



Role of Herbal Medicines in Prevention and Management of Chronic Diseases

Surenbra Katikala*, K.V. Rajasri, CH. Vijaya Lakshmi

Swathi College of Pharmacy, Next to Nellore Toll Plaza, Venkatachalam Mandal, Nellore, A.P-524320

ABSTRACT

The traditional use of medicinal plants can lead to the discovery of new potent botanical agents in the treatment of several diseases. spite of the development of pharmacological agents for the treatment of chronic diseases, the use of medicinal plants continues to flourish. Over the last century, the drastic changes of human life style and eating habits lead to the emergence of various chronic diseases. The decreasing efficacy of some synthetic drugs and the increasing contraindications of their usage make the usage of natural drugs topical again. Herbs and plants can be processed and can be taken in different ways and forms, and they include the whole herb, teas, syrup, essential oils, ointments, salves, rubs, capsules, and tablets that contain a ground or powdered form of a raw herb or its dried extract. Plants and herbs extract vary in the solvent used for extraction, temperature, and extraction time, and include alcoholic extracts (tinctures), vinegars (acetic acid extracts), hot water extract (tisanes), long-term boiled extract, usually roots or bark (decoctions), and cold infusion of plants (macerates). There is no standardization, and components of an herbal extract or a product are likely to vary significantly between batches and producers. Plants are rich in a variety of compounds. Many are secondary metabolites and include aromatic substances, most of which are phenols or their oxygen-substituted derivatives such as tannins. Many of these compounds have antioxidant properties. Ethnobotanicals are important for pharmacological research and drug development, not only when plant constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds. With tremendous expansion in the interest in and use of traditional medicines worldwide, two main areas of concern arise that bring major challenges. These are international diversity and national policies regarding the regulation of the production and use of herbs (and other complementary medicines) and their quality, safety, and scientific evidence in relation to health claims.

Keywords: Medicinal plants, therapeutic agents, secondary metabolites, Ethnobotanicals, Herbs and plants.

ARTICLE INFO

*Corresponding Author:

Dr. Surenbra Katikala
Professor, Department of Pharmaceutical Analysis,
Swathi College of Pharmacy,
Venkatachalam Mandal, Nellore, A.P-524320.

Article History:

Received : 15 July 2024
Revised : 25 Aug 2024
Accepted : 24 Sept 2024
Published : 26 Oct 2024

Copyright© 2024 The Contribution will be made Open Access under the terms of the Creative Commons Attribution-NonCommercial License (CC BY-NC) (<http://creativecommons.org/licenses/by-nc/4.0>) which permits use, distribution and reproduction in any medium, provided that the Contribution is properly cited and is not used for commercial purposes.

Citation: Surenbra Katikala, et al. *Role of Herbal Medicines in Prevention and Management of Chronic Diseases*. A. J. Med. Pharm, Sci., 2024, 12(1): 74-84.

Contents

1. Introduction.	74
2. Traditional Indian Medicine.	76
3. Medical Mushrooms.	80
4. Conclusion	82
5. References.	82

1. Introduction

Global mortality from chronic disease has increased to 16.1% during 2006–2016 and could reach 52 million by 2030. Chronic conditions including cancer, diabetes mellitus, chronic obstructive pulmonary disease, and cardiovascular problems are increasing alarmingly in

Ethiopia and they are associated with increased rates of morbidity and mortality. The national prevalence of cardiovascular disease is estimated to be 15% and the prevalence of both cancer and chronic obstructive pulmonary disease is estimated to be around 4% of the

population. In 2011, the World Health Organization estimated that over 30% of Ethiopians suffer from chronic diseases and/or die from them.

Majority of patients with chronic disease shifted to complementary and alternative medicine modalities to manage their condition because of the chronic nature of the disease and challenges associated with sticking to long-term treatment plans. One of the most common complementary and alternative medicine methods used by many chronically ill patients in the worldwide is the usage of herbal medicine. Traditional medicine (TM) is still widely practicable worldwide, despite the fact that modern medicine has become the predominant medical practice since the 20th century. The magnitude of people who have used TM ranges from 40% to 50% in developed countries like the United States and Australia, whereas the prevalence of TM used to address basic healthcare needs ranges from 60% to 90% in low and middle income countries¹⁻⁴.

According to World Health Organization, traditional medicine is defined as “Health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques, applied singularly or in combination to treat, diagnose and prevent illnesses and maintain well-being”. Herbal medicine is the most widely utilized traditional medical practice in both the general population and people with chronic disease.

Since the beginning of human history, medicinal plants have been used for therapeutic purposes. Complementary use of medicinal plants with prescribed drugs is becoming more widespread concern among people with chronic illnesses like cancer, HIV/AIDS, diabetes, and hypertension. The belief that medicinal plants are completely safe because they are obtained from natural sources is the primary driver for the co-use of these plants with conventional medicine. Additional reason for the preference of medicinal herbs are they are more widely available, affordable, effective, patient report of dissatisfaction and side-effects encountered related with conventional treatment and past good experiences of taking medicinal plants.

Herbal medicine has its origins in ancient cultures. It involves the medicinal use of plants to treat disease and enhance general health and wellbeing. Some herbs have potent (powerful) ingredients and should be taken with the same level of caution as pharmaceutical medications. In fact, many pharmaceutical medications are based on man-made versions of naturally occurring compounds found in plants. For instance, the heart medicine digitalis was derived from the foxglove plant⁵⁻¹¹.

Active ingredients and herbal medicine

Herbal medicines contain active ingredients. The active ingredients of many herbal preparations are as yet unknown. Some pharmaceutical medications are based on a single active ingredient derived from a plant source. Practitioners of herbal medicine believe that an active

ingredient can lose its impact or become less safe if used in isolation from the rest of the plant. For instance, salicylic acid is found in the plant meadowsweet and is used to make aspirin. Aspirin can cause the lining of the stomach to bleed, but meadowsweet naturally contains other compounds that prevent irritation from salicylic acid. According to herbal medicine practitioners, the effect of the whole plant is greater than its parts. Critics argue that the nature of herbal medicine makes it difficult to give a measured dose of an active ingredient.

Medicinal uses for specific herbs

Herbal medicine aims to return the body to a state of natural balance so that it can heal itself. Different herbs act on different systems of the body. Some herbs that are commonly used in herbal medicine, and their traditional uses, include:

Echinacea – to stimulate the immune system and aid the body in fighting infection. Used to treat ailments such as boils, fever and herpes.

Dong quai (dang gui) – used for gynaecological complaints such as premenstrual tension, menopause symptoms and period pain. Some studies indicate that dong quai can lower blood pressure.

Garlic – used to reduce the risk of heart disease by lowering levels of blood fats and cholesterol (a type of blood fat). The antibiotic and antiviral properties of garlic mean that it is also used to fight colds, sinusitis and other respiratory infections.

Ginger – many studies have shown ginger to be useful in treating nausea, including motion sickness and morning sickness.

Ginkgo biloba – commonly used to treat poor blood circulation and tinnitus (ringing in the ears).

Ginseng – generally used to treat fatigue, for example during recovery from illness. It is also used to reduce blood pressure and cholesterol levels, however overuse of ginseng has been associated with raised blood pressure.

Hypericum perforatum – commonly known as St John’s Wort. Studies have suggested that St John’s Wort is just as effective as some pharmaceutical antidepressants in treating mild to moderate depression. It is also used for anxiety and insomnia. However, St John’s Wort can interact with a number of prescription medications, including the oral contraceptive pill, and stop them from working properly¹²⁻¹⁸.

Herbal medicine has been a fundamental component of healthcare systems across cultures for centuries. From ancient China and India to indigenous and traditional cultures in Africa and the Americas, herbal remedies have been integral to promoting health and preventing illness (1). In recent years, there has been a notable interest in holistic and natural approaches to healthcare, with herbalism

emerging as a prominent contender in the realm of preventative medicine (1,2). Herbal medicine can offer a wealth of benefits for maintaining health and preventing illness. Plants have been used for their medicinal properties since ancient times, and their role in disease prevention is arguably more significant than ever.

In recent decades, there has been a resurgence of interest in herbal medicine, driven by factors such as dissatisfaction with pharmaceuticals, concerns about adverse effects, and a growing appreciation for holistic and individualised approaches to health (2). Moreover, advances in scientific research have shed light on the biochemical mechanisms underlying the therapeutic effects of many medicinal plants, validating their traditional uses, and providing insights into their potential applications in disease prevention.

Herbalism is a holistic practice that acknowledges the interconnectedness of the body and mind. Rather than simply targeting isolated symptoms, herbal remedies work to restore balance and harmony within the body, addressing underlying imbalances that may contribute to disease (4). This holistic approach not only treats existing health problems, but it can also strengthen the body's natural defences, helping to prevent future illness and promote overall well-being.

Another strength of herbalism lies in its ability to offer personalised treatment plans tailored to individual needs. Herbalists consider a person's unique constitution, lifestyle, and health goals when selecting appropriate herbs and formulations. By considering the whole person, and by being able to choose herbs that take into account individual needs, herbalism can offer a comprehensive and effective approach to preventative medicine.

2. Traditional Indian Medicine Ayurveda

Traditional Indian medicine has been in existence since antiquity and is inarguably among the most ancient systems of traditional medicine still in existence. It has been proven to date back tens of thousands of years; the longest period determined for any traditional system

Some other arguments have held that the Ayurveda system is the core base of the widely renowned Tibetan medicine, traditional Chinese medicine, and the Unani (Arabic) medicine systems. All these systems ascribe to a common and accepted body–mind–spirit orientation; that holds that disease and health are a product of the interaction of these three fragments. They are also based on the heating and cooling energy processes. There is also an apparent relationship between yoga and Ayurveda. The popularity of both has been on the rise in current times; they are almost inseparable; one cannot be mentioned without the other¹⁹⁻²⁵.

The influence of Ayurveda in the medical world has been so immense, it has come to be referred as 'the mother of healing'. It goes without saying that for one to understand the basis of contemporary medicine, one needs first to

understand the roots of Ayurveda. Most of the natural products utilized in traditional Chinese medicine (TCM) and the modern-day era are also found in Ayurveda. However, even though traditional Indian medicine has been in existence for thousands of years, there is still more to be discovered with the application of modern technology and science. The world we live in is constantly evolving and so is our body, thus, to accommodate these changes. The systems of medicine available, including Ayurveda, will also change to meet the needs and gaps in these changes.

The Ayurveda system holds that the whole universe consists of five main elements, being Vayu (air), Jala (Water), Aakash (space or ether), Prithvi (earth), and Teja (fire). The latter (referred to as Pancha Mahabhoota in Ayurveda) is composed of three vital body humors in different amounts. The three humors are collectively referred to as "Tridoshas," including Vata dosha, Pitta dosha, and Kapha dosha. Each of the elements contain five sub-doshas that control the most important physiological functions of the body. According to this system, the human body contains Saptadhatus (seven tissues), Rakta (blood), Rasa (tissue fluids), Meda (fat and connective tissue), Asthi (bones), Mamsa (muscle), Majja (marrow), Shukra (semen) and three Malas (waste products) of the body, viz. Purusha (feces), Mutra (urine), and Sweda (sweat). The Vata dosha oversees the body's electrolyte balance, transport of cellular components, and getting rid of waste products. Its effects on the body are resonated by dryness. The different tissues interact with one another to maintain the normal physiological functioning of the body. The blood circulation and production of the important blood components in the body are performed by the Rakta Dhatu. On the other hand, the Mamsa Dhatu (Muscle tissue) maintains the support of the skeletal muscles for the adipose tissue (Meda Dhatu). The bones are made up by the Asthi Dhatu, while the Majja Dhatu consists of the fluids that oleate the bones and the bone marrow. The Shukra Dhatu controls the reproductive functions of the body.

The Pitta dosha regulates the body temperature, thirst, hunger, and coordination of the optic nerves. The Kapha dosha is affected by fatty and sweet foods; it enables the lubrication of the body's joints for proper coordination. It is believed that the Vata controls the body's catabolism; the Kapha oversees the metabolism, while the Kapha controls the anabolism of the body. For the body to maintain a healthy state, the three doshas and other related factors and their interactions must have a balance. If there are any significant imbalances between the three, disease or illness will likely result. A balance of the three doshas can be maintained if one follows the basic principles of divine wisdom; this is a major belief of the Ayurveda system²⁶⁻³³.

Siddha System

Protagonists and inheritors of the Siddha system of traditional medicine proclaim that it provides 'Holistic health' to all its users. The system provides rejuvenating, rehabilitative, promotive, and preventive care through a holistic and scientific approach. Siddha is rooted in "Citti," which means achieving accomplishment, internal bliss, and

perfection. The system entails philosophical concepts with four components: medical practice, yogic practice, iatrochemistry, and wisdom. These revolve around the intellectual, psychological, physical, and physiological aspects of all human beings. Some of them are regarded as the most fundamental unit of all the components of the body and the entire cosmos.

The Siddha system include theories of five elements (Aimpotham) that constitute the universe (in terms of properties), three forces/faults (Mukkutram) that help maintaining homeostasis, and eight methods of examination (Envakai Thervukal) that help in proper diagnosis and treatment. The body's physical components identified by this system are also highlighted in the Ayurveda system. The pathological and physiological aspects of these components have been described in the literature of this system and heavily relied upon in practice.

Unani System

Unani is also known as Unani Tibb and is believed to have originated from Greece; its doctrines have been found in the writings of the ancient Greek physicians Galen and Hippocrates. The system was refined and developed with time through experimentation by the Arabs and was made prominent by the Muslim teacher Avicenna. Part of the medicine's principles was adopted from this system during the Muslim political-religious regime in 632 CE. This system has been established through contributions from the Middle East and South Asia; it has become acceptable in different parts of the globe. Healing from the system relies upon principles of balance and harmony that include uniting the spiritual, mental, and physical realms together.

The system holds that the health of the body is maintained by the orderly arrangement of the seven vital physiological principles as stated by the Unani doctrine. These principles are arkan (elements), mizaj (temperament), akhlat (bodily humors), aaza (organs and systems), arwah (vital spirit), afaal (functions), and quwa (faculties or powers). All these components interact with one another to maintain the balance of the normal and natural makeup of the human body. Every human constitution has the capacity and power to regulate itself and maintain the seven components' equilibrium.

There are four entities, thenar (fire), arz (earth), Hawa (air), and maa (water), that make up the basic components of the body and the entire creations of the Earth. The four entities can interact to create consequences that are predictable by man. The elements act upon and rely on each other; they continuously change deterioration and generation due to the body's reaction to the medicines administered. Only skilled healers can observe such changes in the body.

The temperament states are the following four; moist, cold, dry, and hot. The four components are contained in balance by all the entities of the cosmos, such as plants, animals, and minerals. The health of the human body and other entities depends on temperament's balance. Any changes in

the different states may cause ferocious effects on the human body. The temperament has been determined to play a vital role in determining the person's normal state (the social, mental, and physical states) and the natural disease process.

The process of treatment in the Unani system is orderly. Initially, establishing the therapeutic regimen to normalize the balance of external factors (i.e., food, water, and air) involved in diseases and ailments takes priority. Other means that involve treatment with natural medicines are recommended if the latter does not bear any fruits. The prescriptions by the healer are meant to boost and restore the health and well-being of the patients. The healer also uses various therapeutic approaches. One of them is dietotherapy (Ilaj-bi-ghiza), which involves recommending a specific diet to the patient. It is usually a natural course of treatment in the simplest form. In the illustration, in case of fever, the hakim may recommend a nutrient-rich and low-roughage remedy composed of porridge (Daria) and milk broth (kheer). The therapy takes into consideration the amount and the quality of food. Another intervention that may be used is organotherapy, which entails using organs from healthy animals to heal the same diseased organ in the human body³⁴⁻³⁷.

Homeopathy

Homeopathy has been utilized as a healing system in the traditional Indian medical system for over a century. The renowned Dr. Samuel Hahnemann is the protagonist of this system, who popularized it in the mid 17 and 18 centuries. The basic principle of this system is, "like can cure like." If a substance can elicit symptoms in the human body, it can also cure the same symptoms in sick people. The principle has been around for some time, but it was until 200 years ago that it was applied in medicine. Hahnemann believed that the correct and accurate remedy presented the body's vital force with mild disease. For instance, if the disease itself is so strong, it overwhelms the ability of the vital force of the body to correct it. The used substances to treat the initial infections are gentle so that it mounts a response that can correct the imbalance existing in the body due to the disease. Since the symptoms produced by the disease are similar to those induced by the medical disease, the body's responses can lead to healing. The principles of this system are like those of vaccination. A response caused by the disease will protect the body against any amount of disease that can stimulate the body's response. The difference between vaccination and homeopathy is that the body responds to the vibration of energy instead of a product of disease, preventing both infectious and non-infectious diseases.

Yoga

Yoga has become popular in all parts of the world in recent decades. The practice dates to antiquity and has been established as useful to establish physical and spiritual balance in tbody. The relevance of yoga in health care has increased as more attention has been paid to the practice. Published reports have indicated that yoga has helped many master the challenges in their lives and to develop

confidence and control of their lives. The roots of yoga trace back to ancient India. In describing the meaning of the word yoga, union, mastery, and control are of particular importance. Cultural and individual factors influence the practice of yoga. The practice of yoga requires the subject's willingness to practice and study while being dedicated and compliant to yoga. Lifestyle changes may be necessary to meet the objectives set. Multiple studies examined the effects of yoga on the physical fitness aspects such as muscular endurance, balance, flexibility, and spinal mobility³⁸⁻⁴⁰. Cognitive functions have also been studied, such as attention span, memory, processing speed, and executive function.

Different forms of yoga such as Iyengar and Hatha yoga combined with different measures such as the standard sit and reach test have been used to assess the physical flexibility. After several weeks of observation, it was found out that the flexibility of the involved muscles increased over time. Two studies focused on particular postures and the effects they had on specific muscles of the body. One of these studies after three months determined that surface electromyographic signals, while performing the different poses, suggested that the downward facing poses were the most effective to strengthen abdominal muscles. The gluteus maximus muscles could be strengthened by the upward facing poses. Another study that focused on the flexibility of the joints showed that there was increased flexibility and balance in those who performed yoga than those who did not. The practice has been compared to other exercises like stretching and strengthening exercises and calisthenics. Slow movements have been determined to be more effective. At the end of some studies, the mobility of the spine and flexibility of the hamstring had increased. Similarly, yoga also increased the cognitive functioning and the execution speed, and thinking had increased in those who practiced yoga.

Naturopathy

Naturopathy is a healing system that utilizes natural remedies to treat diseases and illnesses. It entails different methods like nutritional counseling, herbs, massage therapy, exercising, and acupuncture to solve health problems. The major objective of this therapy is to bring healing to the entire persona. This includes the spirit of the person, mind, and body. Additionally, the ultimate goal is to cure the base issue or the root cause of the illness and not only the presenting symptoms. The expert takes about an hour or two to examine the patient before identifying the treatment remedy. The patient may be questioned on their entire health history, lifestyle patterns, quantum, and any reason that may lead to the acquisition of an illness.

In contemporary practice, a naturopathic physician must complete a four-year graduate-level course approved by the council of naturopathic medical education. The entire effort of the physician is to utilize the advantages of traditional medicine and other resources to heal the patient. Additionally, it aims to weed the disease from its basic cause and superficial symptoms. At the end of the treatment, the physician explores the emotional, physical,

mental, and mental aspects of one's health. Some of the interventions carried out include changes in the diet patterns of the patient, lifestyle behavior, adoption of hydrotherapy, and some minor surgical procedures. The initial naturopathic appointment tends to be longer, where the physician asks lengthy questions that include the history of the illnesses and the lifestyle habits. He or she can carry out laboratory tests to conclude the diagnosis. The cost of drug therapy and interventions differ from one physician to another. The massage intervention is used to help the patient to be stress-free. It relieves the client of any tension accumulated in the mind and the body via the massage of the specified areas or even the whole body. Acupuncture may induce a little discomfort on the patient, but it has been shown to help reduce the stress that may have accumulated in some part of the body and that triggers any issues related to health. The patient may also go soaking in the sun or a mud bath for some time.

The use of Ayurveda invigorates the users to adopt lifestyle changes and use natural therapies to take control of the balance between the mind, environment, spirit, and body. It usually commences with an internal process of purification, then a special diet, herbal remedies, massage, yoga, and meditation. The healer pays particular attention to the doshas and prescribes herbal medicine and non-pharmacological interventions like meditation and yoga where needed. The Indian Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homeopathy (AYUSH) ministry advocated using Kadha of natural substances such as ginger, curcumin, honey, and cumin seeds during the day to boost one's immunity. Based on these preliminary results, the local Kerala government has collaborated with other public health organizations to expand the use of traditional medicine in the treatment of the COVID-19 pandemic. It has helped shorten the recovery time and reduce the complications usually experienced.

Despite millions of people receiving Ayurvedic therapy across the globe for treatment or prophylaxis, not much information has been published about it. Several lessons can be learned from the use of the therapies. One is that patients' health did not deteriorate during the use of the therapy. On average, the time to recover from the symptoms was about seven days. This was a short time compared to the recovery periods reported by the CDC, which was 3 to 6 weeks. The dosha balance was reported to have been maintained effectively by consuming a regulated diet. The slower digestion time induced by the diet stimulated the body's digestive powers and helped maintain adequate nourishment. The ayurvedic formulations needed may not be available to most of the patients residing outside India; however, the potency of the available formulations cannot be dismissed.

Miscellaneous Natural Products

Curcumin

Curcumin is one of the essential compounds in the turmeric rhizome (*Curcuma longa*), a yellow-orange crystalline material. It does not have a lot of different kinds. This

product has been used as medicine for the last 4000 years, especially in South Asia. It has been named the “Indian saffron” and the “Golden spice” because of its use as a potent agent in medicinal applications. The compound has been used in Unani, Ayurveda, and Chinese medicine.

The geographical locations of its growth have tremendous effects on the quality of the plant and its nutrition composition. It has been used to add flavor to rice, meat, pasta, and vegetable dishes. It is speculated that it has been used for over 2500 years to treat different diseases and illnesses. It has been used in Ayurveda and traditional Chinese medicine for different conditions. Studies on the plant have determined that curcumin has antimicrobial, antioxidant, anti-inflammatory, antiangiogenic, antiplatelet, and antimutagenic properties. These properties have preventive and protective abilities against various diseases such as autoimmune, neurological, metabolic, liver, lung, and cardiovascular.

Studies on curcumin’s physical, organic, and inorganic chemistry have established that the substance acts through various mechanisms; this knowledge has been used to develop nutraceuticals and curcumin-based therapeutic agents. The studies showed that curcumin could react with free radicals, form, and break down nonconjugated substances in the body. Curcumin has been established to be effective in treating lifestyle and chronic illnesses through its pharmacological and chemo-preventive abilities. It has also been used in traditional Indian medicine to expulse gas, strengthen the body’s energy, alleviate arthritis, improve digestion, and dissolve gall stones. In modern medicine, it has been used to heal wounds, stimulate the immune system, and decelerate aging.

Curcumin has been used in the Jiawei-Xiaoyao, a Chinese traditional treatment system, to treat several diseases such as stress, depression, and dyspepsia for thousands of years now. It has also been established that it is effective in treating neurological disease, cardiovascular disease, and other inflammatory diseases. It is also hypothesized to be effective against the pathogenesis of molecular targets to treat and prevent diseases. The modulation of the molecular targets has a role in the development of the disease. Curcumin has been shown to play vital roles in regulating cytokines, kinases, growth factors, metastatic, receptors, and apoptotic molecules in most phases during most diseases’ development. The curcumin structure’s inclination increases its free radical scavenging activities to low-level hydrogenation and a high level of methoxylation. The structure additionally enables the curcumin to have antioxidant, anticancer, and anti-inflammatory effects.

Elderberry (*Sambucus nigra*)

This flowering plant belongs to the Adoxaceae family and is used as a supplement to treat flu and cold symptoms. The berries of this plant contain anthocyanin that has been shown to possess powerful antioxidant properties. Its therapeutic use has effectively treated obesity, influenza, upper respiratory infection, metabolic syndrome, gingival

recession, and hyperlipidemia. The flowers and the plant’s berries contain antibacterial, antioxidant, glucose-lowering anti-inflammatory, and immune-modulating properties. It can be used alone or combined with other agents to treat various health conditions.

The elderberry is an excellent source of free and conjugated amino acids, proteins, fiber fractions, vitamins, antioxidants, and unsaturated fatty acids. Its study shows biological activity elements, primary polyphenols, proanthocyanidins, phenolic acids, and flavonols. The presence of phenols makes the elderberry an ideal medicine and has high antioxidant properties.

Studies established that the processing and storage of the products derived from the elderberry altered the amounts of polyphenols. When fresh fruits are blanched, their composition of polyphenols is decreased, while the anthocyanin content increases; this phenomenon has also been observed in the juices. In the first 30 days, polyphenols decreased by around 40%. In the subsequent days, the amount remained unchanged. Wine from the elderberry showed that anthocyanin content decreased while the flavanols and phenolic acids rose. However, the flavonols and phenolic acids from the plant were relatively stable during the 21-month storage time. These amounts of the content often remain higher in the presence of glucose but lower in ascorbic acid and fructose.

The elderberry has been used in folk medicine to treat many ailments and diseases. It has been heavily applied in managing respiratory infections, mainly in colds and cases of flu, but also in dislocations, burns, skin rashes, hemorrhoids, stings, insect bites, and swellings, among others. Traditional medicine recommends the utilization of the elderberry to manage respiratory illnesses such as cold and catarrh, influenza. It is also a laxative, anti-inflammatory, diuretic, and diaphoretic agent. Its components tackle the levels of reactive oxygen species in the body, reactive chlorine species, and reactive nitrogen species through its antioxidant activity.

A diet consisting of elderberry fruits is likely to be a potential protective agent against the unwanted effects of oxidative stress on the body and growth. The antioxidant activities are exhibited by the elderberry’s extract, it scavenges hydroxyl radicals and 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) while inhibiting the lipid peroxidation in the linoleic acid emulsion. Nitric oxide radicals have also been effectively scavenged by the extracts. The elderberry extracts stimulated the secretion of proinflammatory cytokines IL-1 β , IL-6, IL-8, and TNF- α (tumor necrosis factor) and cytokine IL-10. It increased the production of IFN- β interferon associated with upregulation of TLR-3 (toll-like receptor 3). Elderberry-derived polyphenols caused a 50% decrease in the levels of IL-1 β that is responsible for the long-term inflammation in chronic illnesses. The elderberry also can increase the number of lymphocytes in the body.

The consumption of the elderberry is considered safe if it is eaten when cooked and consumed moderately. It is dangerous to consume it uncooked because of the potential cyanide toxicity. The intake should be cautiously monitored in diabetic patients to promote glucose and insulin metabolism. Some of the side effects that have been reported upon its use include nausea and vomiting, hypokalemia, dehydration, tachycardia, hypotension, and diarrhea⁴¹⁻⁴⁸.

Glutathione

This is an endogenous peptide that possesses both metabolic and oxidative properties. It has been used to prevent neurotoxicity induced by oxaliplatin and cisplatin. It has also been used to prevent other adverse effects caused by radiation therapy and antineoplastic agents and other disorders like poisoning by heavy metals and other elements, corneal disorders, eczema, and liver disorders. Furthermore, glutathione has been employed to treat peripheral vascular disorders and idiopathic pulmonary fibrosis. It is a vital extracellular antioxidant of the lungs, and there is a high concentration of the substance in the epithelial lining fluid of the lungs. It has been shown that a deficiency of glutathione can contribute to the damage of the epithelial lining that is witnessed in different lung disorders. Patients with idiopathic pulmonary fibrosis and cystic fibrosis treated with glutathione had better results over time.

Two cytosolic enzymes, glutamylcysteine glutamate and GSH synthetase, catalyze glutathione synthesis from cysteine, glycine, and glutamate. Feedback inhibition, availability of cysteine, and enzyme activity have all been shown to affect glutathione synthesis. The role of substances in the metabolism of nutrients, defense against free radicals, and regulation of cellular events are all vital for the body. Deficiency of the substance leads to oxidative stress that plays a role in aging and the pathogenesis of many other illnesses such as liver disease, parkinsonism, Alzheimer's disease, and sickle cell anemia, among others.

There is a panoply of the roles played by glutathione in the body. First, it helps to get rid of free radicals and other reactive species of oxygen from the body directly and indirectly via enzymatic actions. The GSH is oxidized to GSSG and then reduced to GSH by NADPH-dependent glutathione reductase. Glutathione peroxidase catalyzes GSH reduction of hydrogen peroxide and other peroxides. Secondly, GSH reacts with several electrophiles and physiological metabolites such as prostaglandins, leukotrienes, melanins, and estrogen to form mercapturates. Glutathione-S-transferase initiates these reactions. The substance also conjugates with nitrogen oxide to form an S-nitrosoglutathione adduct cleaved by thioredoxin to release NO and GSH. NO and GSH are vital in the hepatic action of insulin-sensitizing agents that regulate the utilization of amino acids, glucose, and lipids. GSH serves as a substrate for formaldehyde dehydrogenase that converts GSH and formaldehyde to form S-formyl-glutathione. Formaldehyde is a carcinogen, and its removal from the body, is of great

physiological importance as it is produced from the metabolism of choline, methanol, sarcosine, xenobiotics, and methionine.

It is required to convert prostaglandin H₂ to prostaglandin D₂ and E₂ catalyzed by Endoperoxide isomerase. It is also involved in the glyoxalase system that converts methylglyoxal to D-lactate, a pathway often presents in microorganisms. Due to the vital role of glutathione in the body, adequate concentrations are essential for the proliferation of the cells, including the intestinal epithelial cells and lymphocytes. It is also involved in the process of spermatogenesis in males and the maturation of sperms. Similarly, glutathione is important in activating T-lymphocytes and polymorphonuclear leukocytes and the production of cytokines to mount immune responses against foreign pathogens. Since GSH affects the oxidative, which is an important aspect of the disease process, it can prevent ferocious effects induced by the produced chemicals.

3. Medical Mushrooms

Edible mushrooms are known for their nutritional properties, therapeutic potential, and biological activities. They have emerged as important sources of compounds demonstrating antitumor, antioxidant, and antimicrobial properties. Its bioactive properties enable them with an antioxidant capacity to prevent diseases related to increased oxidative stress and the formation of free radicals. The antimicrobial activities of the compounds and extracts from the mushrooms have been well documented over the years. The use of medical mushrooms has a long tradition in Asian countries. Medicinal compounds from the mushrooms are extracted in multiple ways, through cultivation in the farms or collection from the wild. The fruiting bodies of the mushroom are harvested, or the mycelium is cultivated in the fermenters with solid or liquid substrates.

The mushrooms have been an important therapeutic raw material in folk medicine; for instance, the reishi mushroom (*Ganoderma lucidum*) was regarded as a panacea in traditional Chinese medicine. The therapeutic effects of the traditionally used species have been corroborated with modern research. The species used for food have good amounts of carbohydrates; their structure has chitin that fills the dietary role. They also have large amounts of proteins that contain essential amino acids and may be alternated with animal products. They have low-fat content making them a good source with low calories, but they have adequate stores of polyunsaturated fatty acids (PUFAs) which present many health benefits to the body. The medicinal and dietary uses of the edible mushrooms are supported by the fact that they contain numerous health-promoting and biologically active compounds. They have secondary metabolites that have a range of benefits, such as antiviral, antibacterial, antioxidative, anticancer, the ability to improve the functioning of the cardiovascular system, and anti-inflammatory properties. The most profound application of medical mushrooms is to prevent inflammation.

The glucans and the chitosans have shown antilipemic effects as they decrease the LDL cholesterol levels and the absorption of fat in the gut. They also regulate glycemia; therefore, they prevent the development of obesity, diabetes, and cardiovascular diseases. The β -Glucans, usually contained in the Basidiomycota species, are the biological response modifiers because of their broad-spectrum activities in the immune system. Additionally, they have antioxidant properties, decrease carcinogenic elements' metabolite levels, and prevent DNA damage. They have also been shown to play a role in producing anti-inflammatory and pro-inflammatory cytokines in the body. They have a high binding affinity to the surface of the immune cell receptors with the pattern recognition receptors in the form of pathogen-associated patterns of molecules. Such receptors include dectins-1, toll-like receptors, and complementary receptor 3. Thus, the immune cells' maturation and proliferation, stimulation, and activation of the natural killer cells and the macrophages can be activated by β -glucans. Lentinan from the Lentinula species is one of the most typical β -glucan and has been used for a long in the medical realm.

Lectins contained in medical mushrooms can bind selectively with the membrane carbohydrates of different types of cells, playing an important role in the regulation of the immune system. They promote the process of adhesion of cells, and some of them have been shown to activate the lymphocytes, while others have strong anti-proliferative properties. Lectins that have been extracted from the mushrooms have been established as inhibiting the proliferation of tumor cells, especially in breast cancer, without inducing any toxicity. It has also been tested for use in treating psoriasis, eye disorders, especially glaucoma and diabetes.

The fatty acids of the mushrooms can support human anti-inflammatory processes due to their high composition of unsaturated fatty acids. The PUFAs are precursors of eicosanoids which play a role as signaling molecules necessary for cellular response regulation in the muscles, nerve cells, the immune system, and the blood vessels. They maintain an equilibrium between the anti-inflammatory and inflammatory responses. Therefore, having an adequate supply of fatty acids in the diet helps prevent cardiovascular diseases. α -Linolenic acid (ALA) has been an essential component for normal health and basic nutrition; it is a precursor of long-chained PUFAs. It also has potent anti-inflammatory activities.

Dried edible mushrooms contain high levels of vitamin C, folic acid, thiamine, niacin, and relatively low amounts of α -tocopherol, riboflavin, and β -carotene. Dietary deficiency of folic acids is a common problem; therefore, these diets can be supplemented with edible mushrooms. The mushroom species are also excellent sources of tocopherols and carotenoids. These compounds have powerful anti-inflammatory and anticancer protection of the body. They also inhibit cellular membranes from peroxidation. The carotenoids are very vital for the normal functioning of the eyes with an added role as powerful antioxidants.

Astaxanthin

Astaxanthin pigment belongs to the xanthophylls family, the oxygenated carotenoid derivatives from the plants by lycopene synthesis. It is one of the major components included in the feeds of crustaceans and salmonids. The main role of the pigment is to provide a desirable reddish color to the organisms reared, as most of them do not have access to natural carotenoids.

Andrographis paniculata

Andrographis paniculata, commonly referred to as creat or green chiretta plant has been used as a medicinal food for many centuries now. The roots and leaves of the plants have been used for various medicinal purposes in Asia and Europe. It has been used for medicine because of its 'cold property' to remove heat and expel toxins from the body. It is being used to stimulate the immune system and manage myocardial ischemia, respiratory tract infections, and pharyngotonsillitis in modern medicine. It also contains anti-inflammatory, anti-microbial and anti-hyperglycemic, anti-sclerosis, antiplatelet, anticancer, choloretic, and anti-hyperglycemic properties. Its leaves and stems contain active phytochemicals such as flavonoids and diterpenoids.

The major constituent of the plant is andrographolide (a labdane diterpenoid) and has been used as an herbal medicine in Asia for a long time. It has beneficial effects against virus infection, bacteria dysentery, fever, laryngitis, herpes, and rheumatoid arthritis. The compound protects the body against inflammation by binding to the adenosine A2A receptor, inducing the nuclear factor, subsequently inactivating GSK3 β , which causes the upregulated expression of heme oxygenase 1. The process regulates the body against oxidative stress from diseases like diabetes, neurodegenerative diseases, and osteoporosis.

A. paniculata mitigates the extension of inflammation of the intestine in colitis induced by transfer of naïve T cells. It does this by affecting the early proliferation and differentiation of the T cells. Additionally, it decreases cytokine expression and splenic cell counts and CD4+ IFN- γ + T cells within 4–7 weeks of undergoing treatment. The active compound of *A. paniculata* has been shown to protect the body against infectious agents that destroy the central nervous system. In the process of a CNS disease, the immune responses that protect the body may turn against the host leading to death and morbidity. The plant can prevent the anti-nociceptive activity on hyperalgesia caused by nitroglycerine administration by inhibiting the action of interleukin 6 (IL-6) in the cerebrum and the expression of TNF- α mRNA in the mesencephalon only.

Andrographolide can decrease the LPS-induced expression of the cortical C-X-C and C-C subfamily chemokine in vivo. It can also decrease inflammation of the astrocytes and oxidative stress by mediating the out of the cell signal-regulated kinase and Nrf2-p38-MAPK signaling pathways in the primary astrocytes. Regulating the p38-MAPK signaling pathway can protect the MCAO-induced brain injury. It is also involved in suppressing the generation of

free radicals, brain infarction, and the blood-brain barrier disruption. It has also shown tremendous benefits in Alzheimer's diseases; patients prescribed with andrographolide recover spatial memory, learning performance, and synaptic basal transmission. The compound has also shown neuroprotection on the regulation of the synaptic proteins, reduction of the phosphorylated tau proteins, and the maturation of the amyloid-beta aggregate in the aged degus.

Propolis

This is a resinous material well known and collected by the bees from the plant exudates and the buds. It is mixed with the wax, the pollen, and the bee enzymes. The bees use it in smoothening the out internal walls, carver the carcasses of the intruders in the hive to prevent them from decomposing, and sealing the holes present in the honeycombs. Due to its antimicrobial and antiseptic properties, it protects the colonies of bees from infection. Since antiquity, propolis has been used by different civilizations to manage colds, ulcers, and wounds because of its local anesthetic and antiseptic properties. It was used to embalm the death by the Egyptians and recently in the Boer War to regenerate the tissues and heal wounds. Its uses have also been applied in contemporary medicine owing to its anti-inflammatory, antioxidant, antitumor, and immune-modulatory activities. Its chemical and biological compositions have been studied to gain more insight into it.

Probiotics

Probiotics are living nonpathogenic microorganisms taken to maintain microbial balance, especially in the gastrointestinal tract. They are composed of *Saccharomyces boulardii* yeast or lactic acid bacteria such as *Bifidobacterium* and *Lactobacillus* species, usually through diet supplements and foods. They exert their beneficial effects via various mechanisms like lowering the pH of the intestines, preventing and decreasing invasion by pathogenic organisms, and modifying the hosts' immune response.

Quercetin

Quercetin is an aglycon flavonoid and is widely found in various fruits, plants, medicinal plants including apples, wild berries, brassica vegetables, tea, as well as in many seeds, nuts, Ginkgo biloba and elderberry, etc⁴⁷⁻⁴⁹. It is an auxin transport inhibitor and reported to exhibit useful pharmacological properties such antioxidant, antiprotozoal, anticancer, antiviral, anti-inflammatory, immunoprotective, antidiabetic, etc.

4. Conclusion

The Plants, herbs, and ethnobotanicals have been used since the early days of humankind and are still used throughout the world for health promotion and treatment of disease. Plants and natural sources form the basis of today's modern medicine and contribute largely to the commercial drug preparations manufactured today. About 25% of drugs prescribed worldwide are derived from plants. Still, herbs, rather than drugs, are often used in health care. For some,

herbal medicine is their preferred method of treatment. For others, herbs are used as adjunct therapy to conventional pharmaceuticals. However, in many developing societies, traditional medicine of which herbal medicine is a core part is the only system of health care available or affordable. Regardless of the reason, those using herbal medicines should be assured that the products they are buying are safe and contain what they are supposed to, whether this is a particular herb or a particular amount of a specific herbal component. Consumers should also be given science-based information on dosage, contraindications, and efficacy⁴⁹⁻⁵².

Since the dawn of human civilization, human beings have found remedies within their habitat and have adopted different therapeutic strategies depending upon climatic, phytogeographic, sociocultural, floral, and faunal characteristics. Traditional systems thus contain beliefs and practices in order to avoid, prevent, or avert ailments, which constitute traditional preventive medicine⁵³⁻⁵⁴. The use of medicinal herbs and herbal medicine is an age-old tradition and the recent progress in modern therapeutics has stimulated the use of natural product worldwide for diverse ailments and diseases. The educated public and health care professionals have enormous interests in the medicinal uses of herbs, but there is a great deal of confusion about their identification, effectiveness, therapeutic dosage, toxicity, standardization, and regulation. According to WHO, traditional medicine is popular in all regions of the world and its use is rapidly expanding even in developed countries.

5. References

- [1] Shingina A, Mukhtar N, Wakim-Fleming J, Alqahtani S, Wong RJ, Limketkai BN, et al. Acute Liver Failure Guidelines. *Am J Gastroenterol*, 2023, 118(7), 1128-1153.
- [2] Trey C, Davidson CS. The management of fulminant hepatic failure. *Prog Liver Dis*, 1970, 3, 282-298.
- [3] European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; Clinical practice guidelines panel; Wendon, J; Panel members; Cordoba J, Dhawan A, Larsen FS, et al; EASL Governing Board representative; Bernardi M. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. *J Hepatol*, 2017, 66(5), 1047-1081.
- [4] O'Grady JG, Schalm SW, Williams R. Acute liver failure: redefining the syndromes [published correction appears in *Lancet* 1993, 342(8877):1000]. *Lancet*, 1993, 342(8866), 273-275.
- [5] Lee WM, Stravitz RT, Larson AM. Introduction to the revised American Association for the Study of Liver Diseases Position Paper on acute liver failure 2011. *Hepatology*, 2012, 55(3), 965-967.
- [6] McPhail MJ, Wendon JA, Bernal W. Meta-analysis of performance of King's College Hospital Criteria in prediction of outcome in non-

- paracetamol-induced acute liver failure. *J Hepatol*,2010, 53(3), 492-499.
- [7] Acharya SK, Dasarathy S, Kumer TL, et al. Fulminant hepatitis in a tropical population: clinical course, cause, and early predictors of outcome. *Hepatology*,1996, 23(6), 1448-1455.
- [8] Acharya SK. Acute Liver Failure: Indian Perspective. *Clin Liver Dis* (Hoboken),2021, 18(3), 143-149.
- [9] Freeman RB Jr, Steffick DE, Guidinger MK, Farmer DG, Berg CL, Merion RM. Liver and intestine transplantation in the United States, 1997-2006. *Am J Transplant*,2008, 8(4 Pt 2), 958-976.
- [10] Campsen J, Blei AT, Emond JC, Everhart JE, Freise CE, Lok AS, et al. Outcomes of living donor liver transplantation for acute liver failure: the adult-to-adult living donor liver transplantation cohort study. *Liver Transpl*,2008, 14(9), 1273-1280.
- [11] Bernal W, Auzinger G, Dhawan A, Wendon J. Acute liver failure. *Lancet*, 2010, 376(9736), 190-201.
- [12] Chalasani N, Fontana RJ, Bonkovsky HL, et al. Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. *Gastroenterology*,2008, 135(6), 1924-1934.e19344.
- [13] Koch DG, Tillman H, Durkalski V, Lee WM, Reuben A. Development of a Model to Predict Transplant-free Survival of Patients With Acute Liver Failure. *Clin Gastroenterol Hepatol*,2016, 14(8), 1199-1206.e2.
- [14] Bernal W, Lee WM, Wendon J, Larsen FS, Williams R. Acute liver failure: A curable disease by 2024? *J Hepatol*,2015, 62(1 Suppl),S112-S120.
- [15] McElroy LM, Daud A, Davis AE, Lapin B, Baker T, Abecassis MM, et al. A meta-analysis of complications following deceased donor liver transplant. *Am J Surg*,2014, 208(4), 605-618.
- [16] Bernal W, Hyrylainen A, Gera A, Audimoolam VK, McPhail MJ, Auzinger G, et al. Lessons from look-back in acute liver failure? A single centre experience of 3300 patients, *J Hepatol*, 2013, 59(1), 74-80.
- [17] Craig DG, Bates CM, Davidson JS, Martin KG, Hayes PC, Simpson KJ. Staggered overdose pattern and delay to hospital presentation are associated with adverse outcomes following paracetamol-induced hepatotoxicity. *Br J Clin Pharmacol*, 2012, 73(2), 285-294.
- [18] Katoonizadeh A, Laleman W, Verslype C, Wilmer A, Maleux G, Roskams T, et al. Early features of acute-on-chronic alcoholic liver failure: a prospective cohort study. *Gut*,2010, 59(11), 1561-1569.
- [19] The Risk of Bias in Non-Randomized Studies – of Interventions (ROBINS-I) assessment tool [Internet][Updated Aug 2016]. Available from: <https://www.riskofbias.info/welcome/home/current-version-of-robins-i/robins-i-tool-2016>. Accessed on Dec 15, 2023.
- [20] Revised Cochrane risk-of-bias tool for randomized trials (RoB2)[Internet][Updated Aug 2019]. Available from: <https://www.riskofbias.info/welcome/rob-2-0-tool/current-version-of-rob-2>. Accessed on Dec 15, 2023.
- [21] Barshes NR, Lee TC, Balkrishnan R, Karpen SJ, Carter BA, Goss JA. Risk stratification of adult patients undergoing orthotopic liver transplantation for fulminant hepatic failure. *Transplantation*,2006, 81(2), 195-201.
- [22] Rajekar H, Wai CT, Majeed TA, Lee KH, Wong SY, Leong SO, et al. Prognostic factors in patients with acute liver failure undergoing live donor liver transplantation. *Transplant Proc*,2008, 40(8), 2492-2493.
- [23] Bernal W, Cross TJ, Auzinger G, Sizer E, Heneghan MA, Bowles M, et al. Outcome after wait-listing for emergency liver transplantation in acute liver failure: a single centre experience. *J Hepatol*,2009, 50(2), 306-313.
- [24] Park SJ, Lim YS, Hwang S, Heo NY, Lee HC, Suh DJ, et al. Emergency adult-to-adult living-donor liver transplantation for acute liver failure in a hepatitis B virus endemic area. *Hepatology*,2010, 51(3), 903-911.
- [25] Yuan D, Liu F, Wei YG, Li B, Yan LN, Wen TF, et al. Adult-to-adult living donor liver transplantation for acute liver failure in China. *World J Gastroenterol*,2012, 18(48), 7234-7241.
- [26] Germani G, Theocharidou E, Adam R, Karam V, Wendon J, O'Grady J et al. Liver transplantation for acute liver failure in Europe: outcomes over 20 years from the ELTR database. *J Hepatol*,2012, 57(2), 288-296.
- [27] Urrunaga NH, Rachakonda VP, Magder LS, Mindikoglu AL. Outcomes of living versus deceased donor liver transplantation for acute liver failure in the United States. *Transplant Proc*,2014, 46(1), 219-224.
- [28] O'Grady JG, Alexander GJ, Hayllar KM, Williams R. Early indicators of prognosis in fulminant hepatic failure. *Gastroenterology*,1989, 97(2), 439-445.
- [29] Adam R, Cailliez V, Majno P, Karam V, McMaster P, Caine RY, et al. Normalised intrinsic mortality risk in liver transplantation: European Liver Transplant Registry study [published correction appears in *Lancet* 2001 Apr 21;367(9264):1296]. *Lancet*. 2000, 356(9230), 621-627.
- [30] Pamecha V, Vagadiya A, Sinha PK, Sandhyav R, Parthasarathy K, Sasturkar S, et al. Living Donor Liver Transplantation for Acute Liver Failure: Donor Safety and Recipient Outcome. *Liver Transpl*,2019, 25(9), 1408-1421.

- [31] Yang HR, Thorat A, Jeng LB, Hsu SC, Li PC, Yeh CC, et al. Living Donor Liver Transplantation in Acute Liver Failure Patients with Grade IV Encephalopathy: Is Deep Hepatic Coma Still an Absolute Contraindication? A Successful Single-Center Experience. *Ann Transplant*, 2018, 23, 176-181.
- [32] Sars C, Tranäng M, Ericzon BG, Berglund E. Liver transplantation for acute liver failure - a 30-year single centre experience. *Scand J Gastroenterol*, 2018, 53(7), 876-882.
- [33] Mehrotra S, Mehta N, Rao PS, Lalwani S, Mangla V, Nundy S. Live donor liver transplantation for acute liver failure: A single centre experience. *Indian J Gastroenterol*, 2018, 37(1), 25-30.
- [34] Farmer DG, Anselmo DM, Ghobrial RM, et al. Liver transplantation for fulminant hepatic failure: experience with more than 200 patients over a 17-year period. *Ann Surg*, 2003, 237(5), 666-676.
- [35] Simpson KJ, Bates CM, Henderson NC, Wigmore SJ, Garden OJ, Lee A, et al. The utilization of liver transplantation in the management of acute liver failure: comparison between acetaminophen and non-acetaminophen etiologies. *Liver Transpl*, 2009, 15(6), 600-609.
- [36] Wigg AJ, Gunson BK, Mutimer DJ. Outcomes following liver transplantation for seronegative acute liver failure: experience during a 12-year period with more than 100 patients. *Liver Transpl*, 2005, 11(1), 27-34.
- [37] Yamashiki N, Sugawara Y, Tamura S, Nakayama N, Oketani M, Umeshita K, et al. Outcomes after living donor liver transplantation for acute liver failure in Japan: results of a nationwide survey. *Liver Transpl*. 2012, 18(9), 1069-1077.
- [38] Mendizabal M, Tagliafichi V, Rubinstein F, Rojas P, Marciano S, Yantorno S, et al. Liver transplantation in adults with acute liver failure: Outcomes from the Argentinean Transplant Registry. *Ann Hepatol*, 2019, 18(2), 338-344.
- [39] Ikegami T, Taketomi A, Soejima Y, Yoshizumi T, Sanefuji K, Kayashima H, et al. Living donor liver transplantation for acute liver failure: a 10-year experience in a single centre. *J Am Coll Surg*, 2008, 206(3), 412-418.
- [40] Mallick S, Nair K, Thillai M, Manikandan K, Sethi P, Madhusrinivasan D, et al. Liver Transplant in Acute Liver Failure - Looking Back Over 10 Years. *J Clin Exp Hepatol*, 2020, 10(4), 322-328.
- [41] Ostapowicz G, Fontana RJ, Schiødt FV, Larson A, Davern TJ, Han SH, et al. Results of a prospective study of acute liver failure at 17 tertiary care centres in the United States. *Ann Intern Med*, 2002, 137(12), 947-954.
- [42] Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. *Hepatology*, 2010, 52(6), 2065-2076.
- [43] Larson AM, Polson J, Fontana RJ, Davern TJ, Lalani E, Hynan LS, et al. Acetaminophen-induced acute liver failure: results of a United States multicenter, prospective study. *Hepatology*, 2005, 42(6), 1364-1372.
- [44] Matsui Y, Sugawara Y, Yamashiki N, Kaneko J, Tamura S, Togashi J, et al. Living donor liver transplantation for fulminant hepatic failure. *Hepatol Res*, 2008, 38(10), 987-996.
- [45] Escorsell A, Mas A, de la Mata M; Spanish Group for the Study of Acute Liver Failure. Acute liver failure in Spain: analysis of 267 cases. *Liver Transpl*, 2007, 13(10), 1389-1395.
- [46] Lee SG, Ahn CS, Kim KH. Which types of graft to use in patients with acute liver failure? (A) Auxiliary liver transplant (B) Living donor liver transplantation (C) The whole liver. (B) I prefer living donor liver transplantation. *J Hepatol*, 2007, 46(4), 574-578.
- [47] Russo MW, Galanko JA, Shrestha R, Fried MW, Watkins P. Liver transplantation for acute liver failure from drug-induced liver injury in the United States. *Liver Transpl*, 2004, 10(8), 1018-1023.
- [48] Uemoto S, Inomata Y, Sakurai T, Egawa H, Fujita S, Kiuchi T, et al. Living donor liver transplantation for fulminant hepatic failure. *Transplantation*, 2000, 70(1), 152-157.
- [49] Serrano MT, Sabroso S, Esteban LM, Berenguer M, Fondevila C, Lorente S, et al. Mortality and Causes of Death After Liver Transplantation: Analysis of Sex Differences in a Large Nationwide Cohort. *Transpl Int*, 2022, 35:10263.
- [50] Reddy KR, Ellerbe C, Schilsky M, Stravitz RT, Fontana RJ, Durkalski V, et al. Determinants of outcome among patients with acute liver failure listed for liver transplantation in the United States. *Liver Transpl*, 2016, 22(4), 505-515.
- [51] Fontana RJ, Ellerbe C, Durkalski VE, Rangnekar A, Reddy RK, Stravitz T, et al. Two-year outcomes in initial survivors with acute liver failure: results from a prospective, multicentre study. *Liver Int*, 2015, 35(2), 370-380.
- [52] Ghelichi-Ghojogh M, Rajabi A, Mohammadzadeh F, Shojaie L, Vali M, Afrashteh S, et al. Survival Rate of Liver Transplantation in Asia: A Systematic Review and Meta-Analysis. *Iran J Public Health*, 2022, 51(10), 2207-2220.