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A comprehensive review of the use of plant-derived antioxidants in the management of non-alcoholic liver toxicity

Shubham Verma[1], Akshay Thakur[2], Kaunava Roy[1], and Vir Vikram Sharma[1]

[1]*Department of Pharmacology, School of Pharmaceutical Sciences, CT University Ludhiana, 142024 Punjab, India.*
[2]*Department of Pharmaceutical Chemistry, School of Pharmaceutical Sciences, CT University Ludhiana, 142024 Punjab, India.*

Abstract

With its rising incidence, non-alcoholic fatty liver disease (NAFLD) has become a global health problem. Hepatic lipid buildup, inflammation, and oxidative stress result from complex interactions between metabolic, genetic, and environmental variables in the development of nonalcoholic fatty liver disease. The potential significance of antioxidants generated from phytochemicals in alleviating non-alcoholic liver damage has garnered substantial interest among the many treatment methods. The goal of this thorough review is to summarize and assess the body of research on the application of antiin in the treatment of non-alcoholic fatty liver disease. A comprehensive examination of peer-reviewed research from many databases demonstrates various phytochemicals with antioxidant characteristics and their possible effects on oxidative stress, inflammation, and hepatic lipid metabolism. Prominent phytochemicals such as curcumin, resveratrol, quercetin, silymarin, and green tea catechins are among those whose antioxidative mechanisms are included in the review. Preclinical and clinical research on these substances has revealed encouraging results, suggesting that they may be able to lessen inflammation and hepatic steatosis while also enhancing liver function. We investigate the molecular mechanisms underlying their protective benefits, including reduction of pro-inflammatory cytokines and modification of nuclear factor-erythroid 2-related factor 2 (Nrf2). The study also discusses the shortcomings and difficulties in the existing research, highlighting the necessity of more clinical trials, standardized dosing schedules, and research into the possible synergistic effects of mixing several phytochemicals. To present a fair picture of the therapeutic application of phytochemical antioxidants, safety issues, and possible negative effects are also included. This review emphasizes the potential use of plant phytochemical-derived antioxidants in the treatment of Non-alcoholic steatohepatitis, and non-alcoholic hepatic damage. To provide precise guidelines and maximize their therapeutic potential in the setting of non-alcoholic liver damage or liver toxicity, more investigation and clinical data are necessary.

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*Corresponding author's email: thakurakshay128@gmail.com

Introduction

Obesity, caused by high-fat diets, is a common cause of non-alcoholic fatty liver disease (NAFLD), which is becoming a universal cause of liver disease worldwide, particularly in Western countries. Despite its high prevalence, only a small proportion of affected individuals will become inflamed, followed by fibrosis and chronic liver diseases, and most patients only show simple steatosis. Various mechanisms have been proposed for liver damage, including endoplasmic reticulum stress, perturbation of autophagy, mitochondrial dysfunction, hepatocellular apoptosis, gut microbiota imbalance, dysregulation of microRNAs, genetic/epigenetic risk factors, and an increase in inflammatory responses. These proposed mechanisms allow for a variety of hits acting together on subjects to mediate and offer a more accurate explanation for the progression of NAFLD. (Huang et al., 2020) NAFLD management's US guidelines define steatosis with (Pouwels et al., 2022) ≥5% fat infiltration in imaging or histology and b) no alcohol, drug, or viral-induced steatosis. Patients may present with elevated liver enzymes and often have one or more components of the metabolic syndrome (MS) like systemic hypertension, dyslipidemia, insulin resistance, or overt diabetes. Visceral obesity is increasingly evidenced as a risk factor for NAFLD, and MS is a known risk factor in cardiovascular disease development (Pouwels et al., 2022). NAFLD is a spectrum of the disease characterized by hepatic steatosis when no other causes for secondary hepatic fat accumulation can be identified. It ranges from the more benign condition of non-alcoholic fatty liver to non-alcoholic steatohepatitis (NASH), which is at the more severe end of the spectrum. NAFLD may progress to fibrosis and cirrhosis (Chalasani et al., 2018). The complicated condition known as non-alcoholic fatty liver disease is impacted by a number of variables, including oxidative stress and other pathogenetic factors. A connection exists between the development of NAFLD and the lipotoxic liver damage caused by fatty acids and their metabolites. Hepatic cells are shielded from ROS damage by an antioxidant defense mechanism, which is impacted by both genetic and epigenetic factors. NAFLD can be effectively treated with a healthy diet and exercise regimen, however patient adherence is poor. Antioxidants like Vitamin E are also employed. Probiotics, prebiotics, nutrition, and faecal microbiota transplantation are emerging therapeutic techniques that target gut microbiota dysbiosis, and natural polyphenols have been suggested as a means of preventing and treating non-alcoholic fatty liver disease. In the future, precision medicine may assist in choosing the optimal course of therapy for a given patient by considering genetic or environmental epigenetic risk factors (Delli Bovi et al., 2021).

Pathophysiology

DNA methylation plays a significant role in the progression of NAFLD and liver fibrosis. These changes affect genes involved in glucose, lipid, or acetyl-coenzyme A metabolism, insulin-like signalling, and mitochondrial function. NASH accelerates epigenetic age by promoting changes in methylation associated with hepatic collagen content. An untargeted evaluation of DNA methylation in liver tissues of patients with NAFLD identified almost 70,000 differentially methylated CpG sites in patients with advanced liver fibrosis (F3-F4) compared to those with no or mild fibrosis (F0-F1). 76% of these sites were hypomethylated and 24% were hypermethylated in advanced liver fibrosis in NAFLD, with 7% of reported methylations correlated with gene expression levels (Kitamoto et al., 2015; Murphy et al., 2013).

DNA methylation is particularly involved in the activation of hepatic stellate cells and their differentiation to myofibroblast, which are crucial procedures for hepatic fibrogenesis. Changes in methylation of specific genes have been linked with these processes, with genes promoting fibrogenesis being hypomethylated and highly expressed, while genes inhibiting hepatic stellate cell activation are hypermethylated and lower expressed in the liver of patients with advanced fibrosis compared to those with mild disease. Hepatic alterations in DNA methylation may be associated with systemic

metabolic outcomes, such as decreased mRNA expression of PPARGC1A, a major regulator of mitochondrial biogenesis, and increased insulin resistance. A recent study focused on differentially methylated regions that form networks associated with the progression of NAFLD, identifying two important networks: one affecting cytoskeleton organization, transcriptional activity, and cell proliferation, and another associated with metabolic pathways (Sookoian et al., 2010).

Histone modifications are also important epigenetic changes that affect transcriptional activity and refer to several posttranslational procedures such as acetylation, phosphorylation, methylation, and ubiquitination. Acetylation status has been most vigorously studied and is considered the net result of histone acetylation by histone acetyltransferases (HATs) and histone deacetylation by histone deacetylases (HDACs), p300, a protein involved in the transcription of carbohydrate-responsive element-binding protein (ChREBP), is linked to the development of non-alcoholic fatty liver disease (J. Lee et al., 2017). Glucose-induced activation of p300 increases the transcription of ChREBP, stimulating lipogenic genes through histone acetylation. Tannic acid attenuates the effects of p300, reducing lipogenesis-related genes and improving NAFLD in mice. Inhibition of cdk4 protein reduces the formation of C/EBPα – p300 complexes, reducing liver steatosis and correcting age-associated liver changes. P300 may also be involved in the activation of hepatic stellate cells and their trans differentiation to myofibroblasts. Sirtuins, particularly Sirtuin 1 (SIRT1), regulate hepatic metabolism and insulin sensitivity. Deficiency of SIRT3 leads to insulin resistance, hyperlipidaemia, and steatohepatitis in mice (J. H. Lee et al., 2014). HDAC3, a member of human class I HDACs, is implicated with circadian metabolic rhythm and deletion leads to hepatic steatosis in mouse liver (Perakakis et al., 2020).

Type 2 diabetes, obesity, and MetS are major global health challenges with significant economic impact. Nonalcoholic fatty liver disease often co-occurs with other metabolic disorders, resulting in multiple health challenges and increased risk of serious clinical consequences. The term NAFLD has been proposed by an international expert panel to describe hepatic steatosis associated with metabolic dysfunction. Patients with NAFLD may be primarily under the care of non-hepatology specialists, and optimal patient care requires effective multidisciplinary collaboration and joint protocols (Lu et al., 2018). A combined approach of pharmacotherapy, lifestyle, and behavioral interventions is likely to be most successful due to the complex nature of metabolic disorders. Proactive assessment and rapid intervention of comorbidities by relevant specialist clinicians is necessary. Building on the chronic disease management approach for patients with T2DM or obesity is possible (N. Tanaka et al., 2019). Our understanding of the natural history and pathogenesis of NAFLD and NASH, focused efforts on new diagnostic and interventional approaches, and ability to deliver optimal multidisciplinary care provide opportunities to improve outcomes and reduce healthcare system impact (Cariou et al., 2021).

Antioxidants used for treatment of Non-alcoholic fatty acid damage / toxicity

Glutathione: Pharmacological aspects and implications for clinical use in non-alcoholic fatty liver disease

Although a few medications are being studied, there is currently no authorized treatment for the common liver illness NAFLD (Powell et al., 2021). Glutathione (GSH) is a tripeptide that is produced in the cytoplasm of cells and may exist in two different forms: reduced and oxidized. Because of its antioxidant properties, there has been conjecture on its potential therapeutic use in long-term conditions such as cancer, chronic liver illnesses, and neurological disorders. One of the most common is non-alcoholic fatty liver disease (NAFLD), which is defined by lipid build-up in hepatocytes without alcohol usage or other steatogenic causes. Hepatic steatosis, often referred to as non-alcoholic fatty liver, and its inflammatory progressive form, non-alcoholic steatohepatitis, which is linked to elevated oxidative stress and reactive oxygen species and ultimately results in liver fibrosis, are included in

the term. While oxidative stress plays a well-established pathogenetic role in many disorders, nothing is known about GSH's potential therapeutic benefit in these illnesses (Santacroce et al., 2023).

Impact of vitamin E on redox biomarkers in non-alcoholic fatty liver disease

In NAFLD pathogenesis, oxidative stress—an imbalance between the formation of reactive species and antioxidant defence—is essential. In order to evaluate the efficacy of therapies aimed at redox imbalances and reactive species, new experimental techniques are required. In NAFLD patients, the immunohistochemical identification of 4-HNE protein adducts has been verified (Podszun et al., 2020). In Western nations, non-alcoholic fatty liver disease is a prevalent liver ailment marked by excessive lipid buildup. Free radical-induced oxidation of macromolecules, especially lipids, appears to be a hallmark of NAFLD and NASH, according to data from human studies. In animal tests and liver biopsies, redox indicators can be affected by vitamin E, especially α-tocopherol. Clinical research indicates that NAFLD and NASH are associated with reactive species-mediated damage to macromolecules, primarily lipids. Patients with NAFLD may experience less oxidative stress if they take at least 200 I.U. of α-tocopherol daily (Podszun & Frank, 2021).

Effects of Oral Vitamin C Supplementation on Liver Health and Associated Parameters in Patients with Non-Alcoholic Fatty Liver Disease: A Randomized Clinical Trial

Nutrient deficiencies and excessive calorie consumption are important dietary risk factors that lead to non-alcoholic fatty liver disease (Chakravarthy et al., 2020). Antioxidant treatment together with lifestyle modifications are commonly used to prevent and cure NAFLD (Romero-Gómez et al., 2017). Due to a big experiment that shown vitamin E improves histological and biochemical aspects in people with non-alcoholic steatohepatitis (NASH) more efficiently than pioglitazone, vitamin E is now frequently suggested as an antioxidant (Sanyal et al., 2010). In primary and secondary preventive studies, vitamin E was found to raise insulin resistance, plasma triacylglycerol levels, and even death rates when given over two years (Bjelakovic et al., 2007; Musso et al., 2012). Compared to fat-soluble vitamin E, vitamin C, a water-soluble vitamin, is surprisingly safe when taken orally, even at 10–10 times the recommended daily limit (Khoshnam-Rad & Khalili, 2019). Prior research indicates that vitamin C in combination with other nutrients, such as vitamin E or resveratrol, may mitigate hepatic steatosis; nevertheless, the effect of vitamin C on liver function is yet unknown (Ivancovsky-Wajcman et al., 2019; Izdebska et al., 2017). Vitamin C is essential for preserving lipid homeostasis in hepatic and circulatory tissues, as evidenced by animal studies (He et al., 2021).

Potential role of inflammation in relation to dietary sodium and β-carotene with non-alcoholic fatty liver disease: A mediation analysis

Dietary salt consumption and non-alcoholic fatty liver disease have been linked independently in earlier research. Higher estimated 24-hour urine salt excretion and non-alcoholic fatty liver disease were shown to be significantly correlated in research utilizing data from the Korea National Health and Nutrition Examination Surveys. Greater dietary salt intake was associated with a higher frequency of non-alcoholic fatty liver disease (NAFLD) in young and middle-aged general adults, according to a Korean research. Greater dietary salt intake was shown to be positively correlated with NAFLD in the PREVEND cohort trial, with an OR per SD increase of 1.30 (95% CI: 1.21–1.41). For HSI-defined NAFLD, comparable outcomes were seen, with a matching OR and 95% CI of 1.40 (1.31–1.51) (Choi et al., 2016; Huh et al., 2015; van den Berg et al., 2019). There is an inverse relationship between dietary β-carotene consumption and non-alcoholic fatty liver disease, whereas dietary salt intake is associated with a higher risk of NAFLD. According to the mediation study, inflammation may be involved in this relationship, since a higher salt intake raises the risk of NAFLD by upregulating inflammation (Chen et al., 2022).

The association between non-alcoholic fatty liver disease and advanced fibrosis with blood selenium level based on the NHANES 2017-2018

There is a strong correlation between blood selenium levels and advanced liver fibrosis/NAFLD. NAFLD was regarded as a metabolic disorder up until that point (Nagy et al., 2016). The greatest risk condition was metabolic syndrome, which is characterized by elevated body mass index, a larger waist circumference, poor fasting glucose, and diabetes (Krausova et al., 2020). Furthermore, sedentary behaviour and inadequate physical activity were found to be independent risk factors for NAFLD in recent research (Khambu et al., 2018; Krausova et al., 2021). Smoking increases the risk of non-alcoholic fatty liver disease in obese rats by increasing insulin resistance, hepatic lipogenesis, and hypercholesterolemia (S. Tanaka et al., 2016). Furthermore, exercise helps lessen the oxidative damage brought on by ROS in NAFLD (G.-L. Song et al., 2018). Selenium has demonstrated a critical involvement in several disorders, particularly those related to metabolism (Y. M. Song et al., 2015). However, further research is still needed to fully understand the connection between selenium and NAFLD. Selenium has typically been acknowledged as an antioxidant that can slow the progression of NAFLD (Sun et al., 2018). By directly substituting high-fat diets (HBD) with more selenomethionine, Yang Yi and Seyedeh et al. discovered that high selenium exposure reduced liver steatosis, HOMA-IR, LDL/HDL-c, and TC/HDL-c ratios—all of which are aetiologies of non-alcoholic fatty liver disease in mouse models. Furthermore, the NAFLD mice model's elevated blood selenium and selenoproteins reduced inflammation, lipogenesis, lipid metabolism dysfunction, and oxidative stress. It also delayed the progression of simple steatosis to NASH, and even liver fibrosis and cirrhosis. Nonetheless, a number of clinical investigations revealed a favourable correlation between high selenium intake and NAFLD (Heo et al., 2016). Thus, we looked at the relationship between blood selenium levels and NAFLD in Americans that was identified by VCTE (Pant et al., 2023). The study found a favourable relationship between blood selenium levels and non-alcoholic fatty liver disease in the US population. Less selenium in the blood indicated a higher proportion of individuals with advanced liver fibrosis. The study found that when it comes to blood selenium, changes in selenium homeostasis rather than dietary selenium consumption are more likely to cause NAFLD and liver fibrosis. This suggests that the root cause of both NAFLD and liver fibrosis is an imbalance in selenium homeostasis (Liu et al., 2022).

Non-alcoholic fatty liver disease: The role of quercetin and its therapeutic implications

Because it can lead to liver problems including cirrhosis and hepatocellular cancer, non-alcoholic fatty liver disease is the most common chronic liver disease, with increased morbidity and death (Rafiei et al., 2017). To develop therapies for liver steatosis prevention, the molecular pathways driving lipid build-up, mitochondrial dysfunction, and increased oxidative stress inside hepatocytes are currently being researched (Dongiovanni et al., 2016). Through regulatory processes such as dietary lipids, lipogenesis, FFA absorption, and VLDL production, the liver maintains an equilibrium between fat input and outflow. Hepatic steatosis results from an excessive build-up of TG in liver cells caused by disruption of this homeostatic mechanism. Reactive oxygen species, fibro genic cytokines, and the recruitment of inflammatory cells are all factors linked to liver fibrosis (Tiniakos et al., 2010). In clinical practice, QE, a naturally occurring molecule with anticancer, anti-inflammatory, and antioxidant properties, has demonstrated encouraging outcomes. It is the flavonoid family's most potent free radical scavenger, preventing both non-alcoholic fatty liver disease and liver steatosis. Depending on its quantity and how it interacts with tissue cells, QE may have prooxidant and proapoptotic effects. It possesses strong antioxidative stress activity and inhibitory effects on hepatocyte apoptosis, inflammation, and ROS formation; its hepatoprotective function is still to be investigated. By lowering CYP2E1 levels and decreasing obesity-induced hepatosteatosis, it shields the liver against NASH. It also increases mitochondrial oxidative metabolism through heme oxygenase-1 and stimulates hepatic mitochondrial

oxidative metabolism through the Nrf-2 pathway (Sotiropoulou et al., 2021).

The effect of turmeric on lipid profile, malondialdehyde, liver echogenicity and enzymes among patients with non-alcoholic fatty liver disease: A randomized double-blind clinical trial

We conducted an RCT of the efficacy of turmeric on some parameters of lipid profile, oxidative stress, liver echogenicity and liver functional test (AST, ALT, and GGT) among NAFLD patients. Overall the results of our study showed that supplementation with turmeric extracts (2000 mg/day) could reduce serum levels of ALT and AST. (Jarhahzadeh et al., 2021) Elevated blood ALT and AST are conventional indicators of liver injury and usually measured in investigations on liver disease (Yam et al., 2007). As mentioned, a combination of insulin resistance, oxidative stress, lipid peroxidation and inflammation are involved in pathogenesis of NAFLD (Angelico et al., 2005; Mavrogiannaki & Migdalis, 2013; Samuel et al., 2004). Hence, any compound that controls all of these disorders could consider as a liver-protective compound. In the current research, supplementation with Turmeric significantly reduced serum levels of AST, ALT, and GGT. These findings were in agreement with two recent systematic reviews and meta-analyses that show the beneficial impact of turmeric and its active component, curcumin supplementation on reduction of serum ALT levels in subgroups with ≥ 1000 mg/day as well as serum levels of AST in studies with 8-weeks administration (Jalali et al., 2020; Mansour-Ghanaei et al., 2019). Moreover, another meta-analysis of 4 randomized controlled trials (RCTs) indicated a considerable effect of the curcumin supplementation on lowering AST levels compared to the placebo; while, there was no significant change in ALT blood concentrations following curcumin consumption (Z. Wei et al., 2019). Supplementation with turmeric extracts reduce elevated serum levels of ALT and AST among patients with NAFLD. Decreasing of these two enzymes could indicate improvement in liver function. Therefore, it could be considered as a good adjuvant therapeutic supplement with hypo lipidemic and antioxidant properties for this disease. However, more well-designed randomized clinical trials are needed to investigate other indicators of NAFLD. Furthermore, the beneficial role of curcumin in other liver diseases remained unclear due to the lack of trials on these populations (Jarhahzadeh et al., 2021).

Efficacy of resveratrol supplementation on liver enzymes in patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis

We conducted a systematic review (Darand et al., 2021) to evaluate the effectiveness and safety of resveratrol supplementation for improving liver enzymes in adults with NAFLD. Our results showed that resveratrol cannot effectively reduce AST and ALT concentrations compared with control. Results of subgroup analysis regarding AST revealed that resveratrol supplementation could significantly decrease AST levels in the participants with mean age <45 years, studies with intervention dosage <1000 mg/day, and participants with BMI < 30 kg/m^2. Also, it was observed that resveratrol supplementation significantly decreased the circulating concentrations of ALT levels with duration of follow up >12 weeks. Our findings were in line with recent meta-analysis which examined the effects of resveratrol in adults (Darand et al., 2021). In contrary to our study that only patients with NAFLD were included, they examined subjects with various diseases. Similar results can show that the efficacy of resveratrol is not affected by metabolic status and disease background. Numerous plant species contain the phytoestrogen resveratrol, which has anti-inflammatory and antioxidant qualities. Its anti-inflammatory, anti-aging, cardioprotective, and anti-platelet aggregation qualities have all been demonstrated in studies. Because of these characteristics, resveratrol has an encouraging potential for the management of non-alcoholic fatty liver disease by inhibiting the activity of liver enzymes. It has been shown that supplementing with resveratrol can effectively lower the blood concentrations of hepatic liver enzymes in NAFLD patients, such as ALT and AST (S. Wei & Yu, 2021).

Synergistic protective effects of lycopene and N-acetylcysteine against cisplatin-induced hepatorenal toxicity in rats

CP elicits anticancer effects by interacting with DNA and inducing programmed cell death. Multiple in vitro studies have demonstrated the cytotoxic effects of CP in different cell lines, but only a few in vivo studies have been performed (Ahmad et al., 2019; Alhoshani et al., 2017; Karale & Kamath, 2017; Kumburovic et al., 2019; Li et al., 2017; Rjeibi et al., 2018; Zhu et al., 2017). Our findings are consistent with the in vivo results of other studies, including the involvement of oxidative stress and apoptotic mechanisms in CP-induced hepatorenal damage and the potential use of LP and NAC as protective agents against CP-induced injury. Elevated activities of liver enzymes indicate cellular leakage and loss of functional hepatocyte integrity; the liver enzymes are released into the bloodstream when hepatocyte plasma membranes are impaired (Mohamed & Badawy, 2019). In this study, CP-induced hepatotoxicity was evidenced by significant alternations in serum liver enzymes (AST, ALT, and ALP). CP is taken up by the liver and accumulates in hepatocytes, causing cellular damage that eventually leads to increases circulating liver enzymes. In addition, CP elevated creatinine and urea levels, in agreement with previous studies (Abdel-Daim et al., 2019; Abo-Elmaaty et al., 2020; Elkomy et al., 2020). Elevated creatinine and urea levels are caused by reduced glomerular filtration rate. Moreover, the toxicity of the liver and kidney caused by CP to free radicals that generate in the cells of the liver and kidney, resulting in peroxidation of the lipid and consequently leads to oxidative stress that damage cells (Shahid et al., 2018). A derivative of vitamin A, lycopene (LP) possesses anti-inflammatory, immunostimulant, antibacterial, and anti-mutagenic qualities. It can stop the hepatoxicity and nephrotoxicity that come with chemotherapy, which can seriously harm the liver and kidney's tissue because of oxidative stress and apoptotic processes. By combining LP and NAC, one may significantly protect the hepatorenal system against oxidative stress and apoptosis caused by CP-mediated damage to the liver and kidney (Elsayed et al., 2021).

Efficacy and safety of dietary polyphenol supplementation in the treatment of non-alcoholic fatty liver disease

A systematic review and meta-analysis: NAFLD, a liver disease with a prevalence of 20%-30% in the general population and >25% in most Asian countries, is a complex disease regulated by various mechanisms such as glucose and lipid metabolism, genes, environment, and gut microecology (Pierantonelli & Svegliati-Baroni, 2019; Simental-Mendía et al., 2021). Researchers have been exploring the pathogenesis, prevention, and treatment of NAFLD, with the "second hit" hypothesis being widely recognized (Cobbina & Akhlaghi, 2017).This theory suggests that the pathogenesis of NAFLD is closely related to insulin resistance, which is the central link in the occurrence and development of NAFLD. Abnormal insulin signalling pathways and lipid metabolism disorders jointly promote the occurrence and development of NAFLD (Castera et al., 2019; Cotter & Rinella, 2020; Gallego-Duran et al., 2021; Manne et al., 2018). The major sites of P-oxidation of free fatty acids in the liver are mitochondria, microsomes, and peroxisomes. Insulin resistance and hyperinsulinemia promote the release of free fatty acids from peripheral adipose tissue into the liver (Yang et al., 2022), accelerate the utilization of free fatty acids by hepatocytes, and synthesize excess triglycerides in the liver. This leads to abnormal mitochondrial oxidative phosphorylation and lipid P-oxidation, abnormal triglyceride transport, and reduced low-density lipoprotein secretion, resulting in benign liver fat accumulation, called "simple fatty liver." Steatosis is a necessary condition for the development of NAFLD (Polyzos et al., 2019). The meta-analysis indicates that by lowering BMI, TG, TC, liver enzymes, and insulin resistance, polyphenol supplementation may be able to lower the risk of non-alcoholic fatty liver disease. The advantages vary depending on the kind of polyphenol. For example, curcumin (80–3,000 mg, 8–12 weeks) can successfully lower BMI, TG, TC, liver enzymes, and insulin resistance. On the other hand, silymarin (94–2,100 mg, 8–48 weeks) and

catechin (500–1,000 mg, 12 weeks) can also effectively lower liver enzymes. On the other hand, a smaller number of RCTs and no effectiveness were found for certain polyphenols, such as resveratrol, suggesting that further RCTs are required to assess their safety and efficacy (Carr et al., 2016).

Salubrious Effects of Green Tea Catechins on Fatty Liver Disease: A Systematic Review

Many studies have been conducted on the possible health benefits and therapeutic effects of green tea catechins, namely Epigallocatechin-3-gallate (EGCG), in non-alcoholic fatty liver disease. Green tea extract contains anti-inflammatory, antioxidative, and antilipidemic qualities. It is also high in flavonoids. Clinical investigations and animal models have demonstrated the substantial advantages of EGCG. It has also demonstrated favourable effects in type II diabetes, cancer, cardiovascular disease, and metabolic health (Esmaeelpanah et al., 2021). There are a few possibilities in clinical studies, but there are no FDA-approved treatments for NAFLD at this time (Wong & Singal, 2019). Exercise has been demonstrated to stop the advancement of NAFLD and NASH, which makes EGCG and GTE a safe and effective substitute Exercise helps stop NAFLD and NASH from becoming worse, however EGCG and GTE (green tea extract) could be safe substitutes for people who don't have much time or mobility. The liver may be protected against damage and inflammation by these antioxidants. Even while regular exercise has many health advantages that go beyond liver health, EGCG and GTE may have comparable protective effects on the liver, making them useful for people who are unable to exercise regularly. They may be thought of as supplemental or additional therapies to enhance liver function, but they shouldn't be used in place of exercise. Before making any changes to treatment or lifestyle, it is imperative to consult with medical professionals. (Abunofal & Mohan, 2022; Machado, 2021).

Role of N-Acetylcysteine in the Treatment of Acute Nonacetaminophen, Non-alcoholic and Nonviral Hepatitis: A Meta-analysis

This is the first comprehensive evaluation and meta-analysis assessing the efficacy of NAC in treating acute hepatitis brought on by non-viral, non-acetaminophen, and non-alcohol causes. According to the study, NAC had no beneficial effects on hospital stays, infectious complications, or mortality rates in individuals unrelated to acetaminophen, alcohol, or viral infection. As a mucolytic and in cases of acetaminophen overdose, NAC is now licensed for usage (Kolarov & Zvezdin et al., 2022). Since NAC is now the first-line treatment for acetaminophen toxicity and alcoholic hepatitis, NAC not included in the research (Dludla et al., 2020; Jyani et al., 2019). In cases where information is scarce, the research additionally looked at ischemic, post-liver transplant, hypoxia-induced, non-alcoholic, and post-liver transplant hepatitis (Andrade et al., 2019; Garcia-Cortes et al., 2020). NAC was included in the ACG guideline for addressing idiosyncratic drug-induced liver damage because of its favourable safety profile; nevertheless, definitive remedies are not provided (Darweesh et al., 2017). Larger trials are required, although the data do not support the usage of NAC. Although NAC has been investigated in several contexts, this meta-analysis does not support its utility (Aljohani et al., 2021).

Conclusion

The study emphasizes how phytochemicals including green tea catechins, curcumin, resveratrol, quercetin, and silymarin may be able to lessen the liver damage caused by NAFLD. The many antioxidative processes exhibited by these antioxidants impact several pathways, including the activation of nuclear factor-erythroid 2-related factor 2 and the reduction of pro-inflammatory mediators. The results imply that these antioxidants enhance liver function generally in addition to lowering hepatic steatosis. To close current information gaps, standardize dosing schedules, investigate synergistic effects, and comprehend long-term

safety profiles, further study is necessary. It is imperative to adopt a comprehensive strategy that includes dietary treatments, lifestyle adjustments, and antioxidants derived from plants. The knowledge gathered from this study underscores the need to carry out more research into the therapeutic potential of antioxidants derived from plants, as their incorporation into tailored treatment regimens for non-alcoholic fatty liver disease holds potential for long-term, easily obtainable, and integrative medicine-based liver health.

Authors contributions

M.R.M: Contributes to reference management. M.A.N: Contributed to reviewing & editing. All authors have Read & Agreed.

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Conflict of interest

The authors declare no conflict of interest.

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