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Derleme Makalesi /Review Article

Hindiba Kahvesinin Lipit Biyobelirteçleri ve Kan Şekeri Regülasyonu Üzerine Etkileri: Derleme

Effects of Chicory Coffee on Lipid Biomarkers and Blood Glucose Regulation: A Review

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Öz
*"Cichorium intybus"*tan elde edilen hindiba kahvesi, lipid ve glikoz metabolizmasını düzenlemede umut vadeden bir potansiyele sahiptir. Özellikle hayvan modelleri üzerinde yürütülen klinik öncesi araştırmalar, hindiba kahvesinin düşük yoğunluklu lipoprotein (LDL) kolesterolü ve toplam kolesterolü etkili bir şekilde azaltırken aynı zamanda yüksek yoğunluklu lipoprotein (HDL) kolesterol seviyelerini yükseltebileceğini göstermektedir. İnsülin duyarlılığını artırma ve glisemik kontrolü iyileştirme yeteneği göstermiştir. Ancak, insan klinik deneylerinden elde edilen kanıtlar, özellikle kısa vadeli sonuçlar olmak üzere uzun dönem sonuçlarında da tutarlı değildir. Bu derlemede, hindiba kahvesi tüketiminin glisemik düzenleme ve lipit metabolizması üzerindeki etkileri, diyabet ve kardiyovasküler hastalıklarla ilişkili risk faktörlerle beraber değerlendiren çalışmalar incelenmiştir. Gelecekteki araştırmalar optimum dozajları belirlemeye, olası kronik toksisiteyi değerlendirmeye ve hindiba kahvesinin farklı yaş grupları ve popülasyonlar üzerindeki etkilerini incelemeye odaklanmalıdır. Bu tür çalışmalar, terapötik potansiyeli ve uzun vadeli güvenliği hakkındaki literatürdeki eksikleri tamamlayacaktır.
Anahtar Kelimeler: Hindiba, lipit biyobelirteçleri, kan şekeri düzenlemesi, kardiyovasküler sağlık, diyabet yönetimi

Abstract
Chicory coffee, obtained from *"Cichorium intybus"*, has promising potential in regulating lipid and glucose metabolism. Preclinical studies, especially in animal models, show that chicory coffee can effectively reduce low-density lipoprotein (LDL) cholesterol and total cholesterol while at the same time increasing high-density lipoprotein (HDL) cholesterol levels. It has shown the ability to increase insulin sensitivity and improve glycemic control. However, evidence from human clinical trials is less consistent, especially in short-term results and long-term. This review examines studies evaluating the effects of chicory coffee consumption on glycemic regulation and lipid metabolism, together with risk factors associated with diabetes and cardiovascular diseases. Future research should focus on determining optimal dosages, evaluating possible chronic toxicity, and examining the effects of chicory coffee on different age groups and populations. Such studies will fill the gaps in the literature regarding its therapeutic potential and long-term safety.
Keywords: Chicory, lipid biomarkers, blood glucose regulation, cardiovascular health, diabetes management

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INTRODUCTION

Low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels play a role in assessing the likelihood of diseases occurring in an individual's health status. Elevated LDL cholesterol levels contribute to the formation of plaques. Raise the chances of experiencing heart attacks and strokes[1]. On the other hand, HDL cholesterol might aid in lowering the risk of heart issues by eliminating surplus cholesterol from artery walls. Additionally, triglycerides serve as another indicator. Elevate the probability of developing coronary disease when detected at high levels in the bloodstream[2]. Treatments in medicine that target decreasing LDL and triglyceride levels have also been shown to lower the risk of events like heart attacks and strokes[3].
Blood sugar levels are recognized as another indicator of metabolic well-being in human bodies and their overall health status. Insulin resistance and difficulties in glucose regulation correlate with lipid markers. They are considered a factor in the development of type 2 diabetes and dyslipidemia. Several lipids in the blood often manifest as triglyceride levels, low HDL levels and LDL levels among individuals diagnosed with diabetes[4]. The lipid profile mentioned here raises the chances of heart disease in individuals with diabetes[5]. Research indicates that when glucose metabolism declines in the body, changes occur in the blood levels. Hence, improving blood sugar control can lead to a decrease in LDL and triglyceride levels and an increase in HDL levels in the bloodstream[6]. Contrary to that viewpoint, when glucose tolerance is impaired, it can impact lipid metabolism by developing insulin resistance.
Chicory roots have been utilized as a coffee substitute since the 16th century[7]. When the chicory plant is examined closely, it is found to contain inulin and various compounds such as sesquiterpene lactones like lactucin and lactucopyrin caffeic acid derivatives including acid and di caffeoyl tartaric acid, fats, proteins, flavonoids, alkaloids, steroids, terpenoids, oils, vitamins like alpha-tocopherol and gamma-tocopherol, beta carotene zeaxanthin along, with different minerals. Recent studies have shown that it contains a variety of elements[8]. What particularly stands out are the anti-inflammatory properties of the potent bioactive compounds present in it, which can combat free radicals and significantly reduce cell damage [9].

Fig 1. Chicory Plant (*C. Intybus*)

The fermentation byproducts of chicory that are considered prebiotics include short-chain fatty acids, which are thought to impact the activity of genes controlling liver enzymes in regulating energy metabolism. A study conducted in 2017 using pigs showed that, for the time being, incorporating dried root or inulin into their diet led to changes in the levels of cytoskeletal proteins in the liver[10]. Another study comparing chicory with caffeic acid and ferulic acid highlighted chicory's potential to boost insulin release and improve muscle glucose absorption without any effects on the liver[11].

Fig 2. Components of Chicory Coffee

The impact of the root on lipid biomarkers has sparked interest in its role in promoting cardiovascular health. Research indicates that chicory could help reduce LDL cholesterol and triglyceride levels for guarding against heart disease[12,13]. It has been noted that inulin, a prebiotic derived from chicory, can beneficially alter the metabolic syndrome parameters[14].
Factors in how chicory coffee affects lipid markers and blood sugar levels are at play. (Table 1).

Table 1. Mechanisms of Action of *C. intybus* on Lipid Biomarkers and Blood Glucose Regulation.

Mechanism	Pathway/Enzyme	Effects
Antioxidant Activity	Antioxidant enzymes (e.g., SOD)	↓ Oxidative stress[15,16]
	Nrf2 pathway	↑ Antioxidant protein expression[17]
Lipid Metabolism	HMG-CoA reductase	↓ Cholesterol synthesis[18]
	Lipoprotein lipase	↑ Clearance of triglycerides[19]
	ACAT (Acyl-CoA acyltransferase)	↓ Cholesterol esterification[20]
Glucose Regulation	AMPK (AMP-activated protein kinase)	↑ Glucose uptake by cells[21]
	GLUT4 (Glucose transporter type 4)	↑ Glucose transport into cells[22]
	GSK3 (Glycogen synthase kinase 3)	↓ Glycogen synthesis[23]
Inflammation Reduction	NF-kB pathway	↓Inflammatory cytokines[24]
	COX-2 (Cyclooxygenase-2)	↓Inflammatory response[25]

Effects of Chicory Components on Lipid Biomarkers

Including chicory in your diet as a supplement at doses of 5 to 20 grams per day can help lower levels by blocking the activity of enzymes, like HMG CoA reductase and acetyl CoA carboxylase (ACC) involved in making cholesterol and fatty acids production process. Reduced HMG CoA reductase activity also produces cholesterol while inhibiting ACC, which lowers levels. Additionally, chicory has been proven to lower the levels of a visfatin hormone, which is linked to insulin resistance and inflammation. Studies have noted an increase in the function of antioxidant enzymes like superoxide dismutase (SOD) and catalase that play a role in stress[26]. Research has shown that drinking coffee regularly can help lower oxidative stress markers like malondialdehyde (MDA) and increase levels of antioxidant enzymes such as SOD in the system. Consistent consumption of this coffee suggests protective advantages against heart and related conditions by improving endothelial function and reducing lipid peroxidation[27].

Studies in this field indicate that chicory polysaccharides (CPs) could potentially reduce the complications and progression of fatty liver disease (NAFLD) commonly associated with a diet high in fat. CPs are thought to mitigate fat accumulation in the liver by affecting the function of genes involved in metabolism and controlling inflammation levels. Moreover, they are believed to facilitate the breakdown of fatty acids and reduce inflammation markers well[28]. A study investigating chicory's effects on shielding the liver from harm induced by carbon tetrachloride (CCl_4) found that chicory helped indicators of liver damage such as serum ALT and AST levels[29].

A recent research study looked into the impact of tamoxifen on liver health in rats, as it is known to cause accumulation and worsened lipid levels when used as a chemotherapy drug. Also, chicory extract was given along with the medication group to see its effect on the rat's health parameters, such as serum triglycerides and cholesterol levels, and liver enzyme markers, such as ALT and AST. It was found that chicory extract led to improvements in these parameters, indicating a reduction in liver damage and fat accumulation, supporting the idea that chicory might offer protection against toxicity[30].

For 12 weeks, in a study involving 120 patients with cholesterol levels, regular chicory consumption resulted in lipid profile variations. This included a 15 per cent decrease in cholesterol levels and a significant 20 per cent drop in LDL levels[31]. Chicoric acid can enhance the antioxidant capacity in the liver by boosting the levels of antioxidant enzymes. It is believed that chicoric acid could help combat obesity by improving insulin sensitivity and controlling adipogenesis by regulating adipocytokines and proteins[32]. Chicory extract is known for its capacity to reduce cytokines like TNF alpha and IL 6. Moreover, it also contributes to effectively regulating the factor kappa B (NF kappa B) signalling pathway [33].

A research study examined how chicory extract may help to prevent liver damage in Wistar rats induced by oxymetholone (OM). The rats were split into six groups, including a control group, one group given OM (at 5 mg/kg), two groups administered with varying doses of *Cichorium intybuss* (at 100 or 200 mg/kg), and two groups that received both OM and *Cichorium intybuss.* After undergoing treatment for two weeks and observing changes in liver enzyme levels (AST, ALT, ALP), nitric oxide (NO) and total antioxidant capacity (TAO), as well as examining liver tissue histology, it was found that the OM treatment led to elevated levels of liver enzymes and NO while causing a decrease in serum TAC and changes in body weight. In contrast, the extract administration at both doses notably improved these OM-induced effects, indicating its potential to protect the liver[34].

In a research study conducted on rats by using an extract made from *Cichorium intybus* leaves mixed with alcohol (extract), the impact of this extract on liver damage due to obstructive cholestasis was explored after bile duct blockage in male Wistar rats for seven days at varying doses of 100 mg/kg/day, 200 mg/kg/day and 400 mg/kg/day respectively. The findings showed decreases in prothrombin time and levels of liver enzymes (AST and ALT). TNF alpha and nitric oxide also decreased significantly while serum albumin levels rose compared to the control group results; this suggests that the Cichorium extract effectively shields the liver against harm caused by cholestasis[35].

A different research looked into how the extract from Cichorium root affected liver disease caused by alcohol in Chang liver cells and male Sprague Dawley rats; silymarin was used as the comparison standard in this study of placebo treatment like before. The laboratory tests showed that cychorium did not harm the cells but increased their ability to move. The study results suggested a decrease in liver weight and blood alcohol levels alongside improvements in indicators of liver damage (such as GOT and GPT enzymes) levels and CYP2 E 21 enzyme activity. Furthermore, there was a rise in the functioning of alcohol processing enzymes ADG and ALDH found in Cichorium plants that may suggest its potential use as a treatment for alcohol-related liver harm[36].

The research involved patients suffering from burns treated with seed syrup in an experiment where they were unaware of the trial setup. Sixty individuals took part in the study. They were randomly split into two groups. One group was given seed syrup and placebo capsules; the other group received placebo syrup and capsules with silymarin. Lab tests were conducted over four weeks throughout the study duration. Upon the trial period ending, there were no differences were observed in the levels of liver enzymes between the two groups. Interestingly, both groups showed a decrease in their liver enzyme levels by day 15 compared to the measurements[37].

Including chicory resulted in serum ALT, AST and ALP levels compared to the control group, indicating improved liver function. Additionally, the study found a decrease in stress markers, as shown by MDA levels and higher GSH levels, in the group treated with chicory. Moreover, examinations of liver tissue showed signs of necrosis and inflammation in rats given chicory, suggesting that chicory could offer protection against liver damage, possibly because of its antioxidant properties[38].

In their study, the researchers examined inflammation markers such as C reactive protein (CRP). Also measured IL 6 levels afterwards. The end of the study period showed that consuming coffee reduced overall cholesterol levels and indicators of inflammation. Significant decreases were observed in both total cholesterol and triglyceride levels alongside lower levels of CRP and interleukin IL-6. These results imply that chicory coffee is anti-inflammatory and could benefit lipid metabolism[39].

Influence of Chicory on Glucose Levels and Insulin Response

Extensive research was conducted to explore how *Cichorium intybus* affects metabolic factors related to diabetes, including inflammation levels and blood sugar control in both humans and animals across 23 studies analyzed in the review report findings favourably impacting blood sugar management with a majority of studies and showcasing improvements, in lipid profiles as well. The studies mentioned all indicated a reduction in stress and inflammation, indicating that *Cichorium intybust* may have the ability to enhance metabolic health in individuals with diabetes; however, further investigations are needed to understand the underlying mechanisms at work [40].

Caffeoylolquinic acids (CQA) are crucial for plant production and impact human glucose metabolism. In their study, they were studied to understand their effects on hepatic glucose production in research. The study indicated that three specific di caffeoylquinic acids were able to reduce the activity of enzymes involved in Gluconeogenesis, such as glucose phosphorylase (G) and phosphoenolpyruvate carboxykinase (PEPCK) in rat liver cells. It has been observed that there are connections between the PI3K and MAP kinase pathways that regulate gene expression. They suggest that caffeoylquinic and caffeic acids collaborate to improve function and cellular metabolism by boosting phosphorylation and proton leakage[41].

Several research studies were carried out on an extract derived from seeds containing acid, which demonstrated significant improvements in regulating blood sugar levels during experiments conducted on rats by scientists. The researchers administered chicoric acid extract (NCRAE) doses at 200 mg/kg and 400 mg/kg to evaluate its impact on insulin sensitivity and different metabolic aspects such as glucose and lipid levels. The results indicated enhancements in the body's response to insulin and reductions in fasting blood sugar levels. Moreover, there have been alterations in the way the body handles fats in the form of lipids. These findings highlight the application of acid to address metabolic conditions[42,43].

Another study delved into the impact of Cichorium on hepatic nuclear factor kappa B (NF kappa B), inhibitor of kappa B kinase beta (IKKβ) and serum tumor necrosis factor alpha (TNF alpha) levels in rats with streptozotocin-induced diabetes. The research revealed that Cichorium was able to reduce inflammation related to diabetes by affecting the NF kappa B signalling pathway and decreasing TNF alpha levels. This finding suggests that it may offer benefits in managing complications associated with diabetes[44].

In a research trial investigating seed water extract for alcoholic fatty liver disease (NAFL), 60 participants were randomly assigned to receive either the extract or a placebo for 12 weeks. The findings revealed reductions in body mass index (BMI), liver enzyme levels, and fasting blood glucose among the treatment group using the seed extract as a remedy to improve metabolic factors linked to NAFL based on statistically significant results [45].

In a study involving 50 individuals diagnosed with metabolic syndrome and taking extract for 8 weeks, positive outcomes were observed; reductions in waist circumference and triglyceride levels alongside enhancements in insulin sensitivity were noted among the participants. This indicates that chicory extract may have the potential to manage metabolic syndrome[46]. Additionally, research hints at the benefits of chicory polysaccharides in addressing metabolic issues linked to obesity. According to research findings, individuals with obesity who took supplements showed improvements in insulin sensitivity and lipid profiles suggestive of overall metabolic health[47].

CONCLUSIONS

Recent research indicates that chicory coffee may play a role in improving heart health by influencing cholesterol levels and blood sugar regulation. Some studies suggest that consuming chicory coffee could help reduce LDL cholesterol and enhance insulin sensitivity for blood sugar control. While these findings are promising, extensive research is required to confirm their validity. Moreover, the long-term effects and potential adverse reactions associated with chicory coffee consumption have not been thoroughly explored, underscoring the necessity for more comprehensive investigations in this field.

Chicory coffee could serve as an addition for individuals managing dyslipidemia and glucose regulation concerns in terms of health benefits. Incorporating this product into dietary recommendations could significantly reduce the incidence of metabolic disorders like heart disease and diabetes; however, additional evidence is needed to ensure its effective implementation in practical settings. Understanding this area effectively involves conducting randomized controlled trials to evaluate the long-term health impacts of coffee on various populations. It is essential to investigate the mechanisms through which chicory coffee exerts its effects to establish dosages and confirm its efficacy for therapeutic applications.

Main Points: This study explores the effects of coffee on lipid markers and blood sugar regulation with an emphasis on its health benefits. The findings indicate that chicory coffee can lower LDL cholesterol and triglyceride levels, improving lipid profiles and decreasing heart disease risks. Additionally, the natural compounds found in chicory, such as inulin and caffeoylquinic acids, are known to play a role in these health advantages by boosting insulin sensitivity and managing blood glucose levels, which can have positive effects overall. As a result of metabolic health, coffee's benefits as a functional beverage option are considered to have potential advantages in managing lipid levels and enhancing glycemic control.

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