Investigation Of The Antidiabetic Activity Of Cnicus Benedictus L. In Rats

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Abstract

Cnicus benedictus L.*, commonly known as Blessed Thistle, has been traditionally used in herbal medicine for its diverse pharmacological properties. This study investigates the antidiabetic activity of* Cnicus benedictus L. *in rat models, focusing on its potential to regulate blood glucose levels, improve insulin sensitivity, and mitigate diabetes-related oxidative stress. The bioactive compounds of the plant, including flavonoids and sesquiterpene lactones, are hypothesized to play a pivotal role in these effects. Experimental studies on diabetic rats demonstrated significant reductions in fasting blood glucose and improvements in lipid profiles, with additional evidence of antioxidant and anti-inflammatory activity. These findings highlight the therapeutic potential of* Cnicus benedictus L. *as a natural alternative for diabetes management. However, further research, including clinical trials, is essential to establish its efficacy, safety, and mechanisms of action in humans. The present study aimed to evaluate the efficacy of the Cnicus benedictus leaf methanolic extract (CBHE) in reducing the growth of cervical cancer cells (Hela cancer cell line). Methods: The extraction was achieved using the Soxhlet apparatus. The study utilized a human cervical cancer cell line for antiproliferative evaluation and a human fibroblast cell line for toxicity assessment on normal cells. The incubation periods were 24 and 72 hours, and the concentration of the extract varied between 0.1 and 1,000 µg/ml. Results: The study exhibits that the methanolic extract of Cnicus Benedictus leaves can lessen the growth of human cervical cancer cells. The growth inhibition of the extract was dependent on the concentration and time, with the highest inhibition rate seen at 1,000 µg/ml after 72 hours of incubation. The study also revealed that the extract had minimal impact on the growth of normal cells. Conclusion: The study shows that Cnicus Benedictus leaves methanolic extract has ability to inhibit the growth of human cervical cancer cells in vitro. The extract cytotoxic behavior was (cell cycle and cell non-cycle) specific. The research also found that the extract selectively kills cancer cells rather than normal cells, indicating its safety in their effectivity.*

Keywords : *Antidiabetic Activity , Cnicus Benedictus L.*

INTRODUCTION-

Diabetes mellitus is a chronic and multifaceted metabolic disorder that has emerged as one of the most pressing global health challenges of the 21st century. Characterized by sustained hyperglycemia resulting from impaired insulin secretion, insulin resistance, or a combination of both, diabetes affects millions worldwide, with its prevalence projected to rise significantly in the coming decades. Beyond hyperglycemia, diabetes is associated with disruptions in carbohydrate, lipid, and protein metabolism, often leading to severe long-term complications, such as cardiovascular diseases, neuropathy, nephropathy, and retinopathy. These complications not only diminish patients' quality of life but also place a substantial burden on healthcare systems.Current therapeutic approaches for diabetes include oral hypoglycemic agents, insulin therapy, and lifestyle modifications. While these strategies are effective in many cases, they are often associated with limitations, such as side effects, high costs, and suboptimal glycemic control in certain populations. Furthermore, some pharmacological agents can exacerbate comorbidities or induce weight gain, prompting a growing interest in safer and more accessible alternatives. The exploration of natural products, particularly those derived from medicinal plants, has gained momentum as a promising avenue for diabetes management.One such plant, *Cnicus benedictus L.* (Blessed Thistle), has attracted significant attention due to its extensive historical use in traditional medicine. Belonging to the Asteraceae family, *Cnicus benedictus L.* is native to the Mediterranean region and has been widely utilized for its purported therapeutic properties, including anti-inflammatory, antimicrobial, and hepatoprotective effects. The plant's phytochemical profile is rich in bioactive compounds, including flavonoids, sesquiterpene lactones (such as cnicin), polyphenols, and tannins. These constituents are known to possess antioxidant and anti-inflammatory activities, which are particularly relevant in the context of diabetes, a disease strongly associated with oxidative

stress and chronic low-grade inflammation.Recent preclinical studies using animal models, particularly rats, have suggested that *Cnicus benedictus L.* exhibits antidiabetic activity through multiple mechanisms. These include the enhancement of insulin sensitivity, modulation of glucose metabolism, and attenuation of oxidative damage. Rat models of diabetes, induced through chemical agents such as streptozotocin (STZ) or alloxan, provide an invaluable platform for evaluating the therapeutic efficacy and safety of plant extracts. Such models mimic various aspects of human diabetes, allowing researchers to investigate the biochemical and molecular pathways involved in glucose regulation and insulin action.The antidiabetic potential of *Cnicus benedictus L.* aligns with the broader trend of exploring ethnomedicinal plants as sources of novel therapeutic agents. However, translating preclinical findings into clinical applications requires a deeper understanding of the plant's mechanisms of action, optimal dosages, and potential side effects. Moreover, the standardization of plant extracts and rigorous validation through clinical trials remain critical challenges.This review aims to provide an in-depth analysis of the antidiabetic properties of *Cnicus benedictus L.*, focusing on evidence from rat models. By examining the phytochemical composition, mechanisms of action, and experimental outcomes, this review seeks to highlight the potential of *Cnicus benedictus L.* as a complementary or alternative treatment for diabetes. Additionally, it addresses the current limitations in research and underscores the need for further studies to establish its clinical relevance.

Importance of exploring natural remedies :

Diabetes mellitus is a global health concern with increasing prevalence and associated complications, including cardiovascular diseases, neuropathy, and nephropathy. Conventional treatments, such as synthetic antidiabetic drugs, effectively manage blood glucose levels but are often accompanied by adverse effects, including hypoglycemia, gastrointestinal disturbances, and long-term toxicity. Additionally, the high cost of these treatments poses a challenge for accessibility, particularly in low- and middle-income countries.Natural remedies, derived from medicinal plants, offer a promising alternative in the quest for safer, more affordable, and accessible diabetes management options. These remedies often contain bioactive compounds with multiple therapeutic properties, such as antioxidant, anti-inflammatory, and insulin-sensitizing effects, which address not only hyperglycemia but also its underlying causes and complications.Exploring plants like *Cnicus benedictus L.*, which have a history of use in traditional medicine, can provide valuable insights into novel mechanisms of action. By studying their efficacy in preclinical models, such as rats, researchers can lay the groundwork for developing plant-based antidiabetic therapies that may complement or replace synthetic drugs. This approach also supports the conservation of biodiversity and the integration of traditional knowledge into modern healthcare practices, fostering innovation in drug discovery.

Phytochemical Profile of *Cnicus benedictus L:*

Cnicus benedictus L. (Blessed Thistle) is a medicinal plant with a rich phytochemical composition that contributes to its therapeutic potential, including antidiabetic properties. Key phytochemical constituents of *Cnicus benedictus L.* include:

1. Flavonoids

Flavonoids such as luteolin and apigenin are abundant in *Cnicus benedictus L.*. These compounds exhibit antioxidant, anti-inflammatory, and hypoglycemic effects by scavenging free radicals, reducing oxidative stress, and modulating glucose metabolism.

2. Sesquiterpene Lactones

The primary sesquiterpene lactone present is cnicin, known for its anti-inflammatory and antidiabetic properties. Sesquiterpene lactones have been shown to improve insulin sensitivity and inhibit pro-inflammatory pathways associated with diabetes.

3. Phenolic Acids

Cnicus benedictus L. contains phenolic acids such as chlorogenic acid and caffeic acid, which possess strong antioxidant activities. These compounds help reduce oxidative damage, a key contributor to diabetes complications.

4. Alkaloids

Alkaloids found in *Cnicus benedictus L.* exhibit mild hypoglycemic effects by influencing carbohydrate metabolism and enhancing glucose utilization.

5. Essential Oils

The essential oils derived from *Cnicus benedictus L.* contain a variety of volatile compounds that contribute to its bioactivity. Some constituents of the oil may have indirect roles in enhancing metabolic functions.

6. Tannins

Tannins in *Cnicus benedictus L.* exhibit astringent properties and may assist in managing postprandial blood sugar levels by modulating digestive enzyme activity.

7. Other Bioactive Compounds

Additional compounds such as sterols, lignans, and saponins contribute to the plant's overall pharmacological profile, further supporting its antidiabetic potential.The combination of these bioactive compounds provides a synergistic effect, making *Cnicus benedictus L.* a promising candidate for diabetes management. Further research is warranted to isolate and characterize these compounds for targeted therapeutic applications.

Mechanisms of Antidiabetic Activity :

Cnicus benedictus L. exhibits its antidiabetic effects through multiple biological mechanisms, as observed in experimental studies with rat models. These mechanisms include:

1. Regulation of Blood Glucose Levels

- The bioactive compounds in *Cnicus benedictus L.*, such as flavonoids and sesquiterpene lactones, enhance glucose uptake by peripheral tissues, aiding in blood glucose control.
- These compounds may inhibit intestinal glucose absorption by modulating carbohydrate-digesting enzymes like α-amylase and α-glucosidase.

2. Improvement in Insulin Sensitivity

- *Cnicus benedictus L.* potentially improves insulin receptor sensitivity, allowing better glucose utilization.
- It may upregulate insulin signaling pathways, enhancing glucose transport in muscle and liver cells.

3. Reduction of Oxidative Stress

- Diabetes induces oxidative stress, leading to beta-cell damage and insulin resistance.
- *Cnicus benedictus L.* is rich in antioxidants that neutralize free radicals, protecting pancreatic beta-cells and improving insulin secretion.

4. Anti-inflammatory Effects

- Chronic inflammation is a hallmark of diabetes.
- Compounds in *Cnicus benedictus L.* have been shown to reduce pro-inflammatory cytokines such as TNF-α and IL-6, mitigating inflammatory responses associated with insulin resistance.

5. Lipid Profile Improvement

- Dyslipidemia is a common complication in diabetes.
- *Cnicus benedictus L.* has demonstrated the ability to lower triglycerides, LDL cholesterol, and increase HDL cholesterol, contributing to overall metabolic balance.

6. Enhanced Pancreatic Beta-cell Function

- It may aid in the regeneration of damaged beta-cells in the pancreas, enhancing endogenous insulin production.
- Reduced oxidative damage supports long-term beta-cell viability.

7. Modulation of Gut Microbiota

- Preliminary evidence suggests that the plant may influence gut microbiota, creating an environment conducive to glucose metabolism and insulin sensitivity.

Animal Studies: Evidence from Rat Models :

Most animal studies involved inducing diabetes in rats using agents like alloxan or streptozotocin (STZ), which mimic the pathophysiology of type 1 or type 2 diabetes. After diabetes induction, rats were treated with various doses of *Cnicus benedictus L.* extracts (e.g., aqueous, ethanolic, or methanolic) over a specific period. Parameters measured included:

- Fasting blood glucose levels.
- Glucose tolerance (via oral glucose tolerance tests).
- Lipid profiles (triglycerides, LDL, HDL, total cholesterol).
- Insulin levels and insulin resistance indices.
- Antioxidant enzyme activity (e.g., superoxide dismutase, catalase).
- Histopathological examination of pancreatic tissues.

2. Hypoglycemic Effects

Studies demonstrated significant reductions in fasting blood glucose levels in diabetic rats treated with *Cnicus benedictus L.* extract compared to untreated diabetic controls. The hypoglycemic effect was dose-dependent, with higher doses producing more pronounced reductions in glucose levels. Improvements in glucose tolerance were also observed, suggesting enhanced insulin sensitivity.

3. Antioxidant and Anti-inflammatory Activity

Diabetes is associated with oxidative stress and chronic inflammation, which contribute to its complications. Extracts of *Cnicus benedictus L.* were shown to increase the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase. These effects reduced oxidative damage in pancreatic tissues and improved overall metabolic health.

Anti-inflammatory effects were evidenced by reductions in pro-inflammatory cytokines like TNF-α and IL-6 in treated rats, suggesting a protective role against inflammation-induced beta-cell dysfunction.

4. Lipid Profile Improvements

Rats treated with *Cnicus benedictus L.* extracts exhibited improved lipid profiles, characterized by decreased levels of LDL and triglycerides and increased HDL levels. This indicates a potential role in managing dyslipidemia commonly associated with diabetes.

5. Histopathological Findings

Examination of pancreatic tissues revealed that *Cnicus benedictus L.* treatment preserved the structural integrity of pancreatic beta cells in diabetic rats. This suggests a regenerative or protective effect against diabetes-induced beta-cell damage.

6. Safety and Toxicity

Acute and sub-chronic toxicity studies in rats showed that *Cnicus benedictus L.* extracts were well-tolerated at therapeutic doses, with no significant adverse effects on liver or kidney functions.

Future Directions and Challenges :

Future Directions:

1. **Human Clinical Trials:**
   While preclinical studies in rats have demonstrated promising antidiabetic effects of *Cnicus benedictus L.*, human trials are crucial to confirm its efficacy, optimal dosage, and safety profile.
2. **Mechanistic Studies:**
   Further research is needed to elucidate the precise biochemical and molecular mechanisms underlying its antidiabetic effects, including its impact on insulin signaling pathways, glucose metabolism, and pancreatic beta-cell function.
3. **Standardization of Extracts:**
   Developing standardized formulations of *Cnicus benedictus L.* with consistent concentrations of active compounds will enhance its reproducibility and therapeutic reliability.
4. **Combination Therapies:**
   Investigating the potential synergistic effects of *Cnicus benedictus L.* with conventional antidiabetic drugs or other natural agents could offer innovative strategies for managing diabetes.
5. **Long-term Safety Studies:**
   Assessing the chronic toxicity and long-term impact of *Cnicus benedictus L.* on vital organs in both animal models and humans is essential to ensure its safety.
6. **Exploration of Bioavailability:**
   Studies focusing on improving the bioavailability and pharmacokinetics of its bioactive compounds, such as through nanotechnology or encapsulation methods, could optimize its therapeutic potential.

Challenges:

1. **Variability in Plant Composition:**
   The phytochemical composition of *Cnicus benedictus L.* can vary significantly depending on geographic origin, growing conditions, and extraction methods, posing challenges to standardization.
2. **Lack of Comprehensive Toxicological Data:**
   Although preliminary studies indicate its safety, comprehensive toxicological evaluations, including genotoxicity and reproductive toxicity studies, are limited.
3. **Regulatory Hurdles:**
   Bringing *Cnicus benedictus L.*-based formulations to the market requires navigating complex regulatory frameworks, which can be time-consuming and resource-intensive.
4. **Limited Funding for Herbal Research:**
   Compared to synthetic drugs, herbal medicine research often receives limited funding, slowing the pace of development and clinical validation.
5. **Public Perception and Acceptance:**
   Educating healthcare providers and the public about the scientific basis of *Cnicus benedictus L.* as a complementary therapy is necessary to overcome skepticism regarding traditional remedies.
6. **Interactions with Other Medications:**
   Potential interactions of *Cnicus benedictus L.* with other antidiabetic medications or commonly used drugs need thorough investigation to ensure safe usage.

Conclusion :

The investigation into the antidiabetic activity of *Cnicus benedictus L.* in rat models has provided promising insights into its therapeutic potential. The plant's bioactive compounds, such as flavonoids and sesquiterpene lactones, appear to play a significant role in reducing blood glucose levels, enhancing insulin sensitivity, and mitigating oxidative stress. These findings suggest that *Cnicus benedictus L.* could serve as a natural alternative or adjunct to conventional antidiabetic therapies, particularly for managing type 2 diabetes.Despite these encouraging results, there are several limitations to consider. Most studies to date have focused on preclinical models, and the translational relevance of these findings to humans remains uncertain. Additionally, variations in preparation methods, dosages, and study designs highlight the need for standardization in future research. Comprehensive clinical trials are essential to validate the efficacy and safety of *Cnicus benedictus L.* in human populations.*Cnicus benedictus L.* holds

significant promise as a plant-based antidiabetic agent. Further research, particularly in clinical settings, is crucial to fully understand its pharmacological mechanisms, optimize its therapeutic use, and assess its long-term safety. Such efforts could pave the way for its integration into modern diabetes management strategies.

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