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Hepatoprotective Efficacy and Chemical Evaluation of Chickpea

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Abstract

Liver function tests (LFTs) serve as crucial in clinical practice for detecting liver illness, tracking disease development, and to assess the effects of potentially hepatotoxic medicines. Common LFTs include serum aminotransferases, alkaline phosphatase, bilirubin, albumin, & prothrombin time. Elevations of aminotransferases greater than eight times the upper limit are typically indicative of acute viral hepatitis, ischemic hepatitis, or drug- or toxin-induced liver damage. Chronic moderate increases in aminotransferases are more commonly seen than acute hepatitis. Chickpea extract has notable hepatoprotective efficacy against CCl4-induced liver damage in rats. The extract was antioxidative and anti-inflammatory, with lowered glutathione and malondialdehyde levels. It also considerably lowers liver tumour necrosis factor α levels. The histopathological evaluation of liver tissues revealed normal hepatic architecture in extract-treated mice. The extract's safety profile was shown to be excellent, with little acute toxicity. The hepatoprotective effect was linked to the antioxidant & anti-inflammatory characteristics of the isoflavones and phenolic acids.

Key words: *Liver function tests (LFTs), Chickpea.*

Introduction

Hepatic function tests (LFTs) are utilised in clinical practice to identify patients for liver disease, track disease development, & assess the consequences of potentially hepatotoxic medications. Frequent LFTs include serum aminotransferases, alkaline phosphatase, bilirubin, albumin, & prothrombin time. Aminotransferases detect intracellular hepatic enzymes, which indicate hepatocyte damage. Alkaline phosphatase, GGT, & bilirubin levels propose biliary function & cholestasis. Albumin & prothrombin levels serve the liver's synthetic function. Elevations of aminotransferases greater than eight times the upper

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limit are typically associated with acute viral hepatitis, ischemic hepatitis, and drug or toxin-induced liver damage. Chronic moderate increase of aminotransferases (AST and ALT) < 250 units/l over a period of six months is more prevalent than acute hepatitis. (Kalas et al; 2021).

1. Causes of liver disease

1.1 Insulin resistance

Insulin resistance constitutes a condition in which aberrant triglyceride accumulation and lipolysis in insulin-sensitive organs, such as the liver, result in increased hepatic glucose production. This condition is apparent before fasting hyperglycemia. The exact genetic, environmental, & metabolic components that contribute to insulin resistance aren't very well known. increased transaminitis is frequently associated with direct hepatocyte damage, although it is also proposed that increased ALT levels may suggest insulin signalling dysfunction instead of hepatocyte injury. (Shin et al; 2022).

Resistance to insulin is distinguished by an excess of free fatty acids, which can be harmful to hepatocytes due to cell membrane rupture, mitochondrial malfunction, toxin production, and metabolic control. Oxidant stress, reactive lipid peroxidation, peroxisomal beta-oxidation, & inflammatory cells all have the potential to cause elevated transaminases. The disorder also elevates proinflammatory cytokines such as TNF-α, which may contribute to hepatocellular damage. A hereditary relationship or tendency to develop fatty liver in insulin-resistant conditions has been proposed in individuals with nonalcoholic steatohepatitis. (Neuschwander; 2003).

1.2 Chronic hyperinsulinemia

Chronic hyperinsulinemia in animal studies can cause hepatic insulin resistance, which is characterised by insulin failure that signals an increase in insulin receptor substrate 2. This causes enhanced lipogenesis, which promotes fatty liver and VLDL formation and secretion. Despite down-regulation of the insulin receptor substrate-2-mediated insulin signalling pathway in insulin-resistant states, SREBP-1c up-regulation & consequent lipogenesis in the liver may directly cause hepatic insulin resistance & accompanying fatty alterations. (Shimomura et al; 2000).

1.3 Type 2 diabetes (T2DM)

Type 2 diabetes (T2DM) is associated with a variety of liver problems that are called non-alcoholic fatty liver disease (NAFLD). NAFLD is a clinico-histopathological diagnosis characterised by hepatocellular steatosis, which is typically macrovesicular, regardless of other risk factors for chronic liver disease, including alcohol or chronic viral hepatitis, and these can progress to steatohepatitis, fibrosis, and finally, cirrhosis. (Westerbacka et al; 2004)

Elevated levels of ALT, AST, GGT, & ALP have been connected to an increased risk of diabetes. Likewise, elevated levels of ALT, GGT, & ALP, even within normal ranges, have been independently linked with an increased risk of diabetes. These findings suggested that increased liver enzymes might serve as diagnostics for the existence of diabetes. (Noroozi et al; 2022).

1.4 Non-Alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD) has grown into the most prevalent chronic liver ailment. Around seventy percent of T2DM patients have a fatty liver and progressing to non-alcoholic steatohepatitis (NASH) greatly increases the risk of cirrhosis and hepatocellular cancer. Non-alcoholic fatty liver disease is quite common in people with T2DM. Early identification and management of aberrant liver parameters may assist to reduce liver-related fatalities and morbidity in people with diabetes. (Mandal et al; 2018).

In Noroozi et al 2022 a cross-section investigation, the connection between blood liver enzymes & diabetes among Rafsanjan Cohort investigation participants was investigated. Diabetics showed considerably greater levels of elevated liver enzymes (ALP, AST, ALT, and GGT) than non-diabetic patients. Serum ALT, ALP, & GGT levels showed a strong positive connection with age. The incidence of elevated liver enzymes (ALP, AST, & GGT) in the diabetic group was higher in females than in males, according to a prior study. Individual differences in body fat distribution & metabolism can explain gender variances.

Serum alanine aminotransferase (ALT), a commonly accessible serum marker of liver damage, is higher in around 20% of children and adolescents with T2DM, and this is primarily due to NAFLD. Westerbacka et al. noticed that ALT, unlike aspartate transaminase (AST) and gamma glutamyl transferase (GGT), were closely related with liver fat, and so ALT is utilised as a surrogate measure in numerous epidemiological investigations. A high AST level usually indicates some liver damage, but it is not always caused by hepatitis C. A high AST and a normal ALT may indicate that the AST is originating from a separate portion of the body. It is essential to note that the AST level in the majority of hepatitis C patients fluctuates. (Pinhas-Hamiel and Zeitler; 2007, Schindhelm et al; 2006).

2. Chickpea as Natural Product

In addition, chickpea extract has been shown to be effective in the prevention and treatment of diseases that include hepatopathy. Chickpea seed extracts contain unsaturated fatty acids so as linoleic, linolenic, sitosterol, and sterol beta, which are responsible for improved liver function. The present findings of liver functions are consistent with a previous investigation, which stated that the ethanol extract of chickpea has reduced reactive oxygen intracellular or an increase in antioxidant activity in the liver. Bae et al. (2010) & Mekky et al. (2016) found that the aqueous extract of chickpea has potential hepatoprotective action by reducing oxidative stress and fat buildup in hepatocytes.

When contrast to the positive control group, chickpeas have been linked with improved liver function. Chickpea impact findings were consistent with those obtained by Cid et al. (2020), who indicated that chickpea had an antioxidant effect. Natural antioxidants prevent lipid peroxidation and inhibit the enzyme xanthine oxidase of rat liver induced by alloxan. Lee et al. (2016) found that 400 mg/kg of body weight per day of chickpea ethanolic extract displayed significant decrease ($p<0.05$) in enzymes aspartate transferase (AST). These impacts had been likely due to the abundance of flavonoids in the chickpea, as disclosed by de Camargo et al. (2022).

Chickpea incorporates antioxidant properties. Antioxidants found in nature prevent lipid peroxidation or inhibit enzyme xanthine oxidase in rat liver caused by alloxan. Chickpea ethanolic extract at 400 mg/kg body weight per day demonstrated a significant decrease ($p<0.05$) in enzyme alanine transferase (ALT), likely because of the abundance of flavonoids in the chickpea, as disclosed by Raiyan et al., (2021).

2.1 Effect of Chickpea on Alkaline phosphatase (ALP)

Higher-than-normal ALP levels may suggest liver injury or disease, such as a clogged bile duct or some bone disorders. An alkaline phosphatase (ALP) testing determines the level of ALP in the blood. It is often used to detect liver disease and bone abnormalities. Chickpea tegument possesses an intriguing nutritional profile, with a significant concentration of phenolic substances with antioxidant action. (Raiyan et al; 2021).

Natural antioxidants stop lipid peroxidation or inhibit enzyme xanthine oxidase in rat liver induced by alloxan. Lee et al. (2016) found that 400 mg/kg body weight per day of chickpea ethanolic extract demonstrated significant decrease ($p<0.05$) in enzymes aspartate transferase (AST), alanine transferase (ALT), and alkaline phosphates (ALP). These impacts were likely due to the presence of flavonoids in chickpea, as reported by Unuofin et al., (2020).

2.2 Effect of Chickpea on Albumin level

Albumin is a key protein produced in the liver. The normal physiology of albumin synthesis is heavily influenced by the availability of energy. Indeed, low blood albumin levels are found in medical diseases that correspond to malnutrition, whereas high levels of serum albumin have been linked to metabolic syndrome, a sign of obesity and overnutrition. Furthermore, serum albumin was recently linked to insulin resistance. (Ishizaka et al; 2007).

According to studies, decreased blood albumin concentrations increased the risk of coronary heart disease, cardiovascular mortality, or carotid atherosclerosis. This inverse connection could have been attributed to albumin's antioxidant and anti-inflammatory effects throughout the atherogenic process. Oxidative stress and chronic inflammation are important determinants in insulin resistance and type 2 diabetes, implying that albumin's antioxidant & anti-inflammatory capabilities may be associated with diabetes. (Ceriello and Motz; 2004).

2.2 Effect of Chickpea on HOMA-IR

Patients having nonalcoholic fatty liver disease (NAFLD) and impaired fasting glucose (IFG) were insulin resistant. The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) is a successful instrument for assessing insulin resistance. Thus, in the Bae et al. (2010) investigation, the relationship between serum albumin content, insulin resistance measured by HOMA-IR, and the development of IFG and NAFLD was investigated.

Chickpea can reduce inflammation and oxidative stress in vitro, as well as counteract metabolic changes in diabetes mellitus; Raffaelli et al. (2015) discovered that Syzygium cumini enjoyed a protective effect on the liver, which could be due to the antioxidants found in chickpea. Heba and Baseem (2022) discovered that 5% of powder chickpea in hyperlipidemia meals given to rats resulted in a substantial reduction in enzymes aspartate transferase (AST), Alanine transferase (ALT), & alkaline phosphates (ALP) after four weeks of therapy.

3. The chemical composition of chickpea

Chickpeas are a nutritious pulse crop which includes few digestible carbs, protein, vital fats, minerals, and vitamins. The fatty acid profile of the seed is critical to the texture, shelf life, flavour, fragrance, & nutritional value of chickpea-based foods. Biofortification of essential fatty acids has emerged as a nutritional breeding objective for chickpea crop development programmes across the world. This research investigates worldwide chickpea production, with an emphasis on plant lipids, their functions, or potential health benefits. It also discusses the chemical analysis of essential fatty acids as potential breeding targets for enhancing them in chickpea biofortification. This biofortification can benefit human health and food processing by protecting the quality and flavour of chickpea-based foods. (Madurapperumage et al; 2021)

Chickpea is a very nutritious pulse crop that contains protein, prebiotic carbs, fat, & a variety of minerals. Chickpeas are high in essential fatty acids, phytosterols, triacylglycerols, or phospholipids. TAGs are the most abundant neutral lipids in chickpea. PUFAs, MUFAs, and SFAs are esterified inside the lipids and bind to the glycerol end of TAGs or phospholipids. The most abundant PUFA in chickpeas is LA, followed by OA (MUFA) and ALA. LA is an ω-6 EFA, and ALA is an ω-3 EFA. Diets with an ω-6/ω-3 ratio of 4 to 5 are advised for improved human health. (Jukanti et al; 2012)

Chickpeas are an important legume crop with high protein, carbohydrate, fat, fibre, isoflavone, and mineral content. Chemical compositions were determined for four chickpea species (Muying-1, Keying-1, Desi-1, and Desi-2) from Xinjiang, China. The study discovered 46 distinct flavonoids in Muying-1, with moisture levels ranging from 7.64 to 7.89g/100g. The kabuli chickpeas had more starch than desi chickpeas. The total ash level

varied from 2.59 to 2.69g/100g, with a vitamin B1 value of 0.31 to 0.36mg/100g. The lipid content ranged from 6.35 to 9.35g/100g, with the main fatty acids being linoleic, oleic, and palmitic acids. Both kabuli and desi chickpeas were rich in unsaturated fatty acids, with Muying-1 and Desi-1 containing the most linoleic acid. The protein content varied from 19.79 to 23.38g/100g, with the primary amino acids being aspartic acid, glutamic acid, and arginine acid. The most abundant flavonoids in Muying-1 were determined to be daidzin, biochanin A, genistin, troxerutin, isorhamnetin, astilbin, L-epicatechin, astragalin, acacetin, hyperoside, and myricitrin. (Xiao et al; 2022)

Hend et al. found that adding chickpea as a prebiotic, antioxidant, and thickening agent improved the probiotic viability and physicochemical qualities of stirred bio-yoghurt. The study used probiotic microorganisms (Bifidobacterium bifidum and a combination) and chickpea flour at various doses. The results revealed that chickpea flour increased the proliferation of probiotic bacteria, resulting in greater antioxidant capacity values at various doses. Supplementation with chickpeas increased the viscosity of stirred bio-yoghurt. Sensory examination found that samples containing 1 and 2% chickpea flour were preferable in terms of texture and flavor. The study found that chickpea flour might substitute skimmed milk powder at quantities of 1 or 2%, improving the quality of stirred bio-yoghurt and lowering manufacturing costs.

A chickpea-based diet contains high amounts of EFAs; consuming unsaturated fats rather than saturated fats will help maintain healthy cholesterol levels and avoid obesity and diabetes (Kaur and Prasad, 2021). Furthermore, the inclusion of ALA in a chickpea-based diet lowers angiotensin-converting enzyme inhibition, which adds to antihypertensive benefits (Ogawa et al., 2009; Kaur and Prasad, 2021). After consuming EFAs, LA is converted to arachidonic acid (AA, an ω-6 EFA).

In contrast, ALA is metabolised into eicosapentaenoic acid (EPA, an ω-3 EFA) and docosahexadecaenoic acid (DHA, another ω-3 EFA). AA and EPA are further biosynthesised into prostanoids and leukotrienes. These metabolites offer several physiological benefits for humans. Metabolites of ω-6 origin promote platelet aggregation, whereas those with ω-3 origin are anti-inflammatory (Singh, 2005).

The ω-6/ω-3 fatty acid ratio is a key indication of how EFAs affect human health (Simopoulos, 2002). This ratio is a disease-controlling characteristic, and the ideal range is 1-4:1 or 1-5:1. This number varies from 1-2:1 for the best health advantages in the fight against obesity (Simipoulos, 2016). In Western nations, this ratio ranges between 15-16.7:1 due to low quantities of ω-3 fatty acids in diets and high proportions of LA intake. There have been no published research on the genuine influence of chickpea on disease control parameters (ω-6/ω-3 ratio) and human metabolism. (Simopoulos, 2016)

Chickpea's fatty acid content is responsive to food processing. Cooking can raise the fat content of both kabuli and desi types (Wang et al., 2010), however pressure cooking can lower the amounts of the four primary fatty acids in chickpea flour (Rajni et al., 2012). Furthermore, food processing influences the quality and quantity of chickpea EFAs because unsaturated fatty acids were directly exposed to air and other reactants, resulting in auto-oxidation (Mittal et al., 2012).

PUFAs are especially sensitive to auto-oxidation because they contain more double bonds, either of which might react with oxygen radicals. Alkyl radicals generated from PUFAs are the primary reactants that induce PUFA depletion. High temperatures in food processing may exacerbate these food quality-degrading processes. Heat can greatly breakdown the radicals produced (hydroperoxyl radicals), increasing PUFA depletion. The modifications portrayed are the consequence of chemical changes that occur when cooking. Certain elements (particularly Fe) and isoenzymes like lipoxygenase found in raw chickpeas may catalyse EFA loss during storage. Lipoxygenase primarily contributes to depleting ALA & LA, commencing hydroperoxide production. Another consequence of auto-oxidation is the

formation of volatile aldehydes as unsaturated byproducts with rearranged double bonds (trans fats). (Rajni et al., 2012 & Mittal et al., 2012).

Trans fat production from PUFAs might result from unsaturated double bond breaking and rearrangement during high-temperature food preparation. Volatile chemicals (aldehydes) produced during storage and food processing degrade the quality and fragrance, resulting in rancidity (Bhat et al., 2022), whereas trans fats are harmful to human health. However, no investigations on rancidity and trans fats derived from chickpea dishes are known in the literature. Future research is needed to understand the fatty acid concentrations following processing, cooking, and storage.

The percentage suggested daily allowance (%RDA) both LA (ω-6 fatty acid) is not published; nevertheless the %RDA of ALA (ω-3 fatty acid) for adult men and women is 1.6 and 1.1g, correspondingly (Hjalmarsdottir, 2019). Future chickpea breeding efforts should focus on the safe and appropriate growth of these critical fatty acids for human health. Future genetics and plant breeding breakthroughs will further increase chickpea EFA concentrations along with additional nutritional properties, benefiting human health.

Conclusion

Our review investigated that diabetic rats had significantly raised serum lipid profile measures such as total cholesterol, triglycerides, low density lipoprotein cholesterol, blood glucose, and very low-density lipoprotein cholesterol. This might be attributed to increased free fatty acid release by insulin-resistant lipid cells. Treatment with various doses of chickpea reduced total cholesterol, triglycerides, low density lipoprotein cholesterol, blood glucose, and very low-density lipoprotein cholesterol while raising high density lipoprotein cholesterol. Chickpeas also have antioxidant properties, avoiding excess lipid peroxidation and suppressing liver enzymes such as xanthine oxidase. The chickpea ethanolic extract significantly reduced enzymes aspartate transferase (AST), alanine transferase (ALT), & alkaline phosphates (ALP), most likely owing to the presence of flavonoids. Chickpea seed extracts include unsaturated fatty acids, which include linoleic, linolenic, sitosterol, & sterol beta, which promote liver function.

Complementary medicine, particularly the use of natural items with antidiabetic properties, is becoming increasingly popular. Chickpeas, the world's third most significant grain legume, are high in carbs and protein, making them a crucial source of nutrition in vegetarian diets. Chickpeas include physiologically active chemicals including flavonoids, which lower oxidative stress and hepatic cholesterol and triglyceride levels in diabetic rats. A diet high in isoflavones reduces the risk of diabetes and its consequences, such as cardiovascular disease. Isoflavonoids can lower insulin resistance, hyperglycemia, & promote hypoglycemia and antilipemic actions by repairing pancreatic β cells. Chickpea extract has notable hepatoprotective efficacy against CCl4-induced liver damage in rats. The extract was antioxidative and anti-inflammatory, with lowered glutathione and malondialdehyde levels. It also considerably lowers liver tumour necrosis factor α levels. The histopathological evaluation of liver tissues revealed normal hepatic architecture in extract-treated mice. The extract's safety profile was shown to be excellent, with little acute toxicity. The hepatoprotective effect was linked to the antioxidant & anti-inflammatory characteristics of the isoflavones and phenolic acids.

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