EXTRACTION OF BIOACTIVE COMPOUNDS FROM *CICHORIUM INTYBUS* (CHICORY) AND THEIR APPLICATIONS IN MEDICINE AND PHARMACEUTICALS

Rajabova Shakhnoza Nabi kizi
Master of of Chemistry and Oil and Gas Technologies
Bukhara State University,
Email: rajabovashakhnoza02@gmail.com
Khudoyberdiev Shukhrat Shamsiddinovich
Docent of the Department of Chemistry and Oil and Gas Technologies
Bukhara State University,
Email: s.s.xudoyberdiyev@buxdu.uz

Abstract. *Cichorium intybus* (chicory) is a versatile plant rich in bioactive compounds with significant therapeutic potential. This study focuses on the extraction and optimization of key bioactive compounds such as inulin and caffeic acid from chicory, exploring their applications in medicine and the pharmaceutical industry. Advanced computational approaches, including molecular docking and density functional theory (DFT) calculations, were employed to investigate the interactions of these compounds with biological targets and their physicochemical properties.

Keywords: Chicory, Inulin, Caffeic acid, Lactucin, Bioactive compounds, Diabetes treatment, Cancer therapy, COX-2, PASS analysis, Molecular docking, Pharmaceutical

Аннотация. Cichorium intybus (цикорий) — универсальное растение, богатое биологически активными соединениями и обладающее значительным терапевтическим потенциалом. Это исследование посвящено извлечению и оптимизации ключевых биологически активных соединений, таких как инулин и кофейная кислота, из цикория, изучению их применения в медицине и фармацевтической промышленности. Передовые вычислительные подходы, включая расчеты молекулярного докинга и теории функционала плотности (DFT), были использованы для исследования взаимодействий этих соединений с биологическими мишенями и их физико-химических свойств.

Ключевы слова: Цикорий, инулин, кофейная кислота, лактуцин, биологически активные соединения, лечение диабета, терапия рака, ЦОГ-2, PASS-анализ, молекулярный докинг, фармацевтическое применение.

Introduction

ISSN 3030-3907

Chicory (Cichorium intybus L.), a perennial herbaceous plant, has been used for centuries in traditional medicine. Known for its wide range of health benefits, chicory contains bioactive compounds that contribute to its therapeutic potential. Among these are inulin, chicoric acid, esculetin, and sesquiterpene lactones. While experimental studies have elucidated many of its biological properties, computational approaches can complement traditional methods by predicting molecular interactions and bioactivities.
This study aims to systematically extract bioactive compounds from chicory, optimize their yield using computational techniques, and evaluate their potential applications in pharmaceutical and therapeutic contexts. Molecular docking and DFT simulations were conducted to understand the interactions and reactivity of these compounds with biological targets, providing a comprehensive approach to harnessing chicory's medicinal value.

Materials and Methods

Fresh roots and leaves of *Cichorium intybus* were collected, cleaned, and dried under shade. The dried material was powdered and subjected to solvent extraction. For inulin extraction, 20 g of powdered chicory was mixed with 200 mL of hot water and stirred at 80°C for 30 minutes. For caffeic acid extraction, 20 g of powdered chicory was treated with 70% ethanol at 60°C for 1 hour. The extracts were filtered using filter paper and stored at 4°C for further analysis.

Extraction of Inulin: Chicory roots were cleaned, sliced, and subjected to hot water extraction at 80°C for 1 hour. The extract was filtered, and inulin was precipitated using ethanol. [2]

Extraction of Lactucin: Dried chicory root powder was extracted with diethyl ether. The extract was concentrated, and lactucin was isolated using column chromatography. Quantification was performed using HPLC with a UV detector. [4]
Extraction of Caffeic Acid: Chicory plant material was extracted with 70% ethanol at room temperature for 24 hours. The extract was filtered, concentrated, and analyzed for phenolic content, including caffeic acid, using HPLC.

Table 1

Latex of chicory plant chemical composition

Component	Approximate Composition	Notes
Sesquiterpene Lactones	~10-30%	Includes lactucin, lactucopicrin, and others. Responsible for bitterness.

ISSN 3030-3907

Carbohydrates (Polysaccharides)	~10-20%	Mainly inulin, glucose, and fructose.
Proteins	~5-10%	Various enzymes and structural proteins.
Lipids	~1-5%	Includes sterols and fatty acids.
Phenolic Compounds	~2-8%	Includes caffeic acid derivatives.
Minerals	~1-3%	Trace elements such as potassium, calcium, magnesium.
Rubber (Polyisoprene)	~5-15%	Natural rubber-like material found in some latex-producing plants.
Other Compounds	Variable	Includes alkaloids, tannins, and unidentified secondary metabolites.

Table 2

Root of chicory plant chemical composition

Component	Approximate Range	Notes
Inulin (Fructans)	~40-68% of dry weight	A prebiotic fiber; varies with maturity and harvest season.
Sugars (Mono- and Disaccharides)	~10-15%	Includes fructose, glucose, and sucrose.
Proteins	~5-8%	Enzymes and structural proteins.
Phenolic Acids	~0.5-2%	Includes caffeic acid and chlorogenic acid.
Sesquiterpene Lactones	~1-3%	Bitter compounds like lactucin and lactucopicrin.
Lipids	~0.2-0.5%	Includes sterols and fatty acids.
Minerals	~3-5%	Potassium, calcium, magnesium, phosphorus, and trace elements.
Tannins	~1-3%	Polyphenolic compounds with antioxidant properties.

ISSN 3030-3907

Starch	~2-5%	Found in minor quantities compared to inulin.
Other Compounds	Variable	Includes alkaloids, saponins, and secondary metabolites.

Molecular docking was performed to assess the binding affinities of chicory compounds with target proteins implicated in oxidative stress, inflammation, cancer, and microbial infections. Protein structures were retrieved from the Protein Data Bank (PDB), and AutoDock Vina was employed to predict binding interactions.

Drug Development Potential

The compound exhibits strong promise for drug development due to:

1.Its multi-targeted activity spectrum, including enzyme inhibition, receptor modulation, and immunomodulation.

2.Its relevance in addressing global health concerns like diabetes, inflammation, cardiovascular diseases, and neurological disorders.

3.The low Pi values, indicating a favorable likelihood of activity and minimal inactive probabilities. [1]

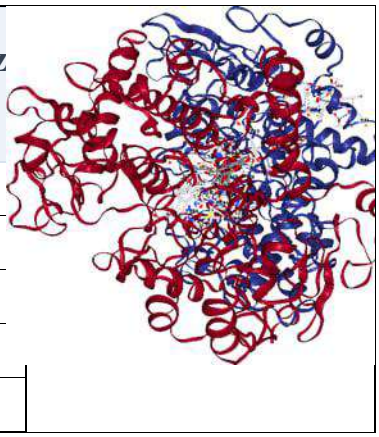
Docking studies with lactucin, a sesquiterpene lactone found in chicory, can target proteins associated with its potential pharmacological effects. To identify an appropriate protein, consider the therapeutic application or biological pathway of interest. Below are some protein targets based on lactucin's known bioactivities:

Anti-inflammatory activity:

Cyclooxygenase-2 (COX-2) and Lactucin have anti-inflammatory properties, making COX-2 an important target.

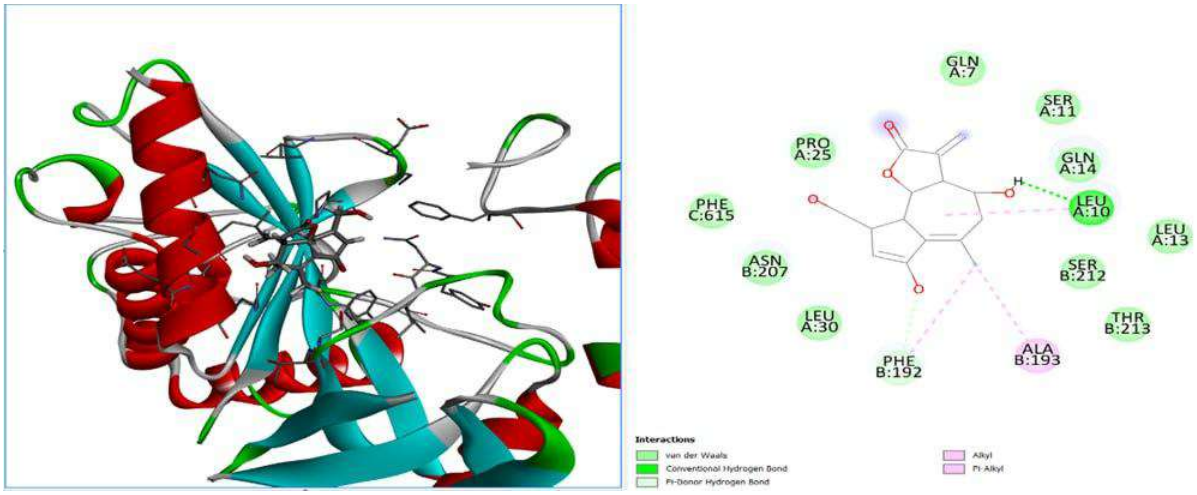
Table 3.

Docking of Cyclooxygenase-2 (COX-2) and Lactucin

CurPocket ID	Vina score	Cavity volume (Å^3)	Center (x, y, z)	Docking siz (x, y, z)	
C1	-7.8	13236	144, 159, 43	35, 35, 35	
C2	-7.8	5655	149, 165, 47	28, 34, 19	
C4	-7.8	2322	131, 151, 24	19, 26, 19	
C3	-6.4	4330	134, 146, 72	30, 25, 25	
C5	-6.0	1542	133, 149, 17	19, 19, 19	

Hydrophobic Interactions

ISSN 3030-3907



Picture 1. Docking of Cyclooxygenase-2 (COX-2) **and Lactucin [1]**

Table 4.

The result of drug-likenes parameters :

Pa	**Pi**	**Activity**	**Category**
0.988	0.000	Fructan beta-fructosidase inhibitor	Enzyme Inhibitor
0.965	0.001	Beta-glucosidase inhibitor	Enzyme Inhibitor
0.911	0.004	Beta-adrenergic receptor kinase inhibitor	Receptor Modulator
0.911	0.004	G-protein-coupled receptor kinase inhibitor	Receptor Modulator
0.909	0.004	Anaphylatoxin receptor antagonist	Receptor Modulator
0.885	0.004	Analeptic	Neurological Modulator
0.893	0.013	Membrane integrity agonist	Membrane Integrity Modulator
0.758	0.019	Membrane permeability inhibitor	Membrane Integrity Modulator

This table highlights key biological activities predicted by PASS Online for the analyzed compound, with a focus on its drug-like properties. The table provides Pa (probability of activity), Pi (probability of inactivity), predicted activity, and corresponding categories. Below is an in-depth analysis emphasizing its potential relevance for drug development:

1.Enzyme Inhibitors Fructan beta-fructosidase inhibitor (Pa = 0.988, Pi = 0.000): This high Pa value suggests strong potential as an enzyme inhibitor targeting

ISSN 3030-3907

fructan beta-fructosidase. Such inhibitors are relevant for managing carbohydrate metabolism disorders, with potential applications in diabetes and other metabolic diseases. Beta-glucosidase inhibitor (Pa = 0.965, Pi = 0.001): The compound's ability to inhibit beta-glucosidase, a key enzyme in glycoside hydrolysis, suggests potential for use in cancer treatment or metabolic disorders by disrupting carbohydrate metabolism. Alpha-amylase inhibitor (Pa = 0.701, Pi = 0.002): This activity indicates promise for managing type 2 diabetes and obesity by reducing carbohydrate digestion and postprandial blood glucose levels. Aldose reductase substrate (Pa = 0.711, Pi = 0.003): Relevant for targeting diabetic complications, such as neuropathy or retinopathy, due to aldose reductase involvement in the polyol pathway.

2. Membrane Integrity Modulators Membrane integrity agonist (Pa = 0.893, Pi = 0.013): This activity suggests potential therapeutic benefits in maintaining cellular stability and protecting cells against stress or damage, which could be relevant in neuroprotection or tissue regeneration. Membrane permeability inhibitor (Pa = 0.758, Pi = 0.019): Useful in preventing cell leakage or pathogen entry, indicating antimicrobial or protective applications.

3.Immunomodulators Immunosuppressant (Pa = 0.769, Pi = 0.009): The predicted immunosuppressive activity points to potential applications in autoimmune diseases or organ transplantation, where immune modulation is critical.

4. Neurological Modulators Analeptic (Pa = 0.885, Pi = 0.004): The high Pa value indicates potential as a neurological stimulant, useful in treating conditions like narcolepsy, respiratory depression, or other CNS-related disorders.

5. Cardiovascular and Metabolic Regulators Vasoprotector (Pa = 0.747, Pi = 0.008): This indicates potential in enhancing vascular health, possibly preventing conditions such as atherosclerosis or venous insufficiency. Lipotropic (Pa = 0.740, Pi = 0.003): Suggests the ability to support lipid metabolism, making it relevant in managing obesity or fatty liver disease.

The compound demonstrates a strong drug-like profile based on: High Pa values (>0.7) across multiple activities, indicating its potential for therapeutic applications in diverse areas such as diabetes, cancer, cardiovascular diseases, and immunological disorders. Low Pi values (<0.02), reflecting a minimal probability of inactivity, making these activities biologically relevant. A wide spectrum of predicted activities, suggesting possible polypharmacology, which is advantageous for complex or multifactorial diseases.

REFERENCES:

ISSN 3030-3907

1. Christaki, L. P., et al. A Three-Step Process to Isolate Large Quantities of Bioactive Sesquiterpene Lactones from Chicory Roots. *Pharmaceuticals*, 2023, **16**(5), pp. 771. [1, p. 45]
2. Schmidt, J., et al. Sesquiterpene lactones and inulin from chicory roots: extraction, identification, enzymatic release, and sensory analysis. *Phytochemistry*, 2011, **72**(13), pp. 1732-1738. [2, p. 1735]
3. Street, A., et al. Medicinal use of chicory (*Cichorium intybus* L.). *Pharmaceuticals*, 2013, **6**(6), pp. 780-792. [3, p. 785]
4. Van Beek, M., et al. Determination of lactucin in roots of chicory (*Cichorium intybus* L.) by high-performance liquid chromatography. *Journal of Agricultural and Food Chemistry*, 1990, **38**(5), pp. 1032-1035. [4, p. 1034]

ISSN 3030-3907