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DIETARY AND NATURAL AID FOR ALCHOLIC LIVER DISEASE STEATOSIS AND CIRRHOSIS

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Abstract

Alcohol use disorders can lead to malnutrition, which has a significant impact on the prognosis of individuals with alcoholic liver disease (ALD). Additionally, these patients often exhibit deficits in vitamins and trace elements, which raises the probability of developing anaemia and experiencing changes in cognitive function. The cause of malnutrition in ALD patients is multiple and complex, involving insufficient food intake, poor absorption and digestion, accelerated breakdown of protein in the skeletal and visceral tissues, and aberrant interactions between ethanol and lipid metabolism. The majority of dietary measurements are based on basic recommendations for chronic liver disease. In recent times, a significant number of individuals suffering from ALD have been identified as having metabolic syndrome, necessitating personalised treatment through nutritional therapy to prevent excessive feeding. As alcoholic liver disease (ALD) advances to cirrhosis, it often becomes worsened by protein-energy deficiency and sarcopenia. As liver failure worsens, nutritional treatment plays a crucial role in managing ascites and hepatic encephalopathy. The objective of the review is to provide a concise overview of significant nutritional therapy and use of Berberine for the treatment of ALD.

Keywords: Alcoholic liver disease(ALD); Alcoholic cirrhosis, Steatosis, Dietary measurement, Berberine extract

1. Introduction

Alcoholic liver disease refers to the damage to the liver caused by excessive alcohol consumption. Alcoholic cirrhosis specifically refers to the advanced stage of liver disease where the liver becomes scarred and dysfunctional due to alcohol abuse. Protein-energy malnutrition is a condition characterised by a deficiency of both protein and energy intake, often seen in individuals with liver disease caused by alcohol abuse.

Alcohol use disorders (AUDs) are a significant contributor to preventable diseases and fatalities associated to liver disease in both the United States and globally. Nevertheless, the occurrence of AUD and ALD has significantly risen in recent years [1]. ALD is the result of consuming an average of at least 60 grammes of pure alcohol each day for a minimum of 5 years. The development and advancement of ALD are impacted by various factors, such as age, gender, the existence of an underlying illness, genetic susceptibility, immune system functionality, obesity, and excessive diet. Complete abstinence is the fundamental basis of treatment, enhancing therapeutic results in all stages of ALD [2]. Approximately 50% of outpatients with ALD and virtually all inpatients with ALD suffer from malnutrition. It is important to note that malnutrition has a negative impact on treatment responses and patient outcomes [2,3]. The extent of nutritional deficiency varies depending on the stage of ALD progression, and the approach to nutritional treatment should be tailored to the specific kind of the disease. Figure 1 demonstrates the histological classification of ALD into three stages [4]:

(i) alcoholic fatty liver or steatosis, characterised by the accumulation of fat in the liver parenchyma;

(ii) alcoholic hepatitis (AH), characterised by inflammation of liver cells and clinical outcomes that vary based on the severity of the damage; and

(iii) alcoholic cirrhosis, characterised by irreversible liver damage that results in complications associated with cirrhosis and portal hypertension.

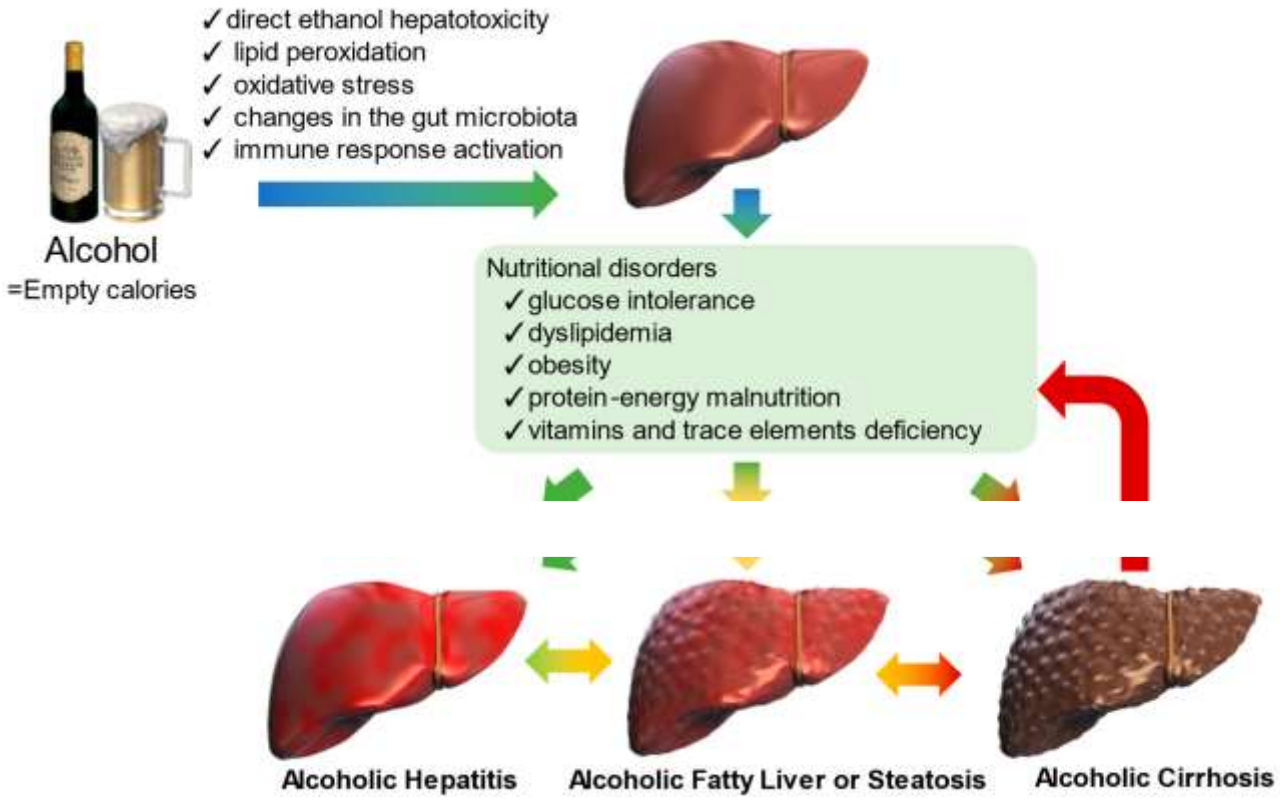

Figure 1.Malnutrition and hepatic illness in individuals with excessive alcohol consumption.
Source: https://www.mdpi.com/2072-6643/15/6/1360

Alcohol can cause harm to liver cells through a variety of routes [5]. Alcohol that is consumed is metabolised by alcohol dehydrogenase (ADH) and cytochrome P450 2E1 (CYP2E1) into acetaldehyde, which is then transformed into acetic acid by aldehyde dehydrogenase (ALDH). Acetaldehyde induces hepatocellular injury. Alcohol metabolism produces reactive oxygen species (ROS) that hinder the antioxidant function in liver cells [6]. Indicators of oxidative stress consist of serum NADPH oxidase (NOX2) [7] and urinary 8-isoPGF2α [8]. Alcohol consumption can cause alterations in the gut flora, which in turn can lead to increased oxidative stress and intestinal hyperpermeability [9]. Probiotics, a form of microbial therapy, enhance the treatment of ALD by reinstating the balance of microorganisms in the intestines and fortifying the protective barrier of the intestines [10]. The activation of Kupffer cells by lipopolysaccharides generated from the gut is a significant contributing element in alcoholic liver disease (ALD). Lipopolysaccharide is detected by the Toll-like receptor (TLR) 4 complex, which is present on both immune cells and parenchymal cells, and triggers the activation of inflammatory cytokines. Repeated and long-term alcohol consumption increases the sensitivity of Kupffer cells to the generation of inflammatory cytokines generated by lipopolysaccharide. In addition, alcohol can directly or indirectly cause hepatotoxicity through its metabolites via several additional routes. Fruits, vegetables, spices, cereals, and teas that can be eaten have been found to be helpful against ALD by several methods [11].

ALD, or alcoholic liver disease, encompasses a range of conditions that start with the accumulation of fat in the liver and can eventually lead to alcoholic hepatitis (AH) and alcoholic cirrhosis. Malnutrition in individuals with ALD is associated with reduced quality of life, heightened susceptibility to infection, frequent hospital admissions, complications, mortality, and increased financial burden. Medical professionals, such as gastroenterologists and hepatologists, should have knowledge on how to evaluate and treat malnutrition, as well as provide nutritional supplements [12]. Alcoholic beverages have minimal to no amounts of protein, vitamins, trace elements, fibre, or other essential nutrients [13]. Nevertheless, the resting energy expenditure (REE) tends to be higher in individuals with alcohol use disorder (AUD), despite their tendency to abstain from food and consume solely alcohol. Patients with traditional ALD often experience common problems such as malnutrition resulting from decreased digestion, nutritional absorption, and organ damage caused by alcohol. The main features of these individuals are primarily marked by reduced body weight, muscle or fat mass, muscle strength, visceral protein levels, and immunological function [14]. Therefore, individuals suffering from ALD frequently experience protein-energy malnutrition (PEM). The presence of malnourishment in ALD patients is a complex phenomenon that involves various factors such as modified olfactory and taste perception, changes in appetite-related hormones, and alterations in gut flora. Patients treated with severe alcoholic hepatitis (AH) frequently have a background of excessive alcohol intake. Therefore, while a patient is hospitalised, management should prioritise providing nutritional support, along with addressing alcohol withdrawal, treating infection and sepsis, managing consequences of cirrhosis and portal hypertension, and administering specialist treatment for alcoholic hepatitis [15,16].

Furthermore, there has been an observed correlation between the rise in ALD patients who are obese and the presence of overnutrition factors, including excessive alcohol intake, obesity, and hyperglycemia, which are strongly linked to the pathological advancement of ALD. Alcohol drinking can contribute to obesity, particularly when combined with excessive consumption of fatty foods and a sedentary lifestyle. Recently, patients with ALD have demonstrated a notable prevalence of obesity and overnutrition. It is well-established that disorders connected to lifestyle might accelerate the progression of ALD. Hence, it is imperative to implement strategies to mitigate lifestyle-related ailments. Among Japanese male patients with ALD, 26% were found to be obese, 34% had diabetes, 23% had hypertension, and 23% had dyslipidemia, according to an observational study [17]. A U-shaped curve was seen, indicating that the risk of type 2 diabetes was lower for individuals who consumed little amounts of alcohol compared to those who did not drink at all. However, the risk of type 2 diabetes increased as alcohol use increased. The controversy about the health advantages of consuming little amounts of alcohol has persisted in recent years. The risk of death from any cause increased as alcohol intake increased, and consuming no beverages was the only way to minimise harm to overall health outcomes [18]. Therefore, there is no justification for suggesting that consuming tiny quantities of alcohol will increase life expectancy, and the primary approach to managing ALD is complete avoidance of alcohol.

Nevertheless, advanced ALD typically exhibits irreversibility and does not ameliorate only by alcohol abstinence. When managing patients with ALD, it is crucial to evaluate and offer advice on lifestyle patterns, such as dietary choices, while also promoting a decrease in alcohol intake. Table 1 displays the calorie and protein levels that are suggested for each stage of ALD. Patients diagnosed with ALD should undergo a thorough evaluation of their nutritional status and be provided with the necessary dietary support [19]. The Nutrition Risk Screening 2002 and Malnutrition Universal Screening Tool are suggested instruments for evaluating nutritional status. These techniques are effective for assessing the risk of malnutrition in hospitalised patients and are endorsed by the European Society for Clinical Nutrition and Metabolism [20,21]. The Royal Free Hospital-Nutritional Prioritising Tool is well regarded for its ability to accurately forecast the risk of malnutrition in patients with cirrhosis [22]. This article discusses the nutritional therapy that health care providers should be familiar with while treating patients with ALD.

Table 1. Recommended nutritional therapy for ALDs.

S.No	Alcoholic Liver Diseases	Recommended Total Energy and Nutrient Intake	References
1	Alcoholic hepatitis	Total energy: 35–40 kcal/kg/day Protein: 1.2–1.5 g/kg/day	[23]
2	Alcoholic fatty liver or steatosis	Total energy: 25–40 kcal/kg/day including LES Protein: 1.0–1.5 g/kg/day, Carbohydrate: 50–60% ,Lipid 15–20% of total energy.	[23,24]
3	Alcoholic cirrhosis	Total energy: 25 kcal/kg/day in the presence of glucose intolerance. Protein: 1.2–1.5 g/kg/day including BCAA preparation.	[25,26]

2. Methods

The authors conducted a comprehensive search of electronic databases to locate all pertinent papers that were currently published. The published publications were obtained through and MDPI from accessible peer-reviewed journals. A search was performed using specific keywords relevant to ALD and nutritional therapy, including alcohol, alcoholic hepatitis, steatosis fatty liver, cirrhosis, and nutrient. Ethanol is a source of calories without any nutritional value, and long-term alcohol consumption without sufficient dietary intake can lead to

many nutritional diseases. Possible mechanisms of liver injury caused by alcohol include direct toxicity of ethanol to the liver, oxidation of lipids, increased oxidative stress, alterations in the composition of the gut microbiota, and activation of the immunological response.

3. Metabolic abnormalities caused by alcohol

3.1. Impaired glucose tolerance

Metabolic disorders, such as diabetes, have a key role in the progression of liver fibrosis and the development of hepatocellular carcinoma [18,27,28]. Alcohol stimulates the liver to produce more glucose, breaks down glycogen, and hinders the release of insulin from the pancreas. These effects collectively contribute to the development of diabetes mellitus [29]. Therefore, type 2 diabetes mellitus frequently occurs as a complication in people with ALD. The impact of moderate alcohol consumption on liver enzymes is positively correlated with higher body mass index (BMI) [30]. In recent years, there has been a rise in the occurrence of glucose intolerance linked to alcoholic fatty liver disease [31]. Research has shown that males with a body mass index (BMI) below 22 kg/m2 are more likely to acquire diabetes if they consume a moderate (23.0 g/day) or high amount of alcohol. Individuals who are susceptible to alcohol intake may exhibit suboptimal compliance with diabetes therapy, resulting in increased rates of illness and death among these individuals. Alcohol use might potentially cause negative effects during the treatment of diabetes. Alcohol has a higher likelihood of causing hypoglycemia when used with sulfonylureas. Consuming alcohol also heightens the likelihood of metformin-induced lactic acidosis.

3.2. Dyslipidemia

Around 30% of alcohol that is ingested is taken up by the body through the stomach, while the remaining 70% is absorbed by the jejunum. More than 90% of the absorbed alcohol is then carried to the liver through the portal vein. Alcohol is metabolised by three different systems: the alcohol dehydrogenase (ADH)-mediated system, the microsomal ethanol oxidising system (a non-ADH system), and the nicotinamide-adenine dinucleotide phosphate oxidase–catalase reaction system (also a non-ADH system) [32]. Chronic alcohol consumption stimulates the production of enzymes that enhance the breakdown of alcohol and aldehyde. Recent research has indicated that alcoholic fatty liver is influenced to some extent by the presence of CYP2E1 [33]. There is an increase in the release of free fatty acids (FFA) from fatty tissues outside the liver into the bloodstream, and any excess FFA is converted into triglycerides (TG) in the liver, leading to its accumulation. Alcohol metabolism worsens fatty liver by suppressing FFA β-oxidation in the mitochondria. In cases of alcoholic fatty liver, there is a decrease in the expression of microsomal TG transfer protein. This protein is responsible for releasing triglycerides (TG) from the liver into the bloodstream. As a result, there is an

imbalance in lipid synthesis and consumption in liver cells, which leads to the buildup of fat inside the liver. There is evidence suggesting that miRNAs play a role in the buildup of fat in the liver caused by ALD. Additional research is needed to fully investigate this relationship.

3.3. Excessive body weight or fat accumulation.

Within the population of patients diagnosed with ALD, 44.5% are classified as obese, whereas 32.4% have metabolic syndrome. These disorders have also been demonstrated to be autonomous prognostic variables in individuals with chronic liver disease, including ALD [34]. Moreover, the combination of obesity and alcohol intake has a synergistic effect on the development of liver cancer [35,36]. Research has shown that obesity lasting for more than 10 years is an autonomous risk factor for fatty liver, acute alcoholic hepatitis, and cirrhosis [37]. Adipose tissue inflammation and fatty liver are linked to the excessive consumption of alcohol. The development of alcoholic liver disease (ALD) may entail the release of adipokines by adipose tissue. An increase in adiponectin levels was found to be linked to more severe liver damage in patients with ALD [38]. It has been proposed that the buildup of fat around the organs may play a role in the advancement of ALD. Obesity, excessive accumulation of iron in the liver, and diabetes are additional risk factors that can independently contribute to fibrosis in alcoholic liver disease (ALD). These factors have significant therapeutic implications in the clinical treatment of ALD [39]. Recently, a new term called metabolic dysfunction-associated fatty liver disease (MAFLD) has been introduced to define fatty liver disease that is accompanied by metabolic dysfunction, regardless of the level of alcohol consumption [40,41]. Research on MAFLD has demonstrated that alcohol intake and metabolic disorders are separate variables linked to liver fibrosis and cardiovascular events, respectively [42]. Even a small amount of alcohol use in patients with MAFLD is linked to the deterioration of liver fibrosis [43]. Nevertheless, there is presently a lack of worldwide agreement on MAFLD, and this is a matter that needs to be taken into account.

4. Nutritional Therapy for ALD

4.1. Alcoholic Fatty Liver, also known as Steatosis

Similar to nonalcoholic steatohepatitis (NASH), a significant number of cases of alcoholic fatty liver (AFL) are further exacerbated by obesity resulting from excessive diet. In Nonalcoholic Steatohepatitis (NASH), the level of fat accumulation in the liver tissue is typically higher compared to Alcoholic Fatty Liver (AFL). At the beginning, there is a formation of microscopic droplets of fat around the central veins. As the disease advances, these droplets move to the periportal area. Alcohol-related liver disease (AFL) is present in 90% of individuals who consume alcohol heavily and can be resolved quite readily by abstaining from alcohol consumption. Excessive alcohol consumption causes fat to build up in liver cells by reducing the production of glucose,

blocking the breakdown of fatty acids, encouraging the production of fatty acids and triglycerides, and releasing fatty acids from fat tissue. Therefore, it is crucial for patients with alcoholic fatty liver (AFL) to abstain from alcohol and make changes to their lifestyle. The suggested diet for AFL is identical to that for NASH, consisting of 20–30 kcal/kg/day and 1.0–1.5 g/kg/day of protein. The diet should have a protein content of 20–25%, carbohydrate content of 50–60%, and total energy from lipids should be 15–20% with minimal intake of saturated fatty acids. Nevertheless, excessive and quick reduction in body weight might result in harm to the liver and encourage the buildup of fat in the liver. Consequently, it is advisable to aim for a weight loss of 1-2 kilogrammes each month [32]. Malnutrition diseases resulting from protein-energy malnutrition (PEM) manifest during the transition from alcoholic fatty liver to cirrhosis. Given the common occurrence of muscle mass loss caused by a lack of BCAA and the potential implications of hepatic encephalopathy, it is recommended to initiate nutritional support therapy promptly. According to the guidelines of the European Society for Clinical Nutrition and Metabolism, oral intake is more effective than tube or intravenous nutrition in improving the function of the intestinal mucosal barrier and preserving the intestinal flora in patients with AFL. This, in turn, reduces the likelihood of infection and mortality [37]. Consequently, the nutritional treatment for individuals with AFL should be determined according to the severity of liver damage.

4.2. Alcoholic cirrhosis

Cirrhosis is commonly linked to malnutrition, and the degree of malnutrition can be indicative of its severity. Individuals with alcoholic cirrhosis experience a catabolic state of starving at a faster rate compared to those without the condition. Alcoholic cirrhosis patients who abstain from eating overnight exhibit similarities to healthy individuals who undergo total starvation for a period of 2-3 days [44]. Patients with cirrhosis may experience a reduction in liver sugar supply and subsequent hunger if they fast for 10-12 hours. In everyday life, this refers to the hours of the evening and early morning. Patients with ALD and cirrhosis can benefit by reducing the time between meals and spreading them out over the course of the day. Furthermore, due to nutritional deficiencies in severe instances of alcoholic cirrhosis, the prevalence of obesity is lower compared to cases of fatty liver, even when the total amount of energy consumed exceeds expenditure. In addition, patients frequently have a body weight that is below the standard, even when taking into account their BMI. Pulmonary embolism (PE) is a frequently occurring complication in patients who are receiving invasive treatment for hepatocellular carcinoma or oesophageal varices.

The fundamental dietary intervention for cirrhosis remains consistent irrespective of the aetiology of the condition. Nutritional intervention is provided for those with PEM (serum albumin level ≤ 3.5 g/dL), Child–Pugh class B or C, or sarcopenia. This intervention includes consuming divided meals (3 to 5 meals per day), using LES (low energy supplements), and incorporating foods that include BCAAs (branched-chain amino

acids). If there is no improvement in the individual's nutritional status or if complications related to cirrhosis arise, it is recommended to rapidly initiate enteral nutrition for liver failure or formulas containing branched-chain amino acids (BCAA) [45]. LES may also be beneficial in enhancing the understanding of the aetiology of alcoholic cirrhosis. The use of BCAA-enriched enteral nutrition in patients with cirrhosis and liver failure is anticipated to elevate serum albumin levels and enhance long-term aberrations in energy metabolism, glucose tolerance, and quality of life. The needs for LES include:

(1) an intake of roughly 200 kcal;

(2) a well-balanced combination of carbs, lipids, and proteins; and

(3) consumption of foods that include branched-chain amino acids (BCAAs). Evening meals that are high in protein can make use of the body's anabolic processes during the night and potentially prevent the loss of muscle mass [46].

According to a study, consuming a blend of BCAAs orally for a long period of time is better than following a regular diet when it comes to increasing blood albumin levels and enhancing energy metabolism. Plasma free amino acid imbalances result in reduced amounts of branched-chain amino acids (BCAA), a fall in Fischer's ratio, or BTR, caused by elevated levels of aromatic amino acids and methionine. The liver metabolises aromatic amino acids and methionine, leading to an elevation in their blood levels as cirrhosis worsens. Branched-chain amino acids (BCAAs) are often broken down in peripheral tissues, such as muscle and adipose tissue. However, in the context of cirrhosis, hepatocytes serve as an energy source and play a role in ammonia metabolism, resulting in a decrease in their blood levels. BCAAs are insufficient even in cases of compensated cirrhosis, such as those classified as Child-Pugh grade A. On the other hand, when cirrhosis advances, the levels of tyrosine in the body increase, leading to a decrease in BTR [47].

There are two types of Oral BCAA formulations available: enteral nutrition for liver failure (or component nutrition for liver failure) and oral granules. Enteral nutritional formulations for hepatic insufficiency contain high levels of the branched-chain amino acids (BCAAs) valine (Val), leucine (Leu), and isoleucine (Ile). A standard dosage of 2-3 packets per day gives a daily intake of 11-17 grammes of BCAAs. These medications are prescribed to treat hepatic encephalopathy in patients with decompensated liver cirrhosis. Due to their inclusion of the essential elements of proteins, carbs, and fat, along with vitamins and minerals, they are prescribed not only to enhance hepatic encephalopathy but also to enhance nutritional well-being. The oral BCAA granule formulation consists solely of BCAAs, specifically Val, Leu, and Ile, at a ratio of 1:2:1.2 [48]. This treatment is recommended for individuals with noncompensated liver cirrhosis who have malnutrition and hypoalbuminemia, but do not have hepatic encephalopathy. Its purpose is to improve their condition. Patients should have the capacity to ingest an adequate amount of meals. A leucine-enriched BCAA mixture was administered to patients with alcoholic cirrhosis in a randomised experiment. This single dose corrected skeletal muscle signalling anomalies and improved the rate of muscle protein synthesis [49]. BCAA granules

shown a significant improvement in blood albumin levels over a timeframe of roughly 8 weeks. Additionally, these granules effectively alleviated symptoms such as edoema of the extremities, general malaise, weariness, and muscle cramps. The aforementioned advantages enhanced the standard of living in individuals with cirrhosis, diminished the occurrence of hepatic encephalopathy, and extended the average lifespan [50]. Implementing nutritional therapy, such as LES, for both short-term and long-term treatment of cirrhosis on an outpatient basis, has been found to enhance nutritional status and prognosis in patients with cirrhosis [51].

Nevertheless, obesity and the buildup of subcutaneous adipose tissue have negative implications for the prognosis of individuals with alcoholic cirrhosis. Therefore, it is crucial to customise nutritional therapy based on each patient's specific circumstances [52]. Alcoholic cirrhosis leads to a mixture of malnutrition and over nutrition, necessitating personalised treatment that involves monitoring the individual's nutritional state and providing nutritional advice. To prevent overfeeding, it is advisable to remove the energy provided by enteral nutrition (which is around 200 kcal) from the total energy intake for patients with liver failure. Without intervention, the inclusion of LES may worsen glucose intolerance [53]. The recommended energy intake is 25–35 kcal per kilogramme of standard body weight per day, assuming there is no glucose intolerance. When there is glucose intolerance, the recommended calorie intake is 25 kcal per kilogramme of body weight per day. Protein requirements, including BCAA preparations, should be based on 1.0-1.5 grammes per kilogramme of body weight per day, unless there is protein intolerance. Meanwhile, for those with protein intolerance, it is recommended to consume 0.5-0.7 grammes of protein per kilogramme of body weight per day, along with enteral nutrition that is rich in branched-chain amino acids (BCAAs), in cases of hepatic failure [28].

Research on enteral nutrition for cirrhosis has not demonstrated any advantages [54]. There is no evidence to support the use of short-term enteral feeding after treating oesophageal varices as advantageous [55]. In patients with cirrhosis, the placement of a percutaneous endoscopic gastrostomy tube is typically not recommended. However, it may be considered if there is no presence of ascites, however the decision to proceed with this procedure should be carefully evaluated [56]. A recent study has shown that introducing solid food early in the diet of conscious patients who have had successful closure of oesophageal varices is safe. The use of immediate nutrition led to improved nutritional status and a reduced occurrence of infection in individuals experiencing bleeding, as compared to delayed nutrition [57].

5. Natural Berberin Therapy

Berberine-Based Advance Drug Delivery System

Berberine is a natural compound extracted from several plants, including Berberis species, It is known for its potential benefits in managing conditions such as diabetes, high cholesterol, and liver diseases like steatosis and cirrhosis.

Berberine also formulated as sustained release formulations uses various techniques such as matrix systems, coated granules, and microspheres to control the release rate of berberine [58-60]

Berberine-sustained release formulations can be used in managing:

i. Type 2 Diabetes: By improving insulin sensitivity and reducing blood glucose levels.[61]
ii. Hyperlipidemia: By lowering LDL cholesterol and triglycerides.
iii. Liver diseases : Steatosis and Cirrhosis.

Table 2. Drug delivery methods and their outcomes

S.no	Drug delivery methods	Results	References
1	**Microparticles**		
	Microparticles in hollow capsular devices (in house 3D printed) via emulsion crosslinking method	Improve sustained and prolonged absorption with oral bioavailability enhancement.	62,65
2	**Nanoparticles/nano-crystals/nanocarriers**		
	Biogenic gold nanoparticles using Trapa bispinosa was developed	Active against folic acid expressing HeLa cells.	66
	Janus magnetic mesoporous silica nanoparticles based on Fe_3O_4 head for magnetic targeting and a mesoporous SiO_2 body for delivery of berberine.	Safe and effective against hepatocellular carcinoma.	67,68
	Janus gold mesoporous silica nanocarriers using folic acid	Triple-therapies strategies for liver cancer.	69
3	**Taste-masked microcapsules containing disintegrating tablets**		
	Orally disintegrating tablets containing microcapsule and coated with Eudragit E100.	Taste masking to improve patient compliance.	70

Some Examples of berberine sustained release Formulation techniques are

i. Matrix Tablets: Using polymers that form a gel-like matrix in the presence of gastrointestinal fluids, controlling the release of berberine.[62]

ii. Coated Pellets: Pellets coated with polymers that dissolve at different rates to achieve a sustained release effect.

iii. Microspheres: Small spherical particles that encapsulate berberine, allowing for controlled release.

To enhance its therapeutic efficacy and bioavailability, advanced drug delivery systems are being developed. Here's an overview of such systems: In Table 2 details on berberine-based advance drug delivery system was discussed. Various drug delivery approaches such as microparticles,[63] nanoparticles/nano-crystals/nanocarriers, and taste-masked microcapsules containing disintegrating tablets[64] were investigated to improve the solubility.

Summary

Nutritional interventions can be beneficial in managing alcoholics, especially individuals with alcoholic liver disease (ALD). Abstinence from alcohol is the primary and crucial treatment for ALD. Nonetheless, due to its high addictive nature, achieving sobriety can be challenging. ALD patients necessitate comprehensive care from a multidisciplinary team. Specifically, advanced ALD necessitates tailored nutritional intervention based on the stage of the disease.

In patients with acute hepatitis (AH), a diet rich in protein and energy should be given through the gastrointestinal tract, as long as there are no issues related to gastrointestinal haemorrhage. It is advised that AH patients ingest 1.2–1.5 grammes of protein per kilogramme of body weight and 35–40 kilocalories per kilogramme of body weight each day.

ALD progresses through these stages, with factors such as genetics, immune function, obesity, and diet influencing its development. Treatment relies on complete abstinence from alcohol, which improves outcomes at all ALD stages. ALD progression is complicated by metabolic issues like impaired glucose tolerance, dyslipidemia, and obesity.

Nutritional therapy is vital for ALD management. For alcoholic fatty liver, a balanced diet with controlled calorie intake and protein is recommended. In alcoholic cirrhosis, frequent meals and evening snacks can help prevent muscle loss. Patients with cirrhosis may require tailored nutritional support, including enteral nutrition and specific dietary supplements.

Overall, managing ALD involves comprehensive lifestyle changes, including dietary adjustments and alcohol cessation. Healthcare providers must assess patients' nutritional status and provide appropriate interventions to improve treatment outcomes and quality of life. Nutritional therapy, and balanced diets, plays a crucial role in managing ALD and mitigating its complications.

Advanced drug delivery systems, such as microparticles, nanoparticles, nanocrystals, nanocarriers, and taste-masked microcapsules with disintegrating tablets, are being developed to enhance berberine's therapeutic efficacy and bioavailability.

Conflicts of Interest: The authors declare no conflict of interest.

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