



Received on 28 September 2021; received in revised form, 20 July 2022; accepted 10 August 2022; published 01 September 2022

## NUTRACEUTICAL APPROACH TO NON-ALCOHOLIC FATTY LIVER DISEASE: A REVIEW

Bhawna Sharma, Ritu Sanwal\* and Sanjay Singh

Department of Pharmacology, Siddhartha Institute of Pharmacy, Near IT Park, Sahastradhara Road, Dehradun - 248013, Uttarakhand, India.

### Keywords:

Nutraceuticals, Dietary supplements, NAFLD, Clinical parameters

### Correspondence to Author:

**Mrs. Ritu Sanwal**

Assistant Professor,  
Department of Pharmacology,  
Siddhartha Institute of Pharmacy,  
Near IT Park, Sahastradhara Road,  
Dehradun - 248013, Uttarakhand,  
India.

**E-mail:** sanwalritu4@gmail.com

**ABSTRACT:** Nutraceutical is employed to explain a medicinal or nutritional component with a food, plant, or natural material that will be purified or concentrated. It is used to improve health by preventing or treating disease. Non-alcoholic fatty liver disease (NAFLD) is a clinical condition characterized by lipid infiltration of the liver with a high prevalence in the general population affecting 25% of adults with a double prevalence in diabetic and obese patients. Nearly 1/3 of NAFLD progresses to non-alcoholic steatohepatitis (NASH), leading to liver fibrosis and cirrhosis. There are currently no specific drugs approved on the market to treat NAFLD. So the treatment is essentially based on lifestyle optimization. However, some nutraceuticals may contribute to developing liver lipid infiltration and related anthropometric, haemodynamic and/or biochemical parameters. The objective of this article is to review the available clinical data on the effect of nutraceuticals on NAFLD and other parameters related to NAFLD. There are relatively few nutraceutical molecules that are adequately studied for their effects on NAFLD and other related diseases. Among them, we have analyzed the effects of nutrients, vitamins, minerals, different bacteria, food supplements, and other nutraceuticals such as carnitine, omega-3 fatty acids, silymarin, and resveratrol. In conclusion, vitamins (such as E and D), silymarin, and omega-3 fatty acids if administered well and for medium to long periods and associated with lifestyle changes that could have positive effects on NAFLD and their related parameters.

**INTRODUCTION:** Lifestyles have changed dramatically in the last 50 years due to urbanization, industrialization speed, and rapid change. These things have changed people's habits and forced them to eat fast, fast and tasty food, fast food, and junk food. These habits directly affect our aspect of healthy eating and gradually reduce the amount and quality of nutrients.

As a result of these changed eating habits, the population has increased the incidence of malnutrition, dementia and degenerative diseases. In recent years, people have become more concerned about health and more concerned about health care. Over the past two decades, changes in medicine, phytomedicine, health science, the food industry and health care have attracted widespread attention among health professionals and the public.

Significant advances have been made in nutraceuticals, food products, and phytonutrients. It is a good idea for pharmaceutical companies to be healthy and to prevent disease and treatment. Ayurvedic treatment regimens depend directly on

<p><b>QUICK RESPONSE CODE</b></p> 	<p><b>DOI:</b> 10.13040/IJPSR.0975-8232.13(9).3411-24</p> <hr/> <p>This article can be accessed online on <a href="http://www.ijpsr.com">www.ijpsr.com</a></p> <hr/> <p>DOI link: <a href="http://dx.doi.org/10.13040/IJPSR.0975-8232.13(9).3411-24">http://dx.doi.org/10.13040/IJPSR.0975-8232.13(9).3411-24</a></p>
---	---

the life of Aahar and Vihaar. Ahirwar is regarded as food and ancient medicine. The concept of Rasayana (re-healing) is widespread in Ayurveda and, in addition to current nutraceuticals <sup>1</sup>.

**Nutraceuticals:** The term "nutraceutical" comes from "nutrition" and "pharmaceutical". It is defined as a diet or part of a diet that provides health benefits of nutritious foods and helps prevent many diseases <sup>2, 3</sup>. Chemicals are natural compounds in our diet by the standards of healthy foods, such as minerals, vitamins, fatty acids, and polysaccharides. Many natural food sources such as fruits, dairy products, vegetables, and poultry contain all the important nutrients in our diet.

For this reason, these nutrients are used to treat and prevent many diseases such as heart disease, diabetes, cancer, osteoporosis, obesity, osteoarthritis and many other diseases. These nutrients contain many water-soluble minerals, antioxidants, fats and vitamins extracted from our diet and are helpful in many of our health problems <sup>4</sup>.

**Reasons for Shift towards Nutraceuticals:**

- ❖ Increase the number of consumers who are concerned about the cost of healthcare.
- ❖ Dissatisfied with medical agents in promoting health. They turn to medication to improve their health and prevent chronic diseases.
- ❖ Healthcare professionals note that our supply of highly processed foods derived from plants grown with chemical fertilizers, pesticides, herbicides, and genetically modified seeds lacks the nutrients needed for good health.
- ❖ People do not believe in prevention more than in healing.

- ❖ Peoplesufferfromchronicdiseasesandhavenotfoundasolutiontoallopathical medicine.
- ❖ Patients with financial problems <sup>5</sup>.

**Benefits of Nutraceuticals:** There are various benefits of nutraceuticals which are given below;

- It can increase the value of our healthy food.
- It can help us to live longer.
- It can help us avoid certain medical conditions.
- You can gain psychological benefits by doing something for yourself.
- It can be seen as more "natural" than traditional medicine and is less likely to cause side effects.
- It is possible to introduce foods for people with special needs (for example, nutritious foods for the elderly).
- It can be easily obtained and inexpensive <sup>6</sup>.
- Reduce the spread and duration of infectious and viral diarrhea.
- Reduce inflammation and symptoms associated with intestinal illness.
- It has protective effects to prevent colon cancer.
- It improves the availability of bioavailability and absorption of minerals such as calcium, magnesium, and possible iron.
- Reduce other risk factors for heart disease.
- It promotes saturation and weight loss and prevents obesity <sup>7</sup>.

**Classification of Nutrients and Minerals as Nutraceuticals:** The classification of nutrients and minerals as nutraceuticals along with their health benefits are given below;

**TABLE 1: NUTRIENTS AND THEIR HEALTH BENEFITS**

Nutrients	Health benefits	References
Vitamin A	Antioxidant, are necessary for growth and development, maintain healthy vision, skin and mucous membranes, and help in the prevention and treatment of certain cancers and skin disorders	8
Vitamin D	Vital for the formation of bones and teeth, helps to body absorb and use calcium, regulates calcium and phosphate absorption	9
Vitamin E	Antioxidant helps in forming blood cells, muscles, lung, and nerve tissue boosts the immune system	10
Vitamin K	Essential for clotting of blood	8
Vitamin C	Antioxidant, and anti-inflammatory nutrients, are important in wound healing and preventing the common cold	11
Vitamin B1	Helps in conversion of food into energy and is essential in neurologic functions	12

Vitamin B2	Helps in the production of energy and other chemical processes in the body, and helps in maintaining healthy eyes, skin, and nerve function	12
Vitamin B3	Helps to convert food into energy and maintain proper brain functioning	13
Vitamin B6	Helps to produce essential proteins and convert protein into energy	7
Vitamin B12	Helps to produce the genetic material of cells, helps in the formation of red blood cells, maintains of central nervous system and synthesizes amino acids and is involved in the metabolism of fats, protein and carbohydrates	14
Folic acid	Produce the genetic materials of cells, essential in first three months of pregnancy for preventing birth defects, RBCs formation, protects against heart disease	15
Pantothenic acid	Aids in the synthesis of cholesterol, steroids and fatty acids, crucial for the intraneuronal synthesis of acetylcholine	7
Amino acid, Tryptophan, Tiramine, Glutamine, Arginine, Cysteine, Caffeine	Hypnotic and sedating effect, Memory improvement, Recuperation of mental fatigue, Stimulation of immune system, Slowdown of the aging process, Stimulation of the central nervous system	16

**TABLE 2: MINERALS AND THEIR HEALTH BENEFITS**

Minerals	Health Benefits	References
Calcium	Essential for building bones and teeth and maintaining bone strength, important in nerve, muscle, and glandular functions	17
Iron	Helps in energy production, and helps to carry and transfer oxygen to tissues.	13
Magnesium	Essential for healthy nerve and muscle function and bone formation, it may help prevent premenstrual syndrome (PMS)	18
Phosphorous	Essential for building strong bones and teeth helps in the formation of genetic material, energy production and storage	13
Zinc	Essential for cell reproduction, normal growth and development in children, wound healing, production of sperm and testosterone	19
Chromium	With insulin helps to convert carbohydrates and fats into energy	7
Cobalt	Essential component of vitamin B12, but ingested cobalt is metabolized in vivo to form the B12coenzymes	7
Copper	Essential for hemoglobin and collagen production, healthy functioning of the heart, energy production, absorption of iron from the digestive tract	7
Iodine	Essential for the proper functioning of the thyroid	7
Selenium	Antioxidant, essential for the healthy functioning of the heart muscle	7

**TABLE 3: DIETARY SUPPLEMENTS AND THEIR HEALTH BENEFITS**

Dietary supplements	Significance	References
Ketogenic diets	Comprised of foods with high fat and low protein and carbohydrate content, they have been reported to improve seizure control. However, these diets are widely acknowledged to be unpalatable	20
Minimally refined grains	Cereals and grains fortified with calcium may reduce the incidence of diabetes and prevents gastrointestinal cancers	12
Phytoestrogens	Found in soya flour and linseeds and have been documented to enhance estrogen levels when hormonal levels are low. This action may prevent against both hot flushes and breast cancer	21
Several species of edible mushrooms	Tonnage, Lentinus, Pleurotus, Auricularia, Flammulina, Tremella, and Grifola have varying degrees of immunomodulatory, lipid-lowering and antitumor without any significant toxicity	22
Glucosamine sulfate and chondroitin sulfate	They are effective and safer to alleviate symptoms of osteoarthritis	23
<b>Peptides/Hydrolysates</b>	Found in casein and whey protein and have A.C.E. inhibitor activity. Buckwheat proteins used as flour reduces cholesterol, hypertension; improve constipation and obesity by acting similar to dietary fibers and interrupting the in-vivo metabolism.	24
<b>Dairy foods</b>	Containing friendly or probiotic bacteria claimed to promote gut health. Bio yogurts containing Lactobacillus acidophilus and Bifidobacteria lead the sector	25

**Classification of Nutraceuticals:** Nutraceuticals are grouped based on their nature and properties, which are given below;

- Chemical constituents.
- Probiotics Microorganisms.

- Nutraceuticals Enzymes.
- Prebiotics.
- Non - traditional nutraceuticals.
- Commercial nutraceuticals.

**A) Chemical Constituents:** It can be divided into nutrients, herbs, and phytochemicals. Phytochemicals plant genes through certain biological functions to support human health, acting in the following ways such as;

- ❖ Substrate for chemical reactions.
- ❖ Cofactors of enzymatic reaction.
- ❖ Inhibitors of enzymatic reaction.
- ❖ Abscesses bind and remove unwanted substances from the intestines.
- ❖ Improves absorption and stability of essential nutrients.
- ❖ Selected growth factor of beneficial bacteria.
- ❖ Substrate fermentation of beneficial bacteria.
- ❖ Selected inhibitors are harmful bacteria in the gut.
- ❖ Active or toxic chemicals.
- ❖ Ligands cause pain or resistance to cell location or intracellular receptors<sup>26</sup>.

**B) Probiotics Microorganisms:** It takes action to remove bacteria such as yeast, other bacteria and

viruses that can cause disease and develop interactions that benefit the human intestinal tract. They have an anti-bacterial effect by altering the microflora, preventing bacterial attachment to the intestinal epithelium, competing with the elements needed to survive the pathogen, producing an antitoxic effect, and eradicating some of the effects of intestinal epithelium infections such as secretion and neutrophils. Probiotics can cure lactose intolerance by producing a specific enzyme ( $\beta$ -galactosidase) that can hydrolyze harmful lactose into its sugar component.

- ❖ In choosing probiotic measurements, safety, operational and technical factors should be considered, as indicated below, as potential health benefits such as.
- ❖ Probiotics must be of human origin.
- ❖ A typical gram-positive environment.
- ❖ It can survive after passing on acid and gallstones.
- ❖ It can attach to human intestinal cells and grow in the intestines.
- ❖ It may show antagonistic action against pathogenic or carcinogenic bacteria.
- ❖ Beneficial clinical outcomes in health care<sup>27</sup>.

**Role of Different Bacteria in the Body:** Different types of bacteria show different health effects, and details about the bacteria are given at the bottom of the table.

**TABLE 4: ROLE OF BACTERIA IN THE BODY AND THEIR BENEFICIAL EFFECTS<sup>5</sup>**

Name of bacteria	Action
<i>L. rhamnosus</i> : (High tolerance to bile salts, surviving in less than favorable environments)	Reduction of viral-associated pulmonary damage, prevention, and reduction of severity of atopic dermatitis in children, Reduction of risk for developing allergic disease, Anti-diabetic potential, Prevention of necrotizing enterocolitis in newborns, prevention or treatment of bacterial vaginosis, Aid in weight loss of obese women, treatment of acute gastroenteritis in children, Reduction of risk for rhinovirus infections in the preterm infant, protection of human colonic muscle from lipopolysaccharide-induced damage
<i>L. acidophilus</i> : ( Present in the lining of the intestine)	Used in the treatment of travellers' diarrhoea, acute diarrhoea, Used in treatment of bacterial vaginosis, Reduction risk of febrile urinary tract infections in children, Reduction of irritable bowel syndrome symptoms, Enhance Immunity by inhibiting pathogens and producing lactocidin and acidophilin, Also show anti-microbial effects against Staphylococcus aureus, Salmonella, E. coli, Candida albicans
<i>L. plantarum</i> : (Synthesis of lactolin and L-lysine: antiviral amino acid)	Prevention of endotoxin production, antifungal activity, Reduction of irritable bowel syndrome symptoms and reduce abdominal pain, bloating, flatulence, and constipation, Eliminates nitrate, promotes nitric oxide levels, Reduces risk of bleeding, Positive effect on immune responses
<i>L. casei</i>	Treatment of functional constipation in adults, reduction of irritable bowel syndrome symptoms, antibiotic-associated diarrhea, Restoration of vaginal flora of patient with bacterial vaginosis and use in intravaginal staphylococcosis which reduces cervix tumors,

	Protection against Salmonella infection, rotavirus infections, clostridium difficile infection, synovitis and show immune modulatory action and decrease lactose intolerance, improvement in cholesterol levels, decrease triglycerides, decrease blood pressure and also decreases systemic inflammatory response syndrome, Show positive effects in Allergy Benefits like Pollen Allergies, Newborn Allergies produce vitamins B1 and B2
<i>L. delbrueckii</i> : (bulgaricus)	Enhancement of systemic immunity, Antimicrobial action against E. coli, Helicobacter pylori, Exhibited antimutagenic activities against 4NQO, a typical mutagen, and faecal mutagen protective action by producing lactic acid
<i>L. brevis</i>	Protective role in bile salt tolerance reduction in plague acidogenicity, Synthesis of Lactic acid, Vitamins D /K.
<i>B. infantis</i>	Reduction of irritable bowel syndrome symptoms, reduction of necrotizing enterocolitis in preterm infants, Simulates the production of cytokines that affect the immune system, Antimicrobial action against clostrida, salmonella and shigella. B. longum colonizes the large intestine. This can decrease the frequency of gastrointestinal problems, such as diarrhea, and nausea during antibiotic use
<i>B. animalis</i> (lactis)	Reduction of the incidence of febrile urinary tract infections in children, Reduction of necrotizing enterocolitis in preterm infants, Reduction of total microbial counts in dental plaque also protect from enterohemolytic pathogen like Escherichia coli, Reduction of total cholesterol, Reduction of risk of upper respiratory illness, Usefull in Crohn's disease, Improvements in immunity, Protection from Salmonella infection reduces the severity of weanling diarrhea associated with rotavirus and E. coli, Used in animal feed(stimulate animal growth, reduce coliform counts by the production of antimicrobial metabolites
<i>B. bifidum</i> : (second most prominent species that identified in breast-fed infants)	Used in treatment of acute diarrhea, Reduction of necrotizing enterocolitis, Reduction of total cholesterol, Boosted immune functions shown anti-ulcer activities, anticancer activity
<i>B. breve</i> :	Prevention and treatment of necrotizing enterocolitis in newborns, reduction of cholesterol, Preventing the intestinal colonization with pathogen microorganisms, May show resistance to streptomycin due to mutation, Eradicated Campylobacter jejuni from their stools, although less rapidly than in patients treated with erythromycin, Induce formation of large amounts of IgA which may used for against food allergens and pathogens.
<i>B. coagulans</i> : (Lactobacillus spore forming lactic acid bacterium)	Treatment of antibiotic-associated diarrhoea, bacterial vaginosis immunological support, increased immune response to viral challenge, prevent respiratory infections, Decrease Irritable bowel syndrome, Clostridium difficile colitis abdominal pain and bloating symptoms. Also used to prevent cancer or the formation of cancer-causing agents.
<i>E. coli</i>	Treatment of functional constipation in adults treatment of inflammatory bowel disease, gastrointestinal disorders pro-inflammatory potential reduction of Salmonella enterica Typhimurium intestinal colonization by iron competition. Promote immune, digestive (produce various digestive enzymes), reproductive health

**C) Nutraceutical Enzymes:** Enzymes are an important part of life without which our body would stop working. Those experiencing medical conditions such as hypoglycemia, blood sugar disorders, digestive problems and obesity can eliminate symptoms by adding enzyme supplements to their diet. These enzymes are found in microbial, plant and animal sources.

**D) Prebiotics:** Prebiotics are foods that we have never eaten before. Instead, they serve as a source of nutrients for good probiotic bacteria.

This encourages probiotic bacteria to grow in a supportive environment, reducing the chances of microbes starting to grow in our digestive tract. Inulin is a prebiotic widely used in processed foods. It is a type of fiber found in the roots of

plants such as chicory, Jerusalem artichoke and dandelion<sup>28</sup>.

**E) Non-traditional Nutraceuticals:** A processed food prepared with the help of biotechnology. Food samples contain organisms designed to produce human life products. They are formulated into nutrient-rich nutraceuticals and synthetic nutraceuticals.

**1) Strengthened Nutraceuticals:** Vitamin and mineral supplements are usually found in that nutrient's 100% Dairy Reference Intake (DRI). Creates enriched agricultural foods or with the addition of nutrients and / or ingredients with the addition of folic acid. Other examples milk is combined with cholecalciferol used in vitamin D deficiency<sup>29</sup>.

**2) Recombinant Nutraceuticals:** Energy foods like bread, alcohol, boiled starch, yogurt, cheese, vinegar *etc.*, are produced with the help of biotechnology. The production of probiotics and the extraction of bioactive elements by fermentation/enzyme technology, as well as engineering technology is achieved through biotechnology.

**F) Commercial Nutraceuticals:** The new molecule is hard to find, more expensive, and more dangerous than before. Many pharmaceutical companies are fenced off to produce healthy food products because there is no doubt a large and growing market. Nutraceuticals offer a wide range of treatments, prescribing anti-arthritis, colds, and coughs, sleep disorders, digestion and prevention of certain cancers, osteoporosis, blood pressure, cholesterol control, pain relief, depression, and diabetes. Recognizing and gaining health in omega-3 fatty acid enriched seafood is one of the most promising developments in human nutrition research and disease prevention over the past three decades. It includes a variety of health food medicines such as dietary supplements, active foods, diet pills, and medications.

**i) Medicinal Foods:** Foods prepared for use or administered internally under the supervision of a physician and intended for the administration of certain foods or the condition of certain nutritional needs, according to a well-known scientific policy, do not stabilize the medicinal value even if it contains a substance a genetic component that is rarely produced due to a specific disease. I quantify non-use of a variety of health conditions leading to infiltration, digestion, consolidation, or physical activity of traditional cybi such as phenylketonuria, celiac disease, and lactose intolerance<sup>30</sup>.

**ii) Active Foods:** active foods, meaning the most commonly accepted parrot, are simply "any food or ingredient that can provide health benefits from other indigenous ingredients. Active foods are designed to bring consumers" strengthened closer to their status, rather than taking dietary supplements in liquid form or capsule. Functional diets have been enriched or fortified, called the diet process. as added to milk. Fat may be a major source of energy for the body. There are the following types of lipids given as;

Saturated, monounsaturated fatty acids (MFA), polyunsaturated (PUFA), eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), saturated fats in animal products and MFA or PUF vegetable origin<sup>31</sup>.

**Metal Binding Proteins:** Some of the examples of metal-binding proteins are as follows;

- Albumin (copper).
- Ceruloplasmin (copper).
- Metallothionein (copper).
- Ferritin (iron).
- Myoglobin (iron).
- Transferrin (iron)<sup>7</sup>.

**TABLE 5: THE BEST HIGH-FIBER FOODS<sup>31</sup>**

Fibrous food	Content of fiber (gms)
Split Peas	16. 3 grams per cup
Lentil	15. 6 grams per cup
Black Beans	15 grams per cup
Lima Beans	13. 2 grams per cup
Brussels Sprouts	10. 3 grams per medium vegetable

**TABLE 6: EXAMPLES OF ANTIOXIDANT & THEIR SOURCES<sup>31</sup>**

Antioxidant	Source
<b>Vitamins</b>	
Vitamin C	Citrus fruits, vegetables
Vitamin E	Grains, nuts, oils
<b>Carotenoids</b>	
Lycopene	Guava, papaya, watermelon, Tomatoes, pink-colored grapefruit
Beta carotene	Carrots, sweet potato
<b>Xanthophylls</b>	
Beta cryptoxanthin	Mango, papaya, oranges
<b>Flavanoids</b>	
Rutin	Tobacco, eucalyptus species
Luteolin	Lemon, red pepper, olive
Quercetin	Onion, apple skin, black grapes
Kaempferol	Grapefruit, tea
Liquiritin	Liquorice

**Market Interest and Growth of Nutraceuticals:** The nutraceutical market is constantly competing with the revenues of major food and pharmaceutical products in the field of nutraceuticals. In addition, many food companies have not yet established their own category of nutraceuticals for a separate product line. Or you can go to the pharmacy; you will be able to buy a food supplement product.

The past few years have marked the entry of major food and pharmaceutical companies into the nutraceutical market, including Kellogg, Heinz, M & M, Quaker Oats, Unilever, Cargill, Ormel, GlaxoSmithKline, Warner-Lambert, Johnson Johnson and Wyeth. The 2004 global nutraceuticals market at the sales level is estimated at \$ 106 million and is expected to grow by 6.0% annual average over the period 2004, 2009 to more than \$ 140 million in 2009<sup>32</sup>.

The nutraceutical market size is unlikely to grow at \$ 180.38 million over the period 2020, 2024, and the rate of rapid market growth during the forecast period. The report provides product market analysis (active food benefits, employment benefits and food ingredients) and geographical location (APAC, Europe, MEA, North America and South America). In addition, the report analyzes the competitive environment in the market and provides details to its various market providers, including Abbott Laboratories, Archer Daniels Midland Co, BASF SE, Cargill Inc., Danone SA, General Mills Inc., Kellogg Co., Nestlé SA, PepsiCo Inc. and CocaCola Co<sup>33</sup>.

**Nutraceuticals Approach in Ayurveda:** The main goals and objectives of Ayurveda are establishing a state of health and eradicating the disease. In Ayurvedic dietetics, importance given to food in the prevention and treatment of diseases, and herbal remedies are part of the daily diet. According to Acharya Charak, foods that should not provide basic nutrients in the body should be used to help maintain good health and prevent the spread of disease.

A lovely verse from Acharya Lolimbaraja about the importance of food is that if healthy food is given in an orderly manner, there is no need to administer drugs. If no healthy food is used, no drugs need to be given as this is not enough. He cured the disease with a lack of healthy food. The concept of Aahar is a perfect way and is beyond the modern view. The Pathyain difference, Hita-ahita and Satmya-asatmya index, is based on an independent process. Ayurveda places great emphasis on the quality of nutritious foods such as Rasayana (preventing degenerative changes), Balya (nutrition after illness), Brihan (provides inadequate nutrients), Jeevaniya (maintains longevity),

Vyadhikshmatva (improves the immune system) and Vajikaran (preserves) and power). The science of nutrition and nutrition in Ayurveda was greatly improved. Acharya Charak divided all food into twelve categories, and Acharya Sushrut became thirteen. There are other divisions based on the compliance of food products such as Ashita (semi-solid, recommended for the elderly), Khadita (solid food, recommended for young people with good digestion), Peeta (consistency fluid, recommended for infants, children, and sick and recommended for summer) and Leeda ( a licked attachment form, recommended for children, recovery and the elderly to prevent or treat high blood pressure, high cholesterol, overweight, osteoporosis, diabetes, arthritis, macular malnutrition, lack of exercise, busy lifestyle, lifestyle<sup>1</sup>.

**Current Trends and Future Prospects of Nutraceuticals:** Over the past 20 years, there has been a rapid increase in the use of nutraceuticals due to the vast amount of information available on Internet resources and the growing public awareness of health problems<sup>34</sup>. Nutraceuticals for medical use are proven on the basis that they cure diseases caused by malnutrition. Strong evidence exists that nutraceutical supplementation improves health and prevents disease<sup>35</sup>.

While nutraceuticals have an important promise in promoting human health and disease prevention, health care professionals and regulatory poisons can also strategically work to develop appropriate guidelines for providing superior medical benefits to people<sup>36</sup>. In terms of nutraceutical production processes, quality controls, such as the composition and content of active ingredients in natural plants and their storage, are very important.

Intensive safety studies involving acute, subacute, subchronic, chronic, and long term terminology studies, animal husbandry, and human clinical studies are required to establish<sup>37, 38</sup>. DNA microarray technology can be used to test the safety and efficacy of drugs, chemicals, dieter supplements, and nutraceuticals. In summary, agriculture, food, and biomedical biotechnologies continue to grow relentlessly to change our lives, and one day our food will likely act as a medicine<sup>39</sup>.

**Liver- The Largest Gland in the Body:** The liver is the largest organ in the body and weighs between 1.2 and 1.5 kg in adults.

**Liver Area in the Body:** It is located in the abdominal cavity below the lid and has two lobes. Hepatic lobes are elements of the structure and performance of the liver consisting of liver cells arranged within cords. Each lobe is covered with a thin layer of connective tissue called Glisson's capsule.

The bile secreted by the liver cells passes through the hepatic ducts and is stored and concentrated in a small muscle sac called the gallbladder. The gallbladder (cystic duct) and the liver duct form the normal bile duct. The bile duct and pancreatic duct open together in the duodenum as a normal hepatopancreatic duct protected by Oddi's sphincter<sup>40</sup>.

Schematic relationships of the liver and other organs: The liver interacts with many other organs. After blood flow, the liver receives its blood from

the hepatic arteries<sup>41</sup>. The hepatic artery is located away from the celiac trunk and the abdominal aorta, so the liver receives its oxygen-rich blood from the heart. Blood rich in nutrients from the digestive system and blood from the digestive tract enters the liver through the hepatic portal artery. Processed blood that flows from the liver through the hepatic arteries enters the inferior vena cava, completing heart contact. The liver influences digestion by forming bile, which is secreted into the small intestine. The gallbladder is a dense area of the gallbladder of the liver. The liver is filled with lymph nodes that provide fluid flow and support for the immune system. The liver comprises many proteins in the blood, indicating its relationship to those organs. The liver has a nervous system that shows its relationship to the nervous system. Finally, the liver disease often causes problems with the kidney system that show relationships with the kidneys. The liver has many important functions in maintaining the balance of the human body<sup>42</sup>.

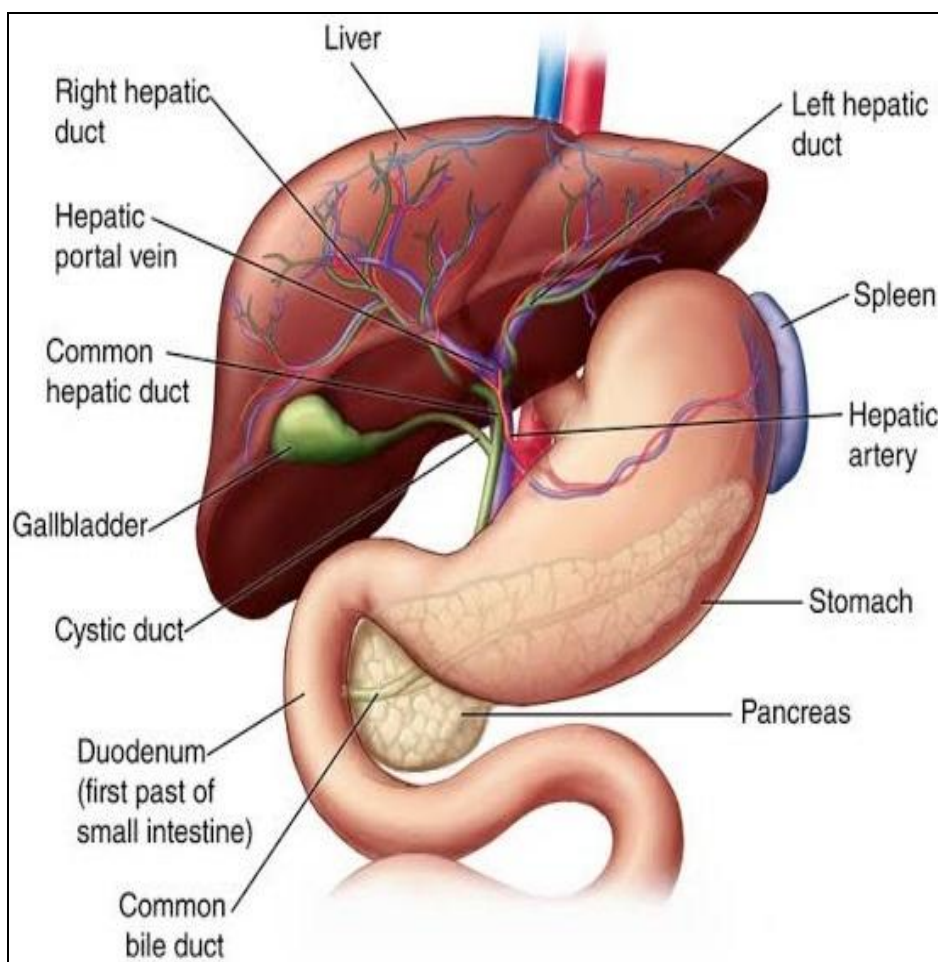


FIG. 1: ASSOCIATION OF LIVER



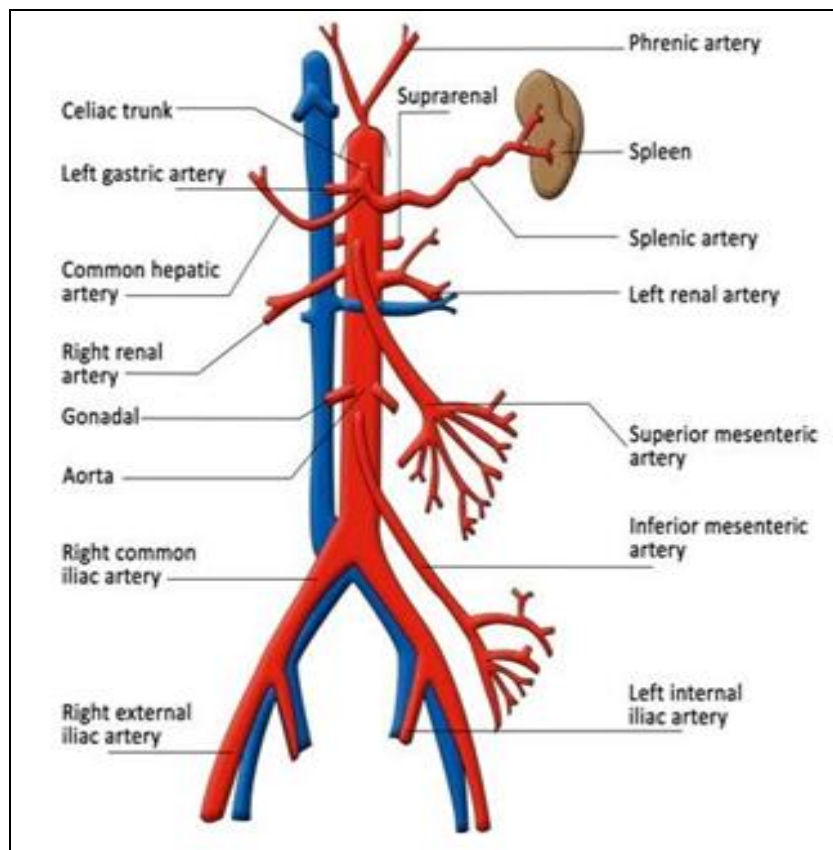


FIG. 2: ARRANGEMENT OF ARTERIES AND VEINS

**Functions of the Liver:** The various types of functions performed by the liver are discussed given below;

TABLE 7: FUNCTIONS OF LIVER

Secretion of Bile
Metabolism of Bilirubin
Vascular and Hematologic Functions: Important blood reservoir
Metabolism of Nutrients Fat: Fatty acid oxidation, synthesis of cholesterol/lipoproteins and production of ketoacids
Protein: Amino acid production, turnover of protein
Carbohydrate: Converts galactose/fructose to glucose, gluconeogenesis and contains 100g of glycogen for release
Metabolic Detoxification: Toxins, Hormones, Drugs
Storage of Minerals and Vitamins: Iron, Copper, Vitamins A, D, E, K and B12, Glycogen
Endocrine functions: Activation of vitamin D, Conversion of thyroxine (T4) to T3, Secretes angiotensinogen, Metabolises hormones
Immunological/ Protective Functions Reticuloendothelial Component: Filters the portal blood from bacteria, Important in antigen presentation, Phagocytosis via kupffer cells, Removes haemolysis products
Inactivation of Toxins and Drugs: Phase I reactions (oxidation, reduction and hydrolysis), Phase II reactions (conjugation/ cytochrome P450 system)

**Non-Alcoholic Fatty Liver Disease (NAFLD):** Non-alcoholic fatty liver disease (NAFLD) is the accumulation of triglycerides (TG) in the hepatocyte without eating alcohol. Fatty liver disease can be caused by the accumulation of TG in hepatocyte to non-alcoholic steatohepatitis (NASH), defined as steatosis accompanied by inflammation, which progresses to fibrosis and then to cirrhosis<sup>43</sup> and eventually to with hepatocellular carcinoma<sup>44</sup>. NAFLD is the first step in developing irreversible changes in the liver parenchyma

leading to cirrhosis (about 1/3 of NAFLD cases are prone to NASH, and 15% of these can turn into cirrhosis) and, on the other hand ' on the other hand, NAFLD itself is a risk factor in the development of heart disease<sup>45</sup>. A recent meta-analysis of 9 observational studies involving data from 96,595 adult studies (34.1% of them with NAFLD) with 4,654 cases of moderate to severe failure during the 5.2-year review period showed a 37% risk of high renal failure in NAFLD patients. The risk was greater than the rate of lipid

penetration into the liver. Since kidney failure and NAFLD are risk factors for heart disease, it is easy to understand how important this association of autoimmune diseases is<sup>46</sup>. Fat intake is called fatty liver disease and may be due to alcohol abuse (fatty liver disease - AFLD) or other metabolic disorders (fatty liver disease NAFLD). The international standard the Scientific community chose to distinguish between AFLD and NAFLD is 2 drinks, equivalent to 20 g per day. NAFLD is the most common condition affecting 25-30% of adults, 15% of children, and over 50% of overweight, obese, and type 2 people. NAFLD could be considered a real disease. If it is completely reversed<sup>47</sup>. The aggressive clinical variation of NAFLD, steatohepatitis (non-alcoholic), characterized by persistent inflammation and degeneration of tissues, affects approximately 5% of adults and 20% of obese individuals<sup>48</sup>.

**NaflD Pathogenesis:** The pathogenesis of non-alcoholic fatty alcohol disease has been identified as a major health problem. Metabolic mutations associated with obesity were collected to explain metabolic syndrome, the leading cause of death and morbidity in developed countries<sup>49</sup>. Metabolic syndrome is characterized by several disorders, including elevated blood pressure, IR, and obesity<sup>50</sup>. The growing epidemic of metabolic syndrome is accompanied by an increase in liver dysfunction, including NAFLD<sup>51</sup>. In particular, NAFLD is an obvious manifestation of the metabolic system<sup>52</sup>. Non-alcoholic fatty liver disease is found in 22 to 30% of the world. The

prevalence of NAFLD in people with normal weight without complaining of a disease that they think affects the body is about 16%<sup>53</sup>. On the other hand, the prevalence of NAFLD is high among obese patients, rising to 73% in obese people and 85% in obese people<sup>54, 55</sup>.

Non-alcoholic disease (NAFLD) is the commonest chronic liver disease. It is characterized by various liver changes that can lead to liver fibrosis and cirrhosis. NAFLD is considered a hepatic component of metabolic syndrome (MetS)<sup>56</sup> but the mechanisms underlying it and its progression are still being investigated. Numerous studies have shown the presence of insulin resistance<sup>57</sup> and increased oxidative stress<sup>58</sup> in patients with NAFLD / steatohepatitis (nonalcohol) steatohepatitis (NASH). Thus, according to the "double hit hypothesis", the first hit represents the accumulation of lipids in hepatocytes, after which oxidative stress can lead to NASH<sup>59</sup>. This traditional theory has been developed within the complex "multiple parallel impact hypothesis" which includes a wide range of similar effects such as insulin resistance, oxidative stress, genetic and epigenetic pathways, natural substances, cytokines, and changes in microbiota<sup>60</sup>. These factors can be related in various ways in the presence and absence of MetS. Various therapies have been suggested so far. However, the only effective strategy for obtaining NAFLD treatment for weight loss and vitamin administration is only designed for non-diabetic NASH patients. Significantly, there is currently no approved treatment for NAFLD<sup>61</sup>.

**TABLE 8: ROLE OF NUTRACEUTICALS FOR THE TREATMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE AND POSSIBLE TARGETS**

Nutraceuticals	Target/mechanism of action	References
Vitamin D	Chronic inflammation, Vitamin deficiency, Insulin resistance	62, 63, 64
Vitamin E	Oxidative stress, Hepatocellular protection	65
Carnitine	Insulin resistanc, Chronic inflammation, Hepatocellular protection	66, 67, 68
Vitamin C	Oxidative stress, Hepatocellular protection	69, 70
Omega-3 fatty acids	Atherogenic dyslipidaemia, Cardiovascular risk, Oxidative stress, Hepatocellular protection	71, 72, 73, 74
Silymarin	Oxidative stress, Chronic inflammation, Insulin resistance and Hepatocellular protection	75, 76, 77
Resveratrol	Oxidative stress, Insulin resistance, Cardiovascular risk	78, 79, 80

### Therapeutic Approaches for NAFLD:

**Non-Medical Treatment:** Many cases of NAFLD are associated with obesity, so exercise and a very low diet are recommended<sup>81</sup>.

Moreover, there is no specific cure for NAFLD other than weight loss, increased exercise, and lifestyle changes, which remain the most important and effective ways to recover from NAFLD<sup>82, 83</sup>.

**Weight Loss:** In a hospital patient with NAFLD, weight loss was accompanied by significant improvement in all parameters of metabolic syndrome, liver function tests and steatosis function<sup>84, 85, 86</sup>, lobular inflammation, ballooning damage, and fibrosis<sup>87</sup>. Improvements in liver function tests associated with weight loss have been observed in 40% of obese patients with NAFLD<sup>88</sup>. In addition, weight loss is the only proven form of NAFLD for children. However, weight loss should be slightly reduced because rapid weight loss can be detrimental to steatohepatitis<sup>89</sup>.

**Exercise:** Exercise has been shown to increase the oxidative capacity of muscle cells and use AF oxidation<sup>90</sup>. It also reduces the accumulation of fatty acids and TG in myocytes and improves insulin sensitivity. In addition, exercise is associated with improved insulin sensitivity<sup>91</sup>.

**Medication Methods:** Most current approaches to treating NAFLD aim to prevent fat absorption, inflammation, and insulin sensitivity<sup>92</sup>.

**CONCLUSION:** There are currently no specific drugs for NAFLD treatment. So, treatment is based on the effectiveness of the lifestyle. However, other nutraceuticals may improve lipid liver penetration and anthropometric, haemodynamic and/or biochemical parameters. Ayurvedic treatment regimens depend directly on the life of Aahar and Vihaar. Aahar was regarded as food and ancient medicine. The concept of Rasayana (rehealing) is a widespread concept in Ayurveda and in addition to current nutraceuticals. This article aims to provide available clinical data on the effect of nutraceuticals based on the NAFLD and NAFLD parameters. Few nutraceutical molecules have been extensively studied for their effects on NAFLD and other related diseases. Among them, we have analyzed the effects of nutrients, vitamins, minerals, various bacteria, dietary supplements, and other nutraceuticals such as carnitine, omega-3 fatty acids, silymarin, and resveratrol. In conclusion, vitamins (such as vitamin E and vitamin D), silymarin, and omega-3 fatty acids, when properly regulated and regulated over a long period, are associated with lifestyle changes that can positively affect NAFLD and their related parameters. It also showed improvements in the

liver function tests (LFT) and a positive impact on liver histology.

**ACKNOWLEDGEMENT:** The authors thanks the Siddhartha group of Institutions for their motivation and support.

**CONFLICT OF INTEREST:** The authors declare that they have no conflict of interest for this study.

## REFERENCES:

1. Nema N, Kumar A, Pillewan M, Mishra and PK Biswas S: Importance of Nutraceuticals in various diseases and human health- A Literature review. *WJPMR* 2018; 4(9): 104-110.
2. De Filippis D, D'amico A and Iuvone T: Cannabinomimetic control of mast cell mediator release: new perspective in chronic inflammation. *J Neuroendocrinol* 2008; 20: 120-125.
3. Keppel Hesselink JM, De Boer T and Witkamp RF: Palmitoylethanolamide: A natural body-own anti-inflammatory agent, effective and safe against influenza and common cold. *Int J Inflam* 2013; 151028.
4. Kumar K & Kumar S: Role of nutraceuticals in health and disease prevention: a review. *South Asian Journal Food Technol Environ* 2015; 1: 116-121.
5. Varigos G: Apoptosis may underlie the pathology of zinc deficient skin. *Immunology and Cell Biology* 2006; 84(1): 28-37.
6. Pandey M, Verma RK and Saraf SA: Nutraceuticals: New era of medicine and health. *Asian Journal of Pharmaceutical and Clinical Research* 2010; 3(1): 11-15.
7. Verma G and Mishra MK: A review on nutraceuticals: classification and its role in various diseases. *International Journal of Pharmacy & Therapeutics* 2016; 7(4): 152-160.
8. Chintale AG, Kadam V, Sakhare R, Birajdar GO and Nalwad DN: Role of nutraceuticals in various diseases: A comprehensive review. *Int J Res Pharm Chem* 2013; 3: 290-299.
9. Pludowski P, Holick MF, Grant WB, Konstantynowicz J, Mascarenhas MR, Haq A and Rudenka E: Vitamin D supplementation guidelines. *The Journal of Steroid Biochemistry and Molecular Biology* 2018; 175: 125-135.
10. Patel CN, Shah N and Anand IS: Probiotic, prebiotic and symbiotic. *The Indian Pharmacist* 2006; 5(47): 20-24.
11. Telang PS: Vitamin C in dermatology. *Indian Dermatology Online Journal* 2013; 4(2): 143.
12. Kumar P, Kumar N and Omer T: A review on nutraceuticals-critical supplement for building a healthy world. *World Journal of Pharmacy and Pharmaceutical Sciences* 2016; 5(3): 579-94.
13. Dureja H, Kaushik D & Kumar V: Developments in nutraceuticals. *Indian Journal of Pharmacology* 2003; 35(6): 363-372.
14. Peralta AMS: Vitamins in Diets: Metabolism Relationship. *Global Journal of Pharmaceutical Education and Research* 2016; 1(2): 50-60.
15. Ziyi Zhou: Effect of smoking and folate levels on the efficacy of folic acid therapy in prevention of stroke in hypertensive men. *Stroke* 2018; 49(1): 114-120.
16. Lopez-Varela S, Gonzalez-Gross M and Marcos A: Functional foods and the immune system: a review. *European Journal of Clinical Nutrition* 2002; 56(3): 29-33.

17. Singh V, Mahaur S & Kushwaha SK: Nutraceuticals: A New Golden Era in Health and Disease. *Asian Journal of Research in Chemistr* 2018; 11(3): 652-658.
18. Kini U & Nandeesh BN: Physiology of bone formation, remodeling, and metabolism. In *Radionuclide and Hybrid Bone Imaging* 2012; 29-57.
19. Wilson D, Varigos G & Ackland ML: Apoptosis may underlie the pathology of zinc-deficient skin. *Immunology and Cell Biology* 2006; 84(1): 28-37.
20. Gupta S, Chauhan D, Mehla K, Sood P & Nair A: An overview of nutraceuticals: current scenario. *Journal of Basic and Clinical Pharmacy* 2010; 1(2): 55.
21. Bilal I, Chowdhury A, Davidson J & Whitehead S: Phytoestrogens and prevention of breast cancer: the contentious debate. *World Journal of Clinical Oncology* 2014; 5(4): 705.
22. Smolskaitė L, Venskutonis PR & Talou T: Comprehensive evaluation of antioxidant and antimicrobial properties of different mushroom species. *LWT-Food Science and Technology* 2015; 60(1): 462-471.
23. Gerlie C, Koda RT & Lien EJ: Glucosamine and chondroitin sulfates in the treatment of osteoarthritis: a survey. In *Progress in Drug Research* 2000; 81-103.
24. Li SQ & Zhang QH: Advances in the development of functional foods from buckwheat. *Critical Reviews in Food Science and Nutrition* 2001; 41(6): 451-464.
25. Dolkar D, Bakshi P, Wali VK, Sharma V & Shah RA: Fruits as nutraceuticals. *Ecology, Environment and Conservation* 2017; 23: 113-118.
26. Dillard CJ and German JB: Phytochemicals: Nutraceuticals and human health. *J Sci Food Agric* 2000; 80: 1744-56.
27. Vouloumanou EK, Makris GC and Karageorgopoulos DE: Probiotics for the prevention of respiratory tract infections: a systematic review. *Int J Antimicrob Agents* 2009; 34: 1-10.
28. Montrose DC, Floch MH: Probiotics used in human studies. *J Clin Gastroenterol* 2005; 39(6): 469-484.
29. Hugenholtz J, Smid EJ, Ladero V and Hols P: Metabolic engineering of lactic acid bacteria for the production of nutraceuticals. *Antonie van Leeuwenhoek* 2002; 82: 217-235.
30. Arrigo FG: Cicero, Alessandro Colletti and Stefano Bellentani. Review - Nutraceutical Approach to Non-Alcoholic Fatty Liver Disease (NAFLD): The Available Clinical Evidence 2018, 1153; doi: 10.3390/nu10091153.
31. Borkar N, Saurabh SS, Rathore KS, Pandit A and Khandelwal KR: An Insight on Nutraceuticals; *Pharma Tutor* 2015; 3(8): 13-23.
32. Chaudhari S P, Powar PV and Pratapwar MN: Nutraceuticals: a review. *World Journal of Pharmacy and Pharmaceutical Sciences* 2017; 6: 8.
33. Dev R, Kumar S, Singh J and Chauhan B: Potential role of Nutraceuticals in Present Scenerio: A Review. *Journal of Applied Pharmaceutical Science* 2011; 01(04): 26-28.
34. Parveen R and Bhargav RK: A review: nutraceuticals & its role in ailments. *World Journal of Pharmacy and Pharmaceutical Sciences* 2020; 9(5): 499-510.
35. Ortega VG, Ramírez JA, Velázquez G, Tovar B, Mata M and Montalvo E: Effect of high hydrostatic pressure on antioxidant content of "Ataulfo" mango during postharvest maturation. *Food Sci Technol* 2013; 33: 561-568.
36. Anita S, Mangesh T, Prasad VS and Singh Meera C: Nutraceuticals-Global Status and Applications: A Review. 2013. Available online: <https://www.semanticscholar.org/paper/Nutraceuticals-Global-status-and-applications>
37. Taylor CL: Regulatory frameworks for functional foods and dietary supplements. *Nutr Rev* 2004; 62: 55-9.
38. Schilter B, Andersson C and Anton R: Guidance for the safety assessment of botanicals and botanical preparations for use in food and food supplements. *Food Chem Toxicol* 2003; 41: 1625-49.
39. Kroes R and Walker R: Safety issues of botanicals and botanical preparations in functional foods. *Toxicol* 2004; 198: 213-220.
40. Roy C, Rink and Khanna S: Body weight and abdominal fat gene expression profile in response to a novel hydroxycitric acidbased dietary supplement. *Gene Exp* 2004; 11: 251-262.
41. Siraj Anwar M, Shveta Uppal, Arun Chitkara, Bibash Kumar Das, Shashi Chadha and Prakash Veer Singh: *Biology Textbook for Class 11, National Council of Educational Research and Training (NCERT)* 260-261.
42. Ozougwu JC: Comparative hepatoprotective and antioxidant effects of *Allium cepa*, *Allium sativum* and *Zingiber officinale* methanolic extracts against paracetamol-induced liver damage in *Rattus norvegicus*. Ph.D Research Thesis, Department Of Zoology and Environmental Biology, University of Nigeria, Nsukka 2014; 222.
43. Allen SE: *The liver: Anatomy, Physiology, Disease and Treatment*. 2002 North Eastern University Press, USA.
44. Than NN and Newsome PN: A concise review of non-alcoholic fatty liver disease. *Atherosclerosis* 2015; 239: 192-202.
45. Farazi PA and DePinho RA: Hepatocellular carcinoma pathogenesis: from genes to environment. *Nat Rev Cancer*. 2006; 6: 674-87.
46. Villela-Nogueira CA, Leite NC, Cardoso CR and Salles GF: NAFLD and increased aortic stiffness: parallel or common physiopathological mechanisms. *Int J Mol Sci* 2016; 17: 460.
47. Mantovani A, Zaza G, Byrne CD, Lonardo A, Zoppini G, Bonora E and Targher G: Non-alcoholic fatty liver disease increases risk of incident chronic kidney disease: A systematic review and meta-analysis. *Metabolism* 2018; 79: 64-76.
48. Araújo AR, Rosso N, Bedogni G, Tiribelli C and Bellentani S: Global epidemiology of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis: What we need in the future. *Liver Int* 2018; 38 (1): 47-51.
49. Townsend SA and Newsome PN: Non-alcoholic fatty liver disease in 2016. *Br Med Bull* 2016; 119: 43-56.
50. Doulberis M, Kotronis G, Gialamprinou D, Kountouras J and Katsinelos P: Non-alcoholic fatty liver disease: An update with special focus on the role of gut microbiota. *Metab* 2017; 71: 182-97.
51. O'Neill S and O'driscoll L: Metabolic syndrome: a closer look at the growing epidemic and its associated pathologies. *Obes Rev* 2015; 16: 1-12.
52. Lonardo A, Sookoian S, Pirola CJ and Targher G: Non-alcoholic fatty liver disease and risk of cardiovascular disease. *Metab* 2016; 65: 1136-50.
53. Athyros VG, Tziomalos K, Katsiki N, Doumas M, Karagiannis A and Mikhailidis DP: Cardiovascular risk across the histological spectrum and the clinical manifestations of non-alcoholic fatty liver disease: An update. *WJG* 2015; 21: 6820.
54. Bellentani S and Marino M: Epidemiology and natural history of non-alcoholic fatty liver disease (NAFLD). *Ann Hepatol* 2009; 8: 4-8.
55. Garcia-Monzón C, Martín-Pérez E, Iacono OL, Fernández-Bermejo M, Majano PL and Apolinario A:

- Characterization of pathogenic and prognostic factors of nonalcoholic steatohepatitis associated with obesity. *J Hepatol* 2000; 33: 716-24.
56. Gholam PM, Flancbaum L, Machan JT, Charney DA and Kotler DP: Non-alcoholic fatty liver disease in severely obese subjects. *AJG* 2007; 102: 399.
  57. Angelico F, Del Ben M, Conti R, Francioso S, Feole K, Maccioni D, Antonini TM and Alessandri C: Non-alcoholic fatty liver syndrome: a hepatic consequence of common metabolic diseases. *Gastroenterol Hepatol* 2003; 18: 588-94.
  58. Polimeni L, Del Ben M, Baratta F, Perri L, Albanese F, Pastori D, Violi F and Angelico F: Oxidative stress: new insights on the association of non-alcoholic fatty liver disease and atherosclerosis. *World J Hepatol* 2015; 7: 1325-36.
  59. Angelico F, Del Ben M, Conti R, Francioso S, Feole K, Fiorello S, Cavallo MG, Zalunardo B, Lirussi F, Alessandri C and Violi F: Insulin resistance, the metabolic syndrome, and non-alcoholic fatty liver disease. *J Clin Endocrinol Metab* 2005; 90: 1578-82.
  60. Angulo P: Non-alcoholic fatty liver disease. *N Engl J Med* 2002; 346: 1221-31.
  61. Takaki A, Kawai D and Yamamoto K: Multiple hits, including oxidative stress, as pathogenesis and treatment target in non-alcoholic steatohepatitis (NASH) *Int J Mol Sci* 2013; 14: 20704-28.
  62. Del Ben M, Polimeni L, Baratta F, Pastori D, Loffredo L and Angelico F: Modern approach to the clinical management of non-alcoholic fatty liver disease. *World J Gastroenterol* 2014; 20: 8341-50.
  63. Roth CL, Elfers CT, Figlewicz DP, Melhorn SJ, Morton GJ, Hoofnagle A, Yeh MM, Nelson JE and Kowdley KV: Vitamin D deficiency in obese rats exacerbates non-alcoholic fatty liver disease and increases hepatic resistin and Toll-like receptor activation. *Hepatology* 2012; 55: 1103-11.
  64. Barchetta I, Angelico F, Del Ben M, Baroni MG, Pozzilli P, Morini S and Cavallo MG: Strong association between non alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes. *BMC Med* 2011; 9: 85.
  65. Targher G, Bertolini L, Scala L, Cigolini M, Zenari L, Falezza G and Arcaro G: Associations between serum 25-hydroxyvitamin D3 concentrations and liver histology in patients with non-alcoholic fatty liver disease. *Nutr Metab Cardiovasc Dis* 2007; 17: 517-24.
  66. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, Charlton M and Sanyal AJ: The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology* 2012; 55: 2005-23.
  67. Flanagan JL, Simmons PA, Vehige J, Willcox MD and Garrett Q: Role of carnitine in disease. *Nutr Metab (Lond)* 2010; 7: 30.
  68. Malaguarnera M, Gargante MP, Russo C, Antic T, Vacante M, Malaguarnera M, Avitabile T, Li Volti G and Galvano F: L-carnitine supplementation to diet: a new tool in treatment of non-alcoholic steatohepatitis – a randomized and controlled clinical trial. *Am J Gastroenterol* 2010; 105: 1338-45.
  69. Somi MH, Fatahi E, Panahi J, Havasian MR and Judaki A: Data from a randomized and controlled trial of L carnitine prescription for the treatment for non-alcoholic fatty liver disease. *Bioinformation* 2014; 10: 575-9.
  70. Duarte TL and Lunec J: Review: when is an antioxidant not an antioxidant? A review of novel actions and reactions of vitamin C. *Free Radic Res* 2005; 39: 671-86.
  71. Harrison SA, Torgerson S, Hayashi P, Ward J and Schenker S: Vitamin E and vitamin C treatment improves fibrosis in patients with non-alcoholic steatohepatitis. *Am J Gastroenterol* 2003; 98: 2485-90.
  72. Hedengran A, Szecsi PB, Dyerberg J, Harris WS and Stender S: n-3 PUFA esterified to glycerol or as ethyl esters reduce non-fasting plasma triacylglycerol in subjects with hypertriglyceridemia: a randomized trial. *Lipids* 2015; 50: 165-75.
  73. Endo J and Arita M: Cardioprotective mechanism of omega-3 polyunsaturated fatty acids. *J Cardiol* 2016; 67: 22-7.
  74. Jump DB, Botolin D, Wang Y, Xu J, Christian B and Demeure O: Fatty acid regulation of hepatic gene transcription. *J Nutr* 2005; 135: 2503-6.
  75. Parker HM, Johnson NA, Burdon CA, Cohn JS, O'Connor HT and George J: Omega-3 supplementation and non-alcoholic fatty liver disease: a systematic review and meta-analysis. *J Hepatol* 2012; 56: 944-51.
  76. Trappoliere M, Caligiuri A, Schmid M, Bertolini C, Failli P, Vizzutti F, Novo E, Di Manzano C, Marra F, Loguercio C, Pinzani M. Silybin, a component of silymarin, exerts anti-inflammatory and anti-fibrogenic effects on human hepatic stellate cells. *J Hepatol* 2009; 50: 1102-11.
  77. Sorrentino G, Crispino P, Coppola D and De Stefano G: Efficacy of lifestyle changes in subjects with non-alcoholic liver steatosis and metabolic syndrome may be improved with an antioxidant nutraceutical: a controlled clinical study. *Drugs R & D* 2015; 15: 21-5.
  78. Feng B, Meng R, Huang B, Shen S, Bi Y and Zhu D: Silymarin alleviates hepatic oxidative stress and protects against metabolic disorders in high-fat diet-fed mice. *Free Radic Res* 2016; 50: 314-27.
  79. Gambini J, Ingles M, Olaso G, Lopez-Grueso R, Bonet-Costa V, Gimeno-Mallench L, Mas-Bargues C, Abdelaziz KM, GomezCabrera MC, Vina J and Borrás C: Properties of resveratrol: *in-vitro* and *in-vivo* studies about metabolism, bioavailability, and biological effects in animal models and humans. *Oxid Med Cell Longev* 2015; 2015: 837042.
  80. Faghihzadeh F, Adibi P and Hekmatdoost A: The effects of resveratrol supplementation on cardiovascular risk factors in patients with non-alcoholic fatty liver disease: a randomised, double-blind, placebo-controlled study. *Br J Nutr* 2015; 114: 796-803.
  81. Poulsen MM, Vestergaard PF, Clasen BF, Radko Y, Christensen LP, Stodkilde-Jorgensen H, Moller N, Jessen N, Pedersen SB and Jorgensen JO: High-dose resveratrol supplementation in obese men: an investigator-initiated, randomized, placebo-controlled clinical trial of substrate metabolism, insulin sensitivity, and body composition. *Diabetes* 2013; 62: 1186-95.
  82. Expert P: Executive summary of the clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. *Arch Intern Med* 1998; 158: 1855-67.
  83. Park HS, Sim SJ and Park JY: Effect of weight reduction on metabolic syndrome in Korean obese patients. *J Korean Med Sci* 2004; 19: 202-8.
  84. Asrih M and Jornayvaz FR: Diets and non-alcoholic fatty liver disease: the good and the bad. *Am J Clin Nutr* 2014; 33: 186-90. <https://doi.org/10.1016/j.clnu.2013.11.003>.
  85. Suzuki A, Lindor K, St Saver J, Lymp J, Mendes F and Muto A: Effect of changes on body weight and lifestyle in

- non-alcoholic fatty liver disease. *J Hepatol* 2005; 43: 1060-6.
86. Park HS, Kim MW and Shin ES: Effect of weight control on hepatic abnormalities in obese patients with fatty liver. *J Korean Med Sci* 1995; 10: 414-21.
87. Ueno T, Sugawara H, Sujaku K, Hashimoto O, Tsuji R and Tamaki S: Therapeutic effects of restricted diet and exercise in obese patients with fatty liver. *J Hepatol* 1997; 27: 103-7.
88. Dixon JB, Bhathal PS, Hughes NR and O'Brien PE: Non-alcoholic fatty liver disease: improvement in liver histological analysis with weight loss. *Hepatol* 2004; 39: 1647-54.
89. Loguercio C, De Girolamo V, de Sio I, Tuccillo C, Ascione A and Baldi F: Non-alcoholic fatty liver disease in an area of southern Italy: main clinical, histological, and pathophysiological aspects. *J Hepatol* 2001; 35: 568-74.
90. Trappoliere M, Tuccillo C, Federico A, Di Leva A, Niosi M and Alessio DC: The treatment of NAFLD. *Eur Rev Med Pharmacol* 2005; 9: 299.
91. Weinstock RS, Dai H and Wadden TA: Diet and exercise in the treatment of obesity: effects of 3 interventions on insulin resistance. *Arch Intern Med* 1998; 158: 2477-83.
92. Kang J, Robertson RJ, Hagberg JM, Kelley DE, Goss FL and Dasilva SG: Effect of exercise intensity on glucose and insulin metabolism in obese individuals and obese NIDDM patients. *Diabetes Care* 1996; 19: 341-9.
93. Carter R, Mouralidarane A, Ray S, Soeda J and Oben J: Recent advancements in drug treatment of obesity. *J Clin Med* 2012; 12: 456-60.

**How to cite this article:**

Sharma B, Sanwal R and Singh S: Nutraceutical approach to non-alcoholic fatty liver disease: a review. *Int J Pharm Sci & Res* 2022; 13(9): 3411-24. doi: 10.13040/IJPSR.0975-8232.13(9).3411-24.

All © 2022 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **Android OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)