oil extracts the oil-soluble active components. Hot-pressed medicinal oils are brought to a slow boil, whereas cold-pressed oils are naturally heated by the sun. Medical oils should not be confused with essential oils, which are natural plant ingredients having medical effects and a unique scent. Adding essential oils to medicinal oils can improve therapeutic effectiveness (253).

C. Advanced extraction methods

Use unique technology to separate desired compounds from a mixture. Advanced extraction methods have various benefits over standard approaches, including: (254)

Increased efficiency: These technologies extract target chemicals more quickly and with better yields.(255)

Reduced solvent consumption: Some modern procedures utilize less solvent, making them more eco-friendly.

Improved selectivity: Advanced procedures can target certain molecules with more precision, resulting in purer extracts.

Milder circumstances: Some procedures employ less severe conditions to maintain heat-sensitive substances.(256)

Here are some of the most popular advanced extraction methods:

Supercritical Fluid Extraction (SFE):

The solvent in this approach is a supercritical fluid, which has both liquid and gas characteristics. (257) Supercritical fluids have high diffusivity and low viscosity, allowing for effective extraction. SFE is especially effective in extracting nonpolar molecules from heat-sensitive materials. (258)

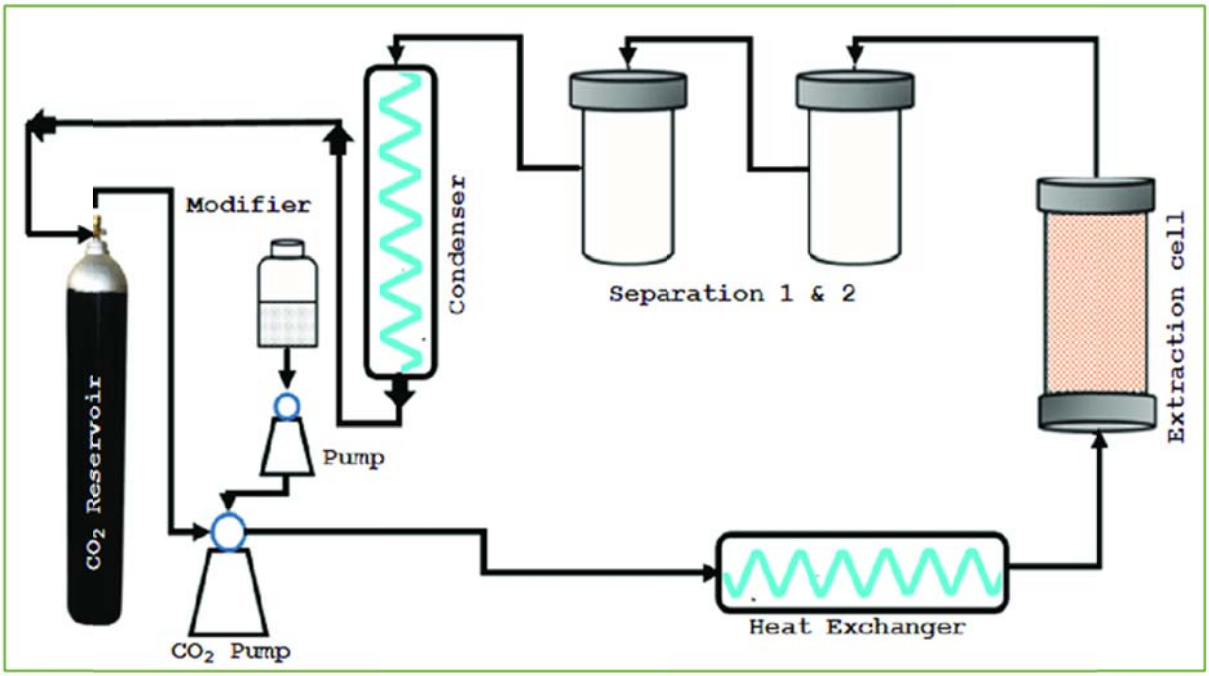


Figure 21: Illustrative diagram of supercritical fluid extraction **(SFE); (259)**

Pressurized Liquid Extraction (PLE):

PLE uses a heated pressurized solvent to extract compounds. The pressure increases the solvating power of the solvent, while the heat accelerates the extraction process.(260) PLE is a versatile technique that can be used to extract a wide variety of compounds from different matrices.(261)

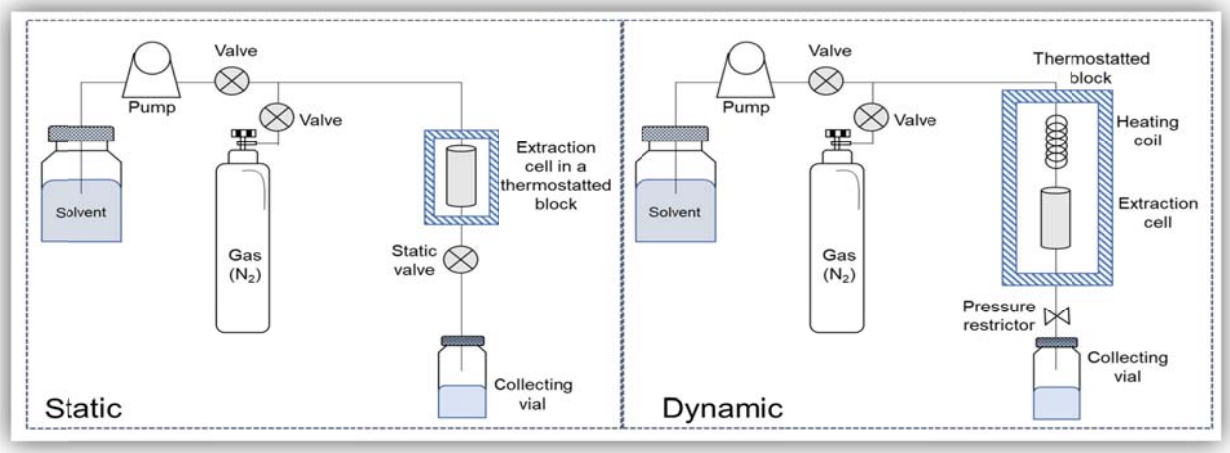


Figure 22: Schematic PLE system configuration for static and dynamic procedures ;(262)

Ultrasound-Assisted Extraction (UAE):

UAE utilizes ultrasound waves to disrupt the cell walls of the material being extracted, which facilitates the release of target compounds. This method is efficient, rapid, and can be used with a variety of solvents.(263)

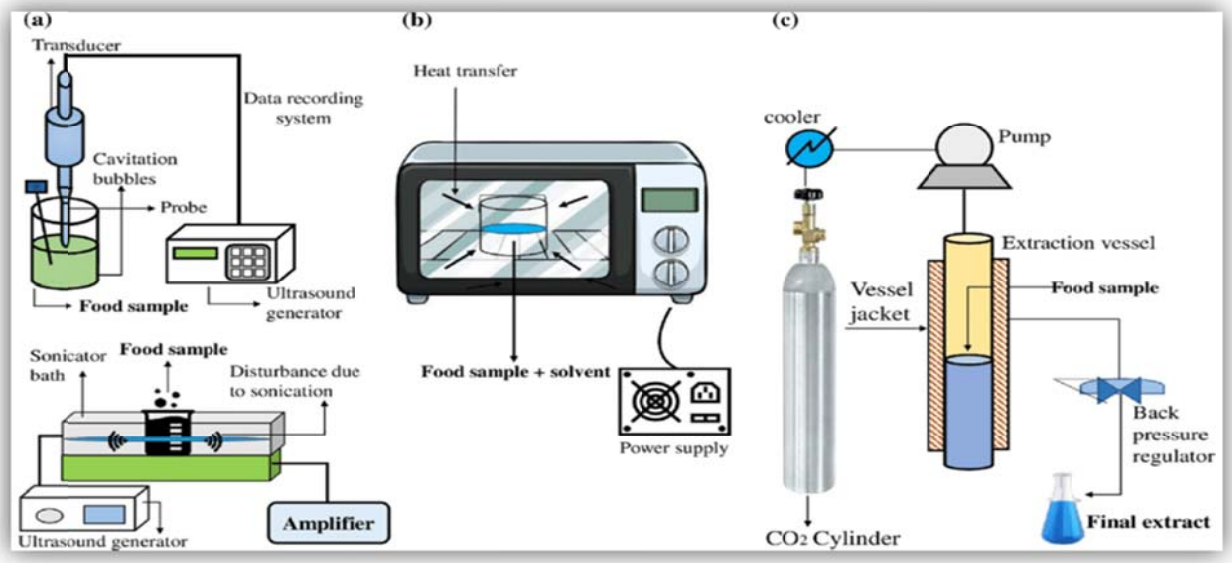


Figure 23: Ultrasound-assisted extraction (UAE) assembly with probe and bath extraction illustrating mechanism of bubble cavitations. ;(264)

Microwave-Assisted Extraction (MAE):

MAE uses microwave radiation to heat the solvent and the sample matrix. This heating enhances the diffusion of the solvent into the material and accelerates the extraction process. MAE is particularly useful for extracting heat-stable compounds.(265)

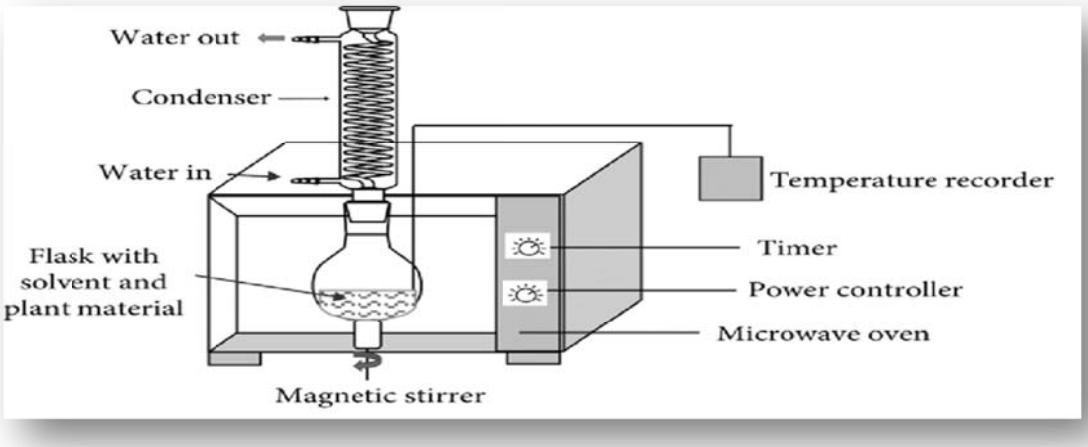


Figure 24: Schematic diagram of Microwave- assisted extraction (MAE).(266)

Enzyme-Assisted Extraction (EAE):

EAE employs enzymes to break down the cell walls of the material being extracted, making the target compounds more accessible to the solvent. This method is particularly useful for extracting polysaccharides, proteins, and other biomolecules.(267)

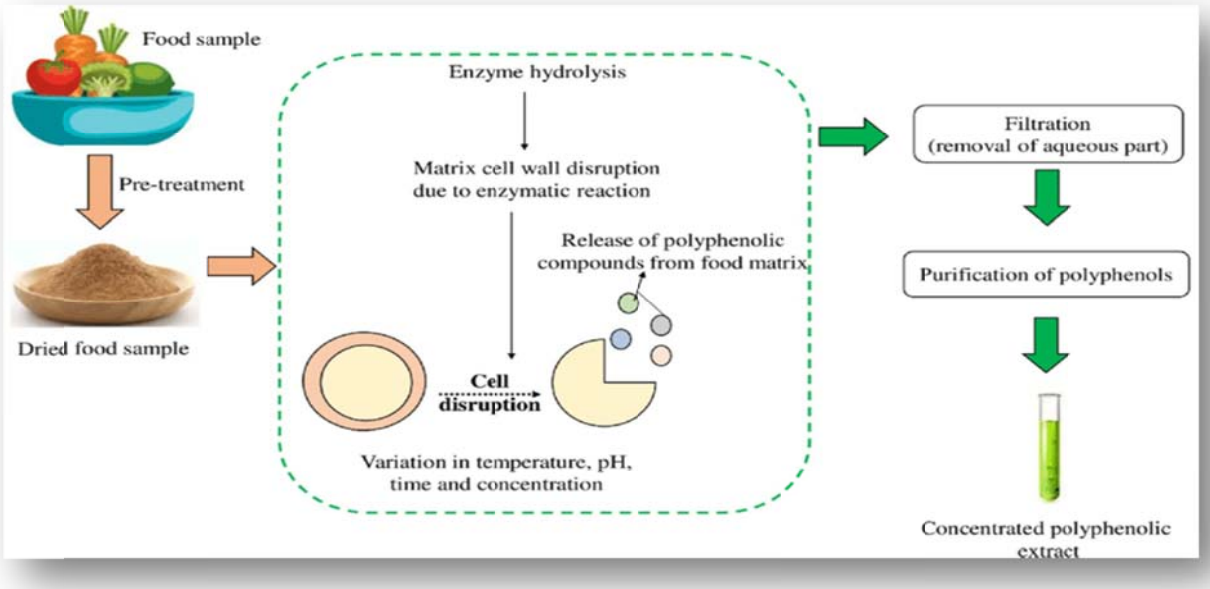


Figure 25: Extraction of phenolics using enzyme-assisted technology (EAE).(268)

The choice of advanced extraction method depends on several factors, including the nature of the target compound, the sample matrix, and the desired purity of the extract

CHAPTER III
Presentation of the Study area
MATERIALS AND METHODS

1. STUDY AREA:

1.1 Presentation of the study area:

1.1.1 Geographical position of the Saida region

This study was carried out in the Wilaya of Saida, which comprises 16 communes spread over 6 Daïras, covering an area of 6,764 km2. Geographically, Saida lies at 34° 50′ 00″ north, 0° 09′ 00″ east.

The wilaya lies in north-west Algeria at an altitude of 800 metres, 461 km from the capital Algiers, and is bordered by the wilaya of Mascara to the north, the wilaya of Sidi Bel Abbès to the west, the wilaya of Tiaret to the east and the wilaya of El Bayadh to the south.

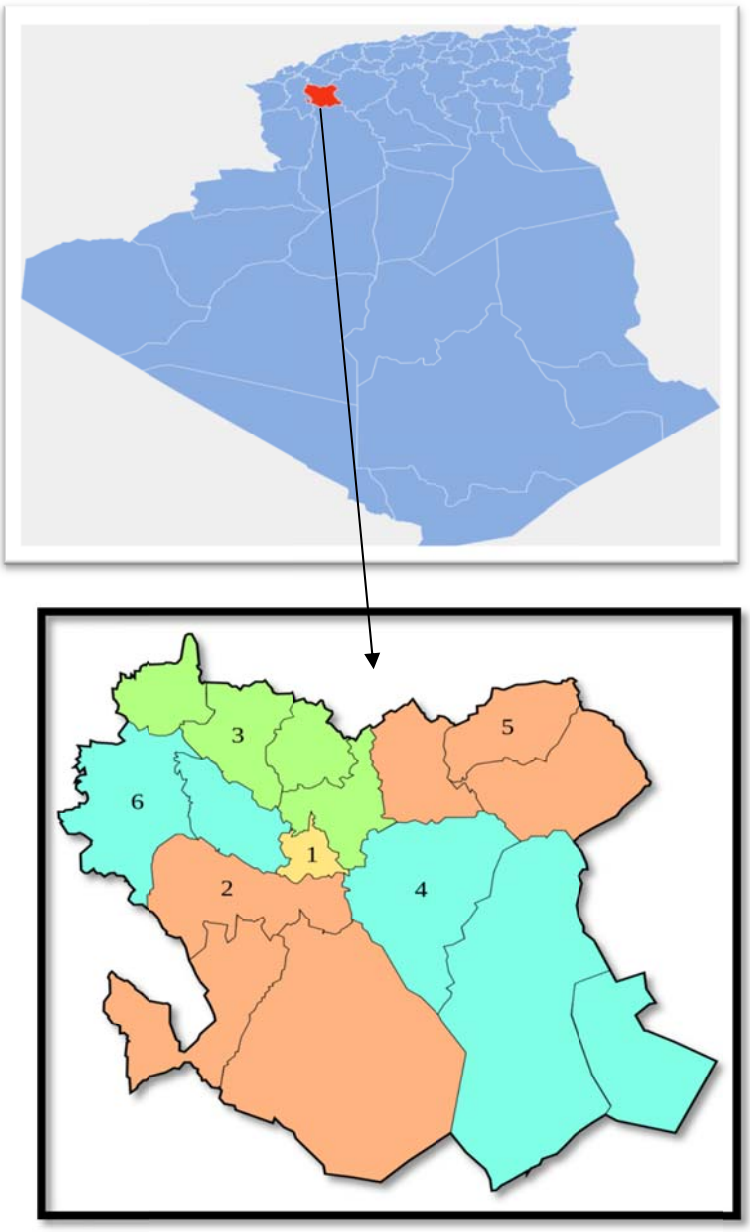


Figure 26: Map showing the study area (Saida).

1.2 Administrative aspect:

The wilaya of Saïda is made up of (06) departments and (16) communes. Saïda is one of the western highlands states. According to the latest statistics, the population of Saïda is approximately 330,000, with a population density of 46.97 inhabitants per km2.

1.3 Climate conditions:

The Wilayat of Saïda is characterised by its continental climate (semi-arid, hot in summer, cold in winter) It is also characterised by two distinct regions: to the north the Al-Dhaya mountains, and to the south the high plateaux.

1.4 LIVESTOCK AND PLANTS:

In addition, it has a rich plant cover such as Aleppo pine, oak, cork and mugwort. Cliptuse....

Around 300 species of medicinal plants have been counted, thanks to the creation of protected steppe oceans, and the medicinal plants of the steppes include many species, such as wormwood, rosemary, watercress, squash, local and steppe phyllo, thyme, vegetal and juniper. It is used ecologically throughout the areas of Al-Mukamin and Lapidation for Punishment in the municipality of Al-Maamoura, Ben Hawar, the municipality of Ain Sokhuna and the Tavernet area in the municipality of Sidi Omar, and is used to treat many human ailments, including kidney disease, influenza, infectious diseases and toothache.

2. ETHNOBOTANICAL SURVEY:

Depending on the purpose of the study, there are several methods for surveying medicinal plants. For our study we have adopted two appropriate approaches which are the most widely used.

2.1 Conduct of the ethnobotanical survey:

The study was carried out over a two-week period up to a month long, during which we conducted interviews with doctorsand patient’s herbalists and some local residents.

During which we conducted interviews with herbalists and a number of inhabitants of the Wilaya of Saida using questionnaire forms containing precise questions about the informant and the medicinal plant used.

During our survey, we were confronted with a number of difficulties, in particular the refusal of some people to complete the questionnaire. But, on the other hand, we mustn't ignore the welcome we received from some people who encouraged and guided us. This enabled us to carry out surveys in the field. The invaluable help of the respondents enabled us to fill in the form correctly, including the questions related to our work, and to explain the content of the questionnaire through our interventions in order to obtain more precise answers.

The taxonomic identification of plants was carried out thanks to herbalists and a number of documents, in particular.

2.2 Public surveys:

This survey involves asking people aged between 19 and over 60, spread across different intellectual levels, questions about medicinal plants and their use, the parts of the plant used.

This was achieved by organising several outings in the town of Saida and their State institutions such as The hospital of saida

2.4 Statistical processing of data:

The results obtained were entered into Excel in order to identify the population taking part in the survey, the plants used and all the local traditional therapeutic uses.

2.5 Working methodology

2.5.1 Objectives of the study

The purpose of this study is

- To carry out an inventory of the use of medicinal plants by the population for the treatment of LIVER disease.

Population for the treatment of LIVER diseases.

- Gather as much data as possible on the various uses and ways in which these plants are used for self-medication.
- Identify the most interesting species with potential therapeutic

Therapeutic potential

2.5.2 Materials

- Survey sheets
- Notepad
- Pencil

2.5.3 Working methodology

2.5.3.1 Choice of sites

Our study is an exploration of traditional care practices for liver and hepatic diseases by the population of the town of Saida.

To do this, we associated to some hospitals and travelled to different areas of the city to carry out our study. In order to obtain the most diverse sample of the population, we visited several hospital services.

2.5.3.2 Period of the ethnobotanical survey

The ethnobotanical surveys on medicinal plants were carried out during the period from 05 February to 05 March.

2.5.3.3 Survey and questionnaire

We drew up an exhaustive questionnaire containing 10 questions, 03 concerning the identification of the informant and on care using plants. These forms were distributed to a random sample of people and patients.

2.5.3.4 Statistical analysis

The data collected were analysed manually before being coded and entered using Excel software, Windows office version Excel 2007.

Chapter IV:

"Survey results and analysis"

1 Survey results and analysis

1.1 Presentation of the survey:

The survey was carried out in the town of Saida. The various survey forms were distributed to people of different genders, ages and educational levels, without distinction or prior choice, and were offered to anyone wishing to contribute to the study,

They were offered to anyone wishing to contribute to the study.

1.2 Analysis of the results

1.2.1 Information about the informant:

1.2.1.1 Sex:

i. Results by number:

people questioned	Number per Sex	
	male	female
Number of people questioned	07	39

ii. Analysis of results:

A total of 46 people responded to the questionnaire, men, representing 15 % of respondents, and women, representing 85% of respondents.

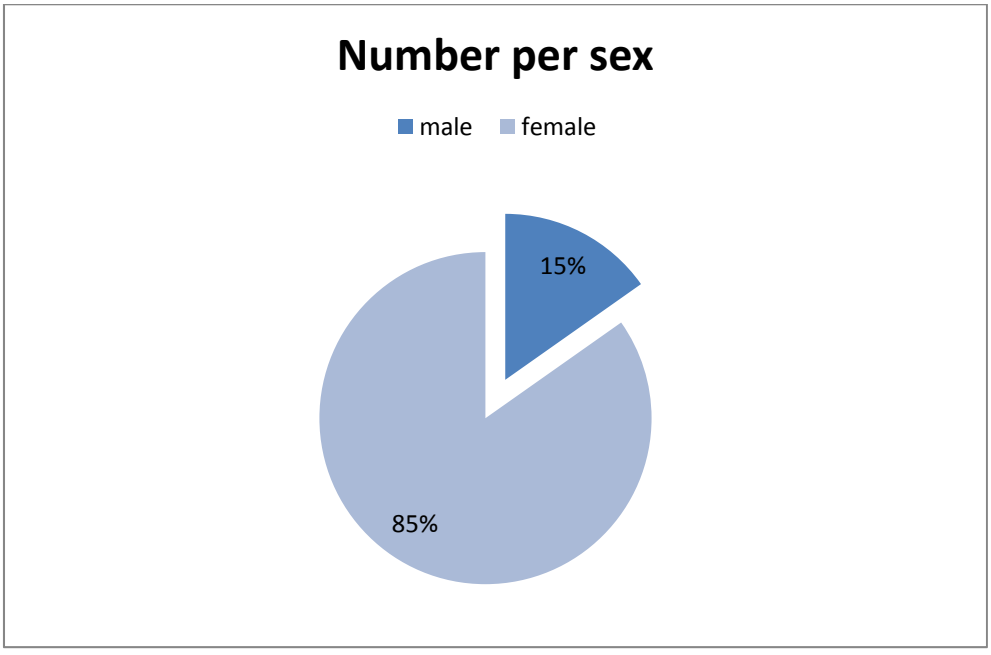


Figure 27: Diagram showing the use of herbal medicine in both sexes.

1.2.1.2 Age:

i. Earnings per figure:

Age range	Under than 20 years	20-40 years	40-60 years	More than 60 years
Number of person	02	09	14	21

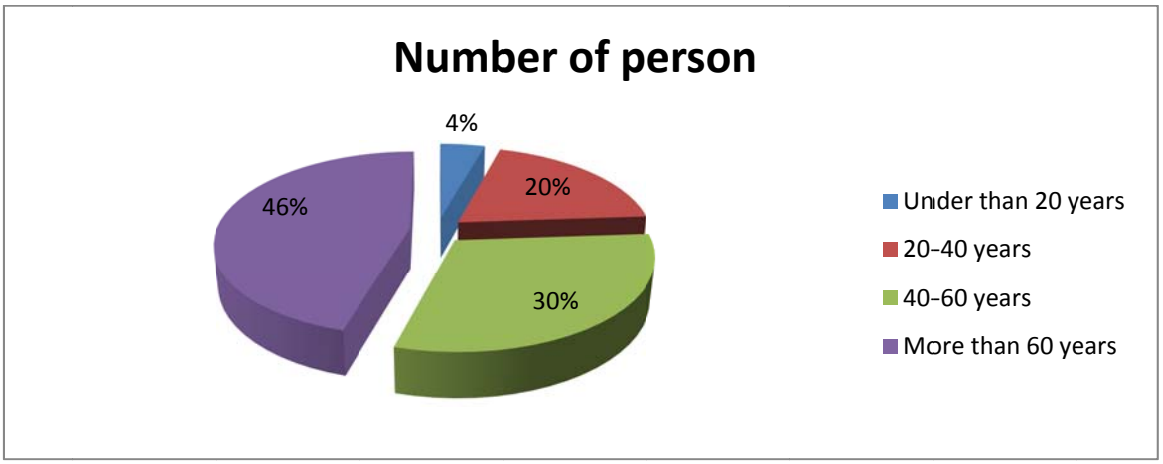


Figure 28: Diagram showing the distribution of informants by age.

ii. Analysis of results:

According to the figures presented, the dominant age group participating in the survey was the over-60s, with 46 %, followed by the 40-60 age groups with 30. %, the 20-40 age groups with 20 % and the under 20 age group with 4 % of respondents.

1.2.1.3 Educationl level:

i. Result per numbers:

Level of education	No education level	Primary/middle	Secondary	University
Number of people questioned	10	17	08	11

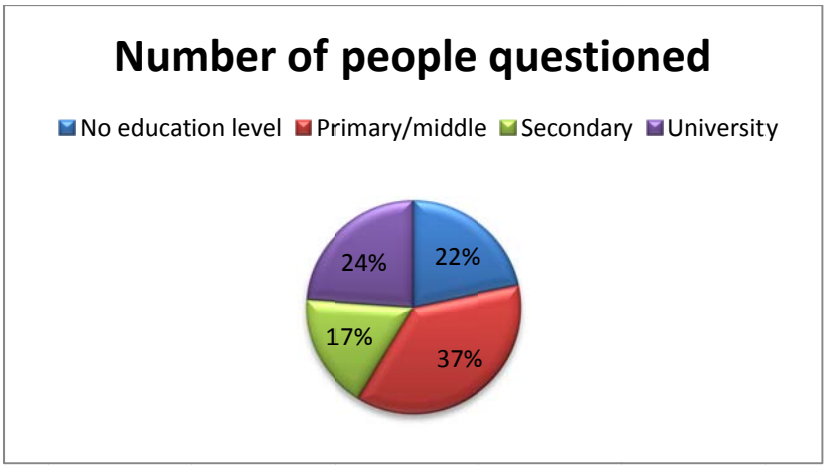


Figure 29: Diagram showing informants by school level.

ii. Analysis of results:

The number of participants according to academic level was established by analysing the figures offered from the largest number to the smallest, such as: those with a primary/medium level which they have an equal percentage of 37 % followed by university students with 24% those with no level 22% and lastly high school students 17 % .

1.2.2 Questions about therapeutic practices:

1.2.2.1 Informants' therapeutic practices:

i. Earnings per share:

Practices therapeutics	Modern Only	Traditional Only	Modern and Traditional
Number of people	13	09	24
Main reasons	Confidence in science science, habit, speed of results observed, ease (acquisition and use), availability, méfiance des plantes inconnues et a résultat lent ou inexistant.	Fear of pharmaceutical products; family practice, boosts the immune system immune system, inexpensive.	Obtain better results by combining, alternating according to availability.

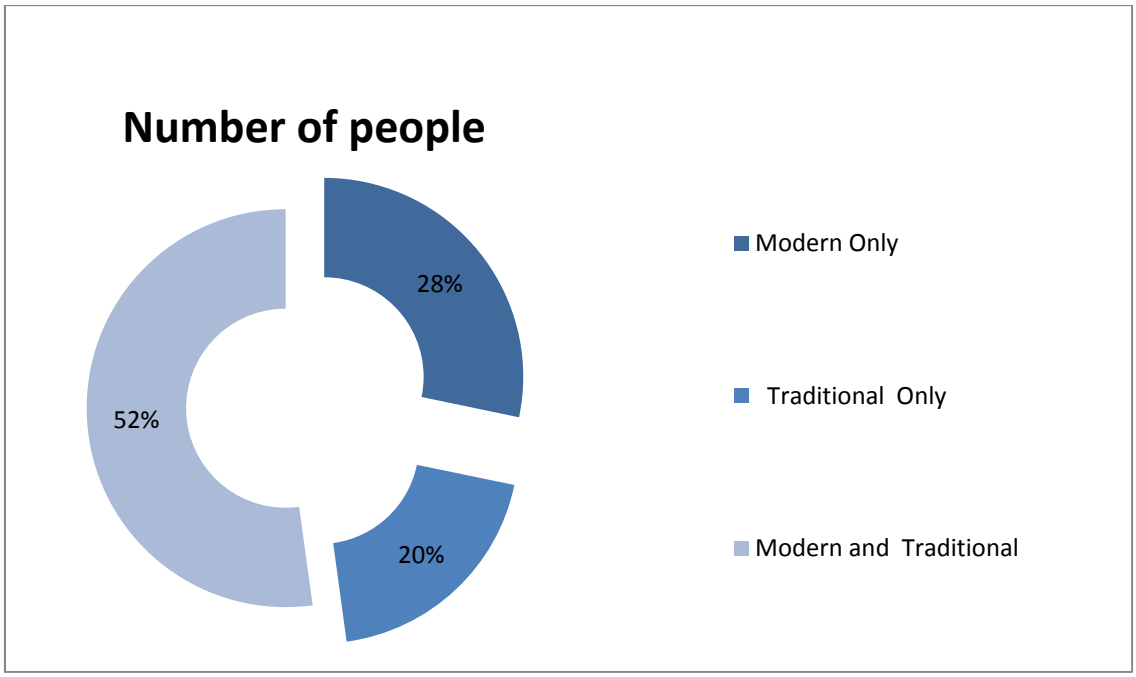


Figure 30: Diagram showing the therapeutic practicesof the informants.

ii. Analysis of results:

According to their responses, the most popular therapeutic practice among participants was modern, with 28 % preferring the speed and ease of acquisition and use provided by pharmaceutical products over the use of unknown plants, which are difficult to obtain and produce slow or non-existent results. Regarding the remaining contestants, 52 % of the population employs a combination of contemporary and traditional medicines to get the benefits of both, and occasionally they do so simply because solutions are available, without regard for choice. Traditional therapy supporters 20% are devoted to it because it is less expensive, they respect family practices, or they trust natural materials' power to increase immunity, as compared to medicines, which frequently have negative side effects. These data, and the underlying reasons, lead us to believe that pharmaceutical medicine has been able to dethrone traditional therapeutic techniques without eradicating them and that therapeutic practices are frequently guided by the price/results ratio rather than prior knowledge and understanding.

1.2.2.2 Frequency of doctor visits:

i. Result by Number:

Frequency visits	none	frequent control	In case of illness only
Number of people	01	17	28

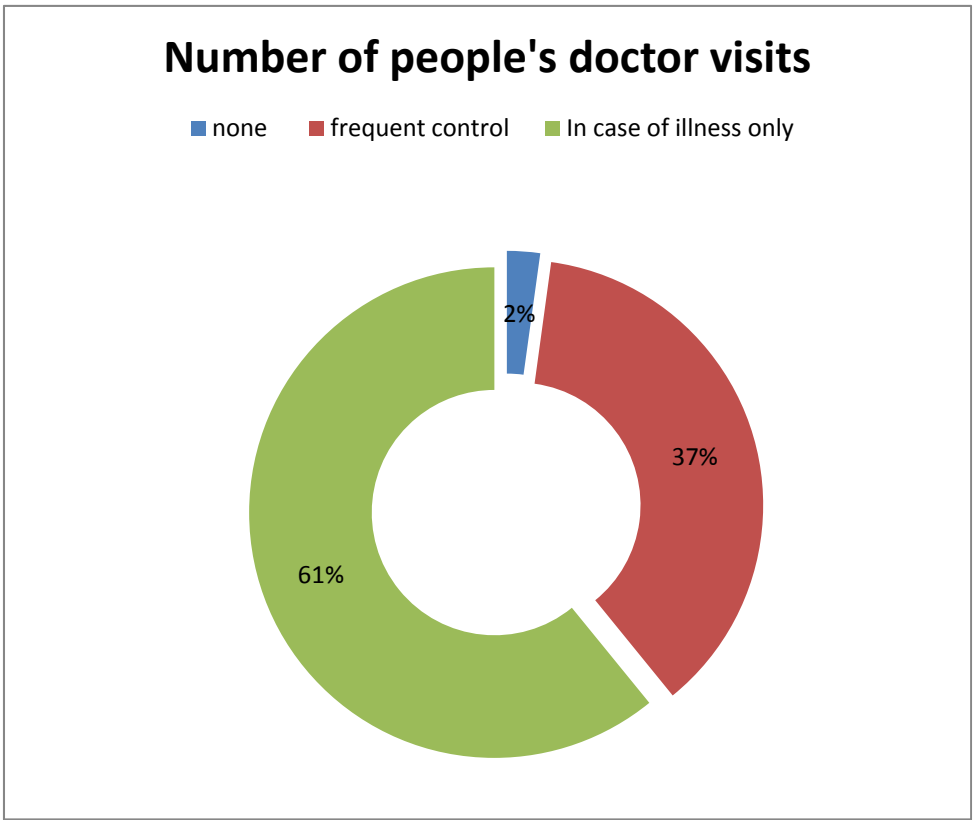


Figure 31: Diagram showing the frequency of visits to the doctor.

Ii.Results analysis:

More than 61% of respondents said they only went to the doctor when they were sick, whereas 37% had regular checkups. Unfortunately, such data indicate our fellow citizens' misunderstanding of the significance of frequent check-ups and disregard for health monitoring.

1.2.2.3 Knowledge of toxic plants in the region.

i. Results by figure:

Knowledge of toxic plants	Yes	No
Number of people	22	24
Cited plants	Nettle, mushroom, Flax seed	/

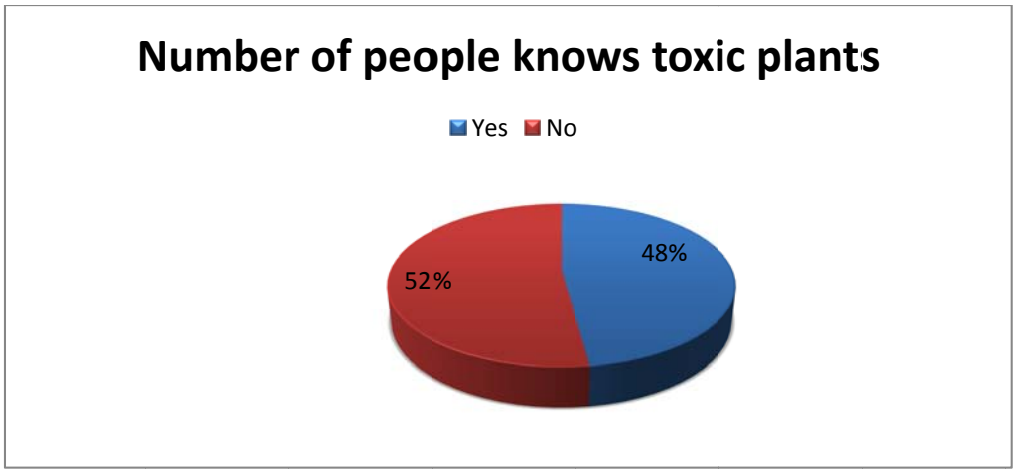


Figure 32: Diagram showing the people knowledge about toxic plants

ii. Analysis of results:

More than half of respondents 52 % were ignorant of the presence of dangerous plants in the region, and those who claimed to know 48 % were not primarily harmful, highlighting a lack of knowledge about medicinal plants.

1.2.2.4 Employment of Phytotherapeutic Plants

i. Result by number:

Utilization	Uses	Does not use
Number of people	27	19

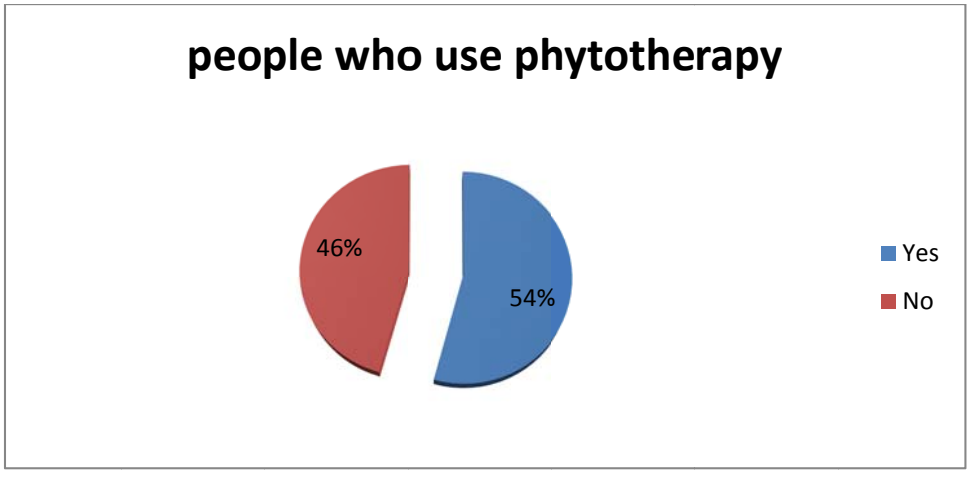


Figure 33: Diagram showing the percentage use of phytotherapeutic plants.

ii. Analysis of results:

As shown above, the combination of two categories using traditional medicine meant that the number of users was little higher than the number of non-users, for a ratio of 54 to 46 %.

1.2.2.5 Use of Plants with Specific Doses:

i. Result in numbers:

Using precise doses	Yes	Non
Number of people	25	21

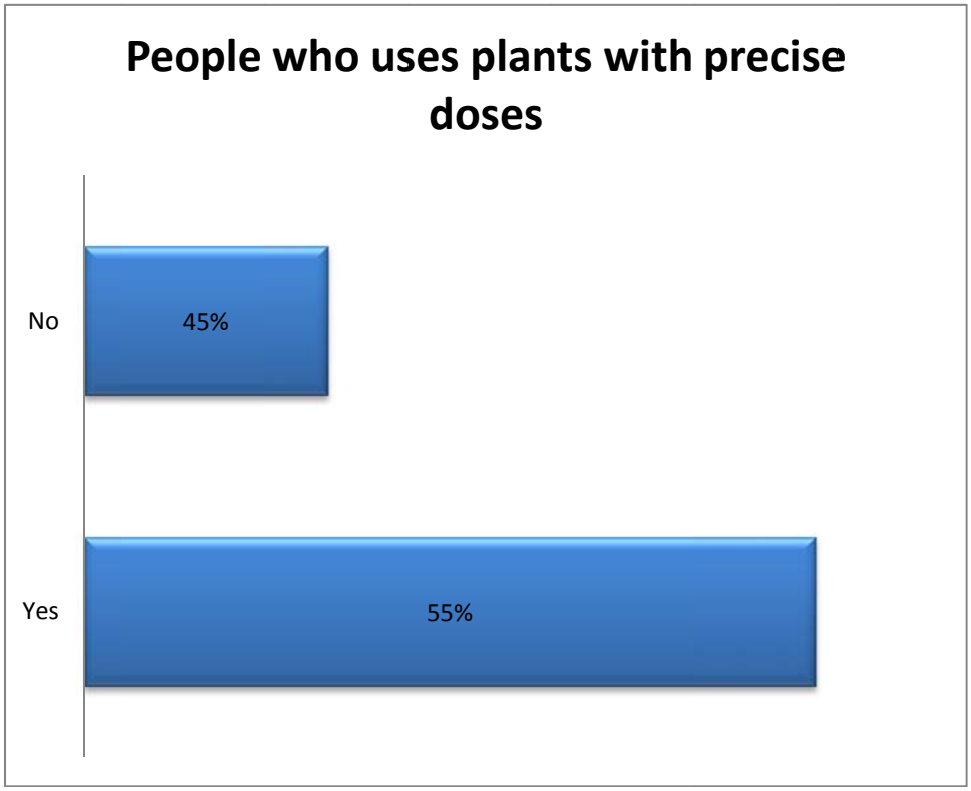


Figure 34: Diagram of the use of plants with precise dosage.

Ii.Results analysis:

The table shows that 45% of plants are used without specific dosages, whereas 55% use precise doses. These statistics also show a poor therapeutic practice based on ignorance, leading to an empirical approach that cannot provide differentiated and long-lasting results.

1.2.2.6 The outcome of your care:

i. Results by number:

Results of treatment	Healing	Improvement	No effect	Harmful effect
Number of people	12	18	09	07

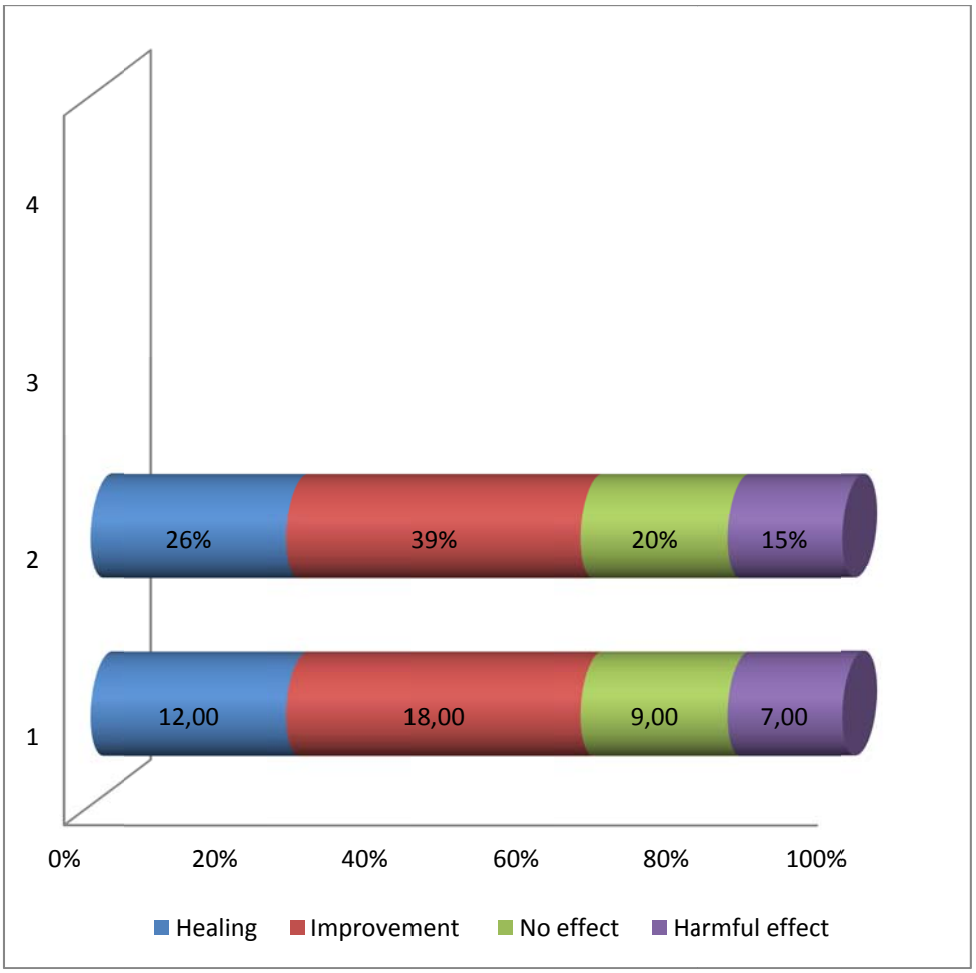


Figure 35: Diagram showing the results observed by informants on herbal treatments.

ii. Analysis of results:

The majority of herbal remedies users, 39%, claimed an improvement, followed by 26% who reported a full cure and 20% who reported no impact at all, with 15% reporting negative consequences. These figures indicate the pleasure and efficacy of herbal treatments. The 15% who felt such therapies were hazardous might be attributed to ignorance and overuse.

1.2.2.7 Source of information for plant use:

i. Result per number:

information Sources	Experiences of other	herbalists	Phytotherapist	documentation
Number of people	21	09	10	06

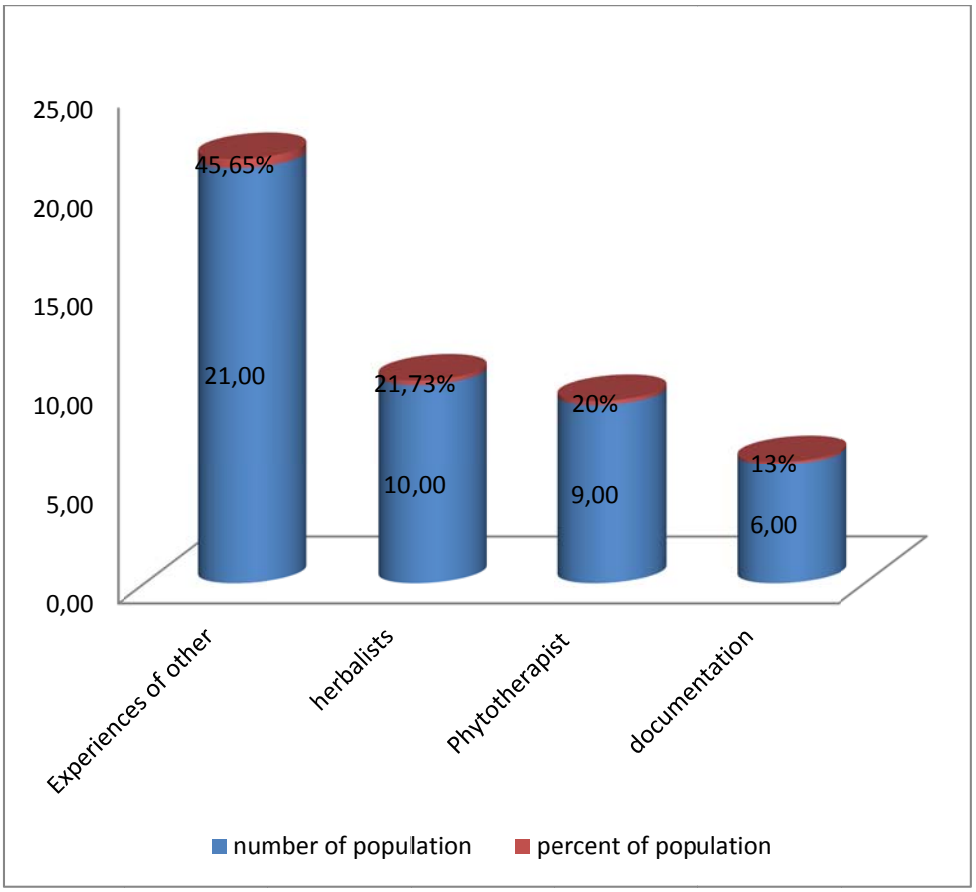


Figure 36: Diagram showing sources of information on natural remedies given by informants.

ii. Analysis of data:

Among informants confirming the use of pharmaceutical therapy, the majority 45.65% found guidance in the advice supplied by past users. Those seeking information from books and the internet had the lowest rate of 13%, with the remaining 21.73% and 20% seeing a specialized herbalist or phytotherapist, respectively. Again, the results show the acceptance of remedies based on substandard practice, as contacting a specialized doctor has the lowest rate.

1.2.2.8. Identification of a LIVER disease:

i. Result by number:

Possibility of identifying a liver disease	No	Yes
Number of people	31	15

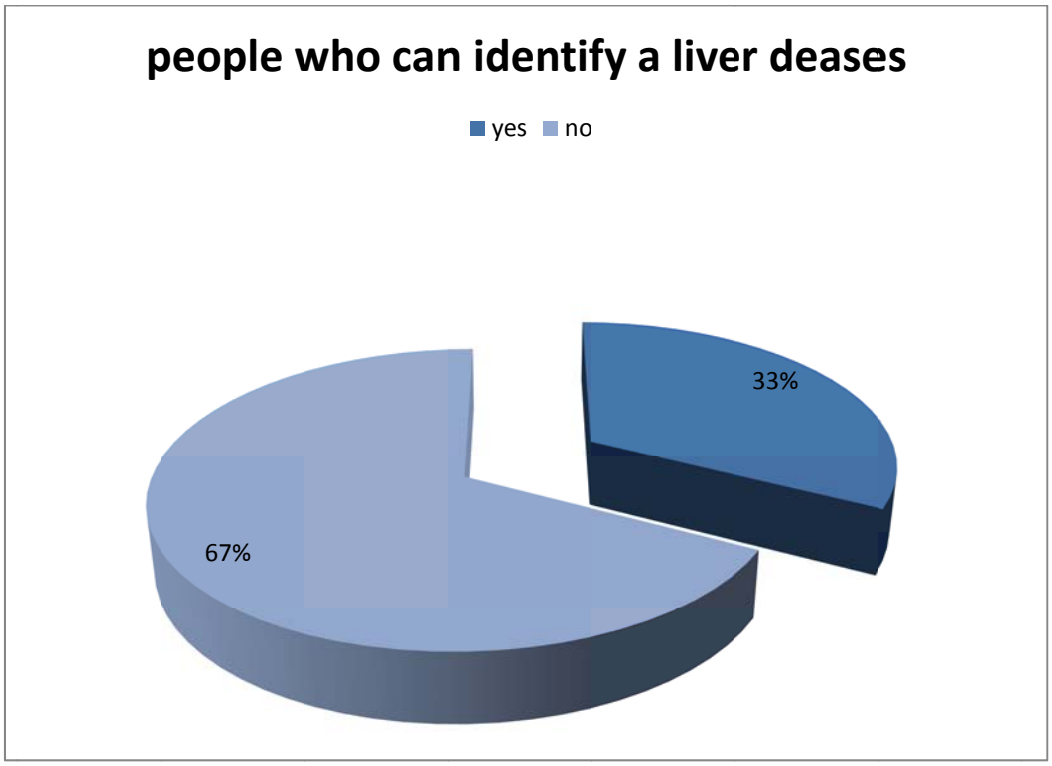


Figure 37: Diagram showing how informants identified liver disease by informants.

ii. Results analysis:

33 % participants replied 'Yes', whereas reported a lack of knowledge of liver diseases. The greatest percentage was among those who did not know 67%, highlighting our society's lack of health knowledge.

1.2.2.9 Symptoms to help identify liver disease:

i. Result by number:

Symptômes identifiés	Tiredness	Loss of appetite	Nausea and vomiting	Dark urine	Abdominal pain	diarrhea	Jaundice
Number of people	12	08	15	11	04	07	17

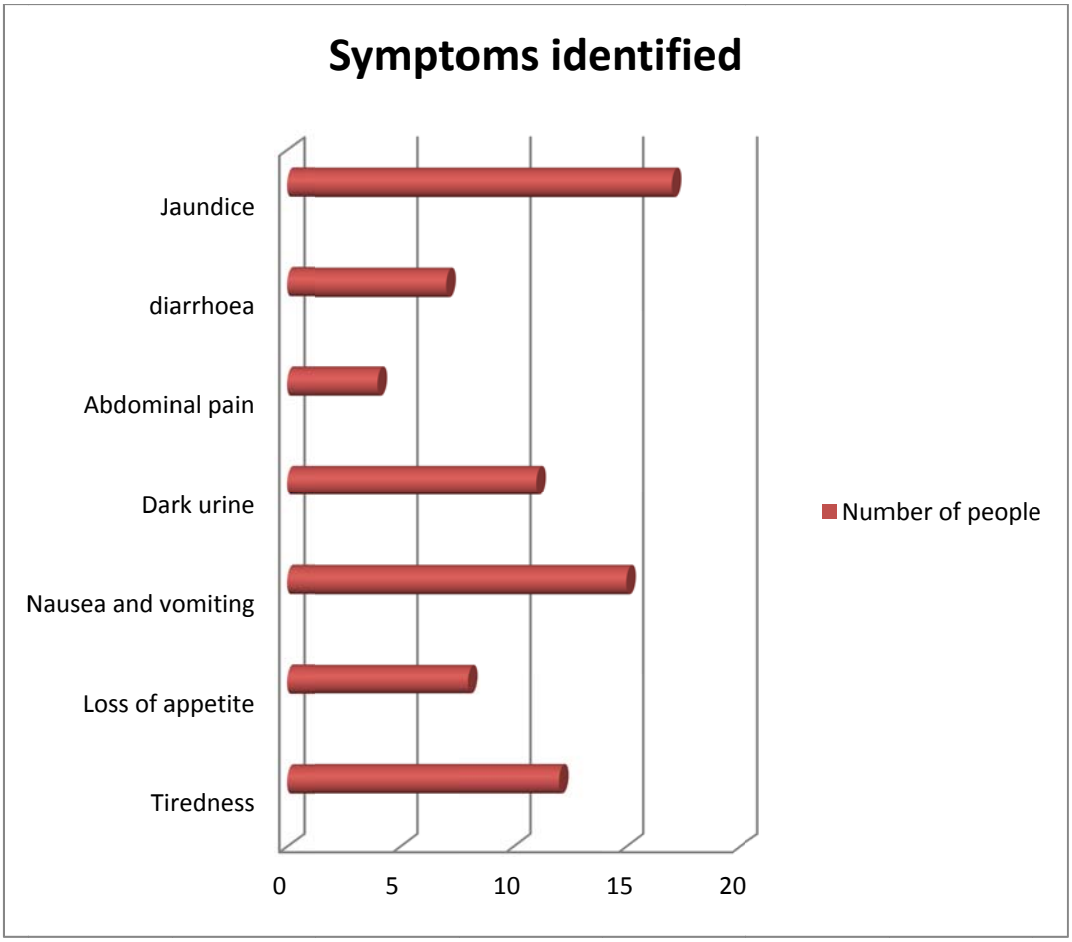


Figure 38: Diagram showing the symptoms of liver disease identified by informants.

ii. Analysis of results:

According to the analysis of the answers given, the symptoms reported by the various stakeholders

- Tiredness, Loss of appetite, Nausea and vomiting, abdominal pain, diarrhea, Jaundice (yellowing of the skin and whites of the eyes), Dark urine

Are the correct answers and they are the most frequently reported symptoms of liver disease.

1.2.2.10 Herbs known to treat liver disease:

i. Result by number:

Name of plants	Number of people	Method of use	Part of plant used
Zygophyllum cornutum (Cosson)	05	Powder or infusion	Roots and flowers
Genista ferox Poiret	07	poultice	Leaves
Cynara cardunculus L.	*05*	Raw or cooked	Fruit
Atriplex halimus L	13	decoction	Leaves
Beta macrocarpa Guss	16	Raw and decoction	Leaves
Beta vulgaris L.	11	Raw , juice	Roots, Leaves
Spinacia oleracea L	14	raw or cooked	Leaves
resedifolia (L.) O. Kuntze.	*18*	herbal tea	Leaves
marianum (L.) Gaertn	*06*	decotion	Root
Cichorium intybus L	*15*	Infusion and raw	Leaves, Roots
Convolvulus arvensis L.	*17*	Infusion and decoction	Leaves, roots
Ecballium elaterium (L.) A.Rich.	*13*	Maceration and nasal instillations	Fruits, roots
Vicia faba L.	*26*	raw or cooked	Grains

Lens culinaris Medik	*21*	Cooked and decoction	Grains
Cicer arietinum L	*11*	Cooked and decoction and puré	Grains
Ajuga iva (L.) schreb	*09*	Powder and decotion	Above ground
Olea europoea L	*28*	fluid extract	Fruits
Apium graveolens L	*23*	Raw and soup	Leaves
Reseda lutea L	*20*	Raw and infusions	Leaves, flowering tops.
Rhamnus alaternus L	*14*	Infusions	Leaves, wood

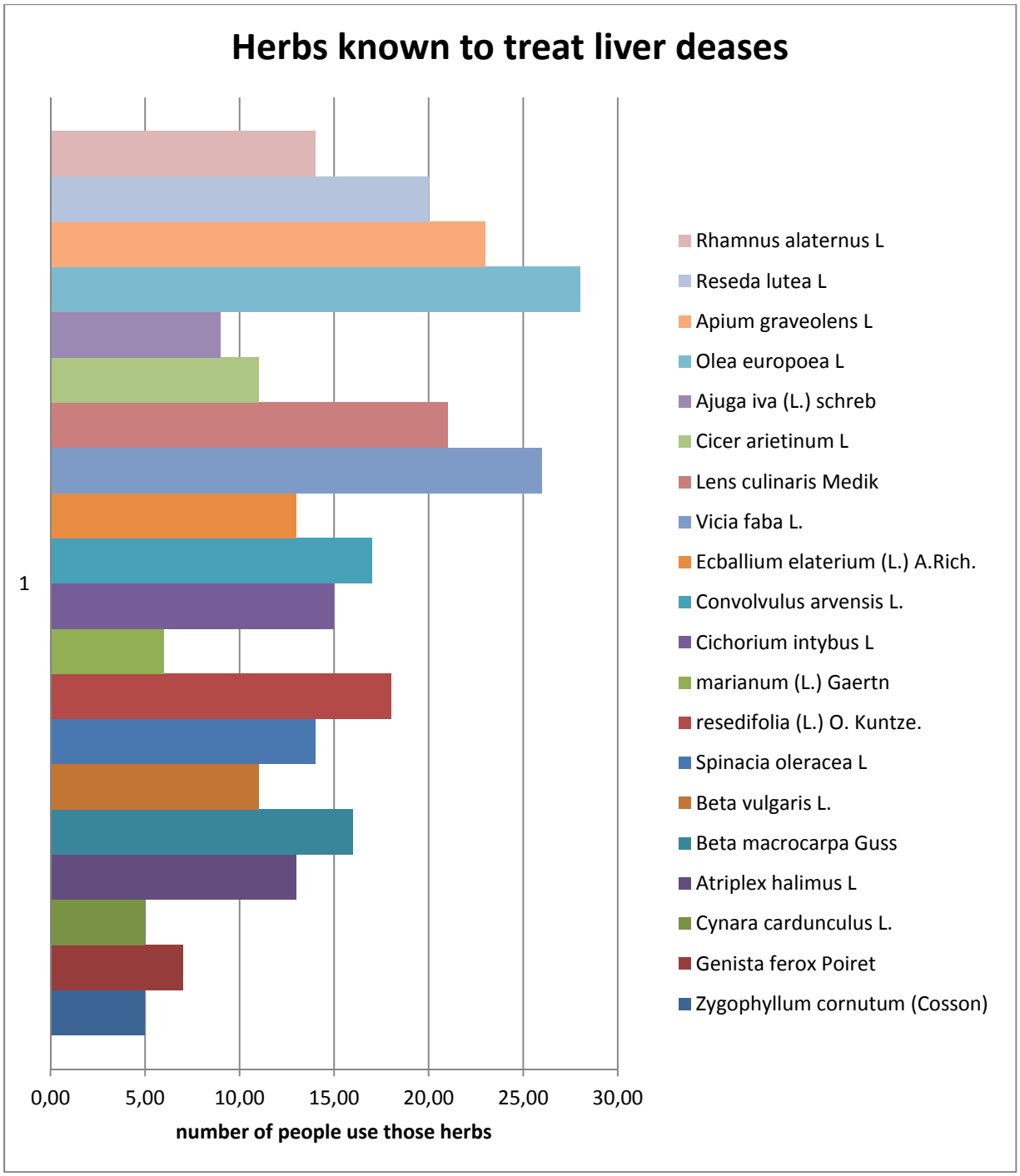


Figure 39: Diagram showing the plants recognised by informers.

ii. Analysis of results:

The various plants mentioned by the informants are exactly those used to treat liver diseases, with more or less effective effects, depending on the use and the case. This shows that the informants have a good knowledge of the plants used to treat liver diseases and the ways in which they are used.

1.2.2.11 Preparation method for medicinal plants:

i. Result per digit:

decoction	powder	infusion	cooked	raw	extract fluid	juice	cataplasme	Maceration
10	04	10	08	14	02	02	01	01

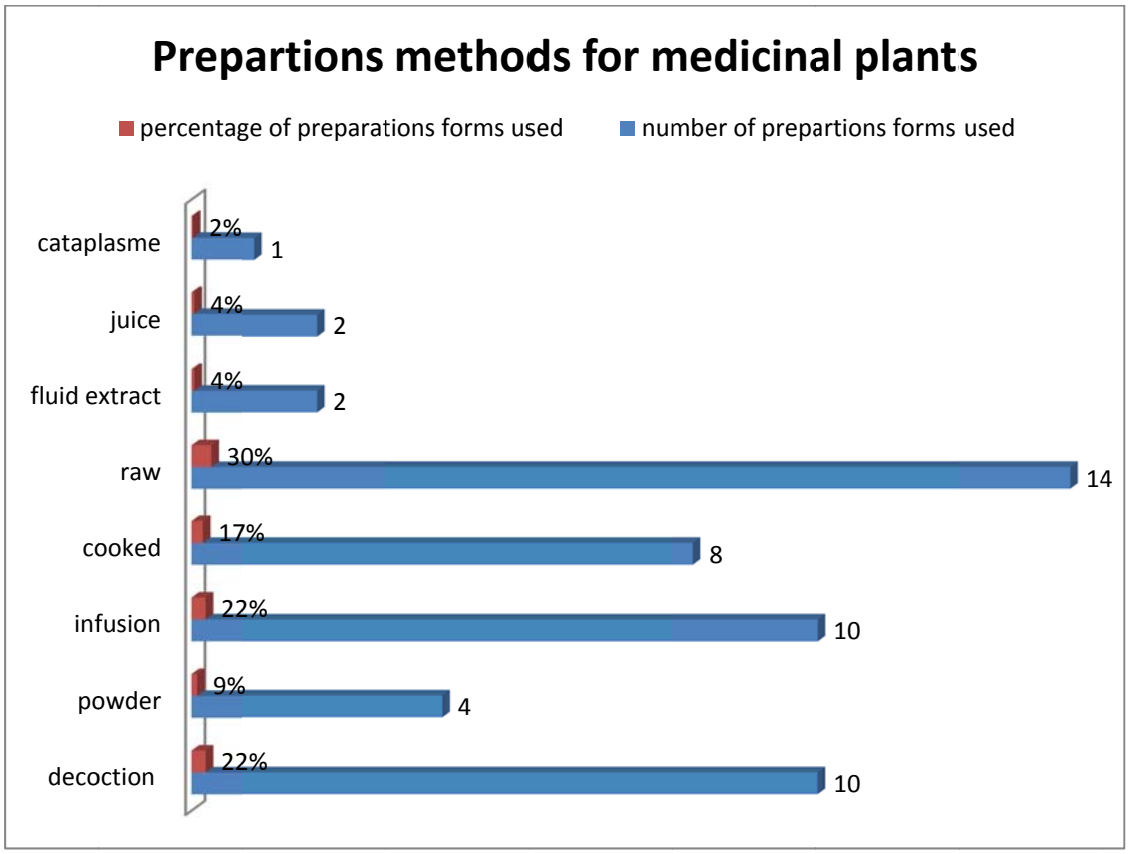


Figure 40: Diagram showing the distribution of preparation methods recognised by informants.

ii. Analysis of results:

In order to treat the various illnesses using traditional herbal remedies, there are several forms of preparation applied, namely infusion, decoction, powder, cooked, raw, juice and fluid extract.

The most common method used in the Saida region is raw compounds 30%, followed by decoction 22% in the same level with infusion. Followed by cooking with 17% and powder method with 9% However, the rest of the population agreed with close percentages for fluid extract 4% and juice 4% and cataplasm 2% and maceration with 1%.

General conclusion

General conclusion

Traditional medicine in Algeria is thriving. Many Algerians who do not have access to a modern health system are turning to medicinal plants for their therapeutic benefits. The purpose of this investigation is to identify natural materials, mostly aromatic and medicinal plants that are utilized by patients, traditional healers, and herbalists in the treatment of liver diseases in Algeria. Plants have always been and continue to be a valuable source of treatment due to their medicinal capabilities. These plants play a significant role in scientific study due to their biological properties.

This is why the knowledge gathered over the centuries about the effects of plants on a common disease such as: liver diseases.

The present work devoted to the ethnobotanical study of the population of the city of Saida for the treatment of hepatic diseases that the bibliographical research on the medicinal plants by survey carried out on the inhabitants of this area, enabled us to draw several conclusions on the ethnobotanical reality of our area of investigation.

We discovered that 54% of the population uses herbal therapies, compared to 46% who rely only on pharmaceutical therapy for recovery. Despite the existence of phytotherapist specialists, only an average for 20% of the population consults them, while herbalists 21% are widely regarded as the professionals of herbal medicine. However, 55% of those who use the treatment use an empirical dosage that has not been studied (based on indications from others).Herbal medication.

It's vital to remember that one of the main reasons people avoid using plant-based remedies is the slower results compared to pharmaceutical products.
Although phytotherapy is an ancient medicine, further research on its therapeutic and toxic potential is necessary to validate and expand on current findings.

Medical plants continue to be a reliable source of active ingredients with therapeutic properties.

Despite encouraging results from this study on phytotherapy, its use in the region of Saida remains limited. Medicinal plants, like medicines, must follow precise standards to which only a phytotherapy specialist can respond. As a result, more emphasis should be placed on the cultivation, exploitation, and commercialization of these plants, which have the potential to generate significant external revenue.

Perspectives and recommendations.

• Conduct a thorough analysis of the therapeutic efficacy of medicinal plants, including toxicity.
• Conduct more in-depth studies on medicinal plants to isolate and identify active principles using advanced methods. Discover new bioactive substances that can address various health issues and potentially replace synthetic medications.
• Determine the mechanism of action of the active principles on microorganisms.
• Using medicinal plant active principles to create plant-based medicines.
• Conduct in-depth and complementary scientific research on this survey to help pharmacological industries in the future to inventing qualified medications and remedies.

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« Annexes »

"Ethnobotanical survey on medicinal plants used in liver diseases".

Questionnaire

« Les plantes a utilisées pour traiter des maladie de foie (hépatique) »

Date :…….. Localité :…….

1. Informations sur l'informateur :

1. Sexe : *Masculin ….. Féminin …..*

2. Age : - de *20 ans ….. 20-40 ans ….. 40-60 ans …. +de 60 ans …..*

3. Niveau scolaire : *Néant …. Primaire /moyenne ….. Secondaire ….. Universitaire….*

2. Questions sur les pratiques thérapeutiques :

1. Quelles sont vos pratiques thérapeutiques ?

- **Modernes Seul …….** **Pourquoi ?.....**
- **Traditionnelles Seul ……** **Pourquoi ?.....**
- **Modernes et traditionnelles ….** **Pourquoi ?.....**

2. Fréquences de visites chez le médecin :

Aucune … **contrôle fréquent……..**
En cas de maladie uniquement……

3. Connaissez-vous des plantes toxiques dans la région ? Prière de les motionner

Si oui …. Les quelles ? :…. Non …..

4. Utilisez-vous des plantes phytothérapique?

Utilise ….. N'utilise pas …..

5. Utilisez-vous les plantes avec des doses précises ?

Oui …… Non …….

6. Résultats de vous soins :

Guérison ….. Amélioration …… Aucun effet …. Effet nocif……..

7. Lorsque vous utilisez une plante, à qui vous adressez-vous ?

Expériences des autres …. Herboristes …… Phytothérapeute…..

Documentation (article internet et livre) ……

8. Pouvez-vous identifier une maladie de foie?

Oui …… Non …….

9. Quelle sont les symptômes qui vous aident à identifier une maladie de foie ?

……..…….

10. Quelle sont les plantes traitant une maladie de foie (hépatique) que vous connaissez?

……

Nom des plantes	Modes d'utilisations	Partie des plantes utilisées

"Ethnobotanical survey on medicinal plants used in liver diseases".

استبيان

"الأعشاب المستخدمة لعلاج أمراض الكبد."

التاريخ..... الموقع.....

1.معلومات عن المبلِّغ:

1. الجنس: ذكر..... أنثى.....

2. العمر: أقل من 20..... 20-40 سنة..... 40-60 سنة..... فوق 60 سنة.....

3. المستوى التعليمي: لا يوجد.... ابتدائي/متوسط..... ثانوي..... جامعي....

2. أسئلة حول الممارسات العلاجية:

1. ما هي ممارساتك العلاجية؟

- **الحديثة وحدها ..... لماذا؟.....**
- **التقليدية وحدها ..... لماذا؟.....**
- **الحديث والتقليدي.... لماذا.....**

2. تكرار زيارة الطبيب:

لا شيء... فحوصات متكررة..... في حالة المرض فقط.....

3.هل تعرف أي نباتات سامة في المنطقة؟

إذا كانت الإجابة بنعم.... أي منها؟ ..... ؛ لا.....

4.هل تستخدم الأدوية العشبية؟

استخدم ..... لا تستخدم.....

5.هل تستخدم الأعشاب بجرعات دقيقة؟

نعم ..... لا.....

6.نتائج علاجك:

الشفاء.التحسن. التحسن ..... لا يوجد تأثير .... تأثيرا ضار.....

7.عند استخدامك للنبات، إلى من تلجأ؟

تجارب الآخرين.... المعالجون بالأعشاب ..... المعالجون بالنباتات.....

الأدب (مقالات وكتب على الإنترنت.....)

8.هل يمكنك تحديد مرض الكبد؟

نعم ..... لا.....

9. ما هي الأعراض التي تساعدك على

.....

(10ما هي النباتات التي تعرفها والتي تعالج أمراض الكبد؟

اسم النبات	طريقة الاستخدام	جزء النبات المستخدم

"Ethnobotanical survey on medicinal plants used in liver diseases".

Questionnaire

"Herbs used to treat liver disease".

Date:…… Location:……

1. Information about the informant:

1. Sex: Male..... Female.....

2. Age: under 20..... 20-40 years..... 40-60 years.... over 60 years.....

3. Level of education: None.... Primary/middle..... Secondary..... University....

2. Questions about therapeutic practices:

1. What are your therapeutic practices?

- **Moderns Alone..... Why?**
- **Traditional Alone..... Why?**
- **Modern and traditional.... Why?**

2. Frequency of visits to the doctor:

None ... frequent check-ups..... In case of illness only.....

3. Do you know of any poisonous plants in the region?

If yes.... which ones? : No .....

4. Do you use herbal remedies?

Use..... Do not use.....

5. Do you use herbs in precise doses?

Yes..... No.....

6. Results of your treatment:

Healing..... Improvement..... No effect.... Harmful effect.....

7. When you use a plant, who do you turn to?

Experiences of others.... Herbalists..... Physiotherapist.....

Literature (internet articles and books).....

8. Can you identify a liver disease?

Yes..... No.....

9. What are the symptoms that help you identify liver disease?

.....

10. What plants do you know that treat liver disease?

.....

Name of plant	Method of use	Part of plant used