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A COMPREHENSIVE REVIEW ON THE PHYTOCHEMICAL, PHARMACOLOGICAL, AND ETHNOBOTANICAL PROFILE OF *CICHORIUM INTYBUS* WITH SPECIAL REFERENCE TO IN-DEPTH HEPATOPROTECTIVE MECHANISMS

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ABSTRACT

Cichorium intybus L. (chicory) is a medicinal plant. Belongs to the family of Asteraceae, traditionally used for centuries for its nutritional and therapeutic properties. It contains various bioactive components like inulin, sesquiterpene lactones, flavonoids, phenolic acids and other phytochemicals, which are responsible for its wide range of biological activities. Different parts of the plant, such as roots, leaves, seeds and flowers have been traditionally used for the management of various ailments, including hepatic disorders, digestive disorders, diabetes, inflammation and microbial infections. Several pharmacological studies have revealed antioxidant, anti-inflammatory, antimicrobial, antidiabetic, anticancer and hepatoprotective activities of Cichorium intybus. The hepatoprotective effect of *Cichorium intybus* is mainly due to its capacity to reduce oxidative stress, antioxidant defence systems, lipid peroxidation, and to improve the liver function biomarkers. This review provides a detailed overview of the ethnobotanical significance, phytochemical composition, pharmacological activities and hepatoprotective mechanisms of *Cichorium intybus*. In addition, recent findings related to molecular docking studies and

clinical investigations are discussed to emphasise its therapeutic potential as a promising medicinal plant for liver protection and drug development.

KEYWORDS: *Cichorium intybus*, Phytochemical, Hepatoprotective activity, antioxidant activity, Molecular docking, Mechanism of hepatoprotection.

INTRODUCTION

Cichorium intybus L. (chicory) is a medicinal plant that has been traditionally used for its therapeutic and nutritional properties. It is valued for its rich phytochemical composition and wide range of pharmacological activities, making it an important plant in both traditional and modern medicine.[1] Recent studies have suggested that *Cichorium intybus* possesses antiviral potential, including inhibitory activity against SARS-CoV-2, highlighting its possible role in the development of novel therapeutic agents.[2] The roots of *Cichorium intybus* are widely utilised as a coffee substitute and serve as an important source of inulin, a prebiotic dietary fibre with significant health benefits.[1,2] Other parts of the plant, including the leaves and stems, are used in the food, pharmaceutical, and nutraceutical industries owing to their bioactive constituents. Growing scientific interest in *Cichorium intybus* is attributed to its diverse phytochemical profile and its multiple medicinal and industrial applications.[3] Furthermore, *Cichorium intybus* exhibits promising antimicrobial activity, which has been largely attributed to the presence of phenolic compounds, flavonoids, sesquiterpene lactones, and other bioactive metabolites. These compounds contribute to its potential use as a natural antibacterial agent and support its therapeutic significance.[3]

Geographical Distribution

Cichorium intybus L. is native to Europe, Western Asia, and North Africa and has been widely cultivated and naturalized in many parts of the world due to its medicinal and nutritional importance. It is well adapted to a variety of climatic conditions and soil types, which has contributed to its widespread distribution across temperate and subtropical regions.[4] In India, *Cichorium intybus* commonly grows in roadsides, cultivated fields, grasslands, and wastelands. It is distributed in several states, including Punjab, Uttar Pradesh, Maharashtra, and parts of South India, where it is cultivated and also found growing naturally.[4] The genus *Cichorium* comprises several wild and cultivated species distributed across different geographical regions. Studies have reported the occurrence of 36 wild taxa, with 13 species identified in Bulgaria, 18 species in Sicily, and 5 species common to both regions, indicating considerable geographical diversity within the genus.[5]

Description of Genus

The *Cichorium* genus comprises six recognised species most of which are native to Europe and Asia. A few species are distributed in North and South Africa, but they are not as common. The Cichorium genus has plants that are characterised by the presence of laticifers that produce a milky latex and have distinctive capitula (flower heads) inflorescences.[1] Some of the types of Cichorium plants are *Cichorium intybus*, *Cichorium endivia, Cichorium spinosum and Cichorium pumilum.*[6] *Cichorium intybus* is the most economical and medicinally important species.

Botanical Description

Cichorium intybus is an erect perennial herb that grows to a height of approximately 30-150 cm. It possesses a well-developed taproot and stiff, branching stems. Basal leaves are arranged in a rosette and are deeply lobed, while the leaves at the top are smaller and do not have stems.[6] The flowers are blue, purple or sometimes white and arranged in capitula(flower heads). The fruit is a dry, indehiscent achene containing a single seed. The plant usually flowers in the spring and summer. Cichorium species can benefit from genomic techniques. The study showed that successful isolation and regeneration of protoplasts. This finding implies that DNA-free genome editing, in chicory, could help improve crops and breeding methods efficiently.

Chicory and its genome editing could lead to crop improvement strategies.[7] The chicory-legume mixtures really helped to increase the productivity of the pasture. They found that subterranean clover works well with the chicory-legume mixtures. This is because the subterranean clover is very good at staying alive and regrowing, which makes it a great choice for the chicory-legume mixtures. The chicory-legume mixtures and subterranean clover are a team; the subterranean clover is the best one to use with the chicory-legume mixtures.[8]

The morphology of *Cichorium intybus* includes

Root: shaped like a spindle and filled with inulin. Stem: Erect, angular, branched and rough. Leaves: The basal leaves are arranged in a rosettes and are pinnate lobes, whereas the upper leaves are smaller, sessile, and less deeply lobed. Flowers: Arranged in capitula (flower heads) with involucral bracts at the base. Fruits:Dry, indehiscent achenes, each containing a single seed.

Fig.1 **Fig.2**

Fig.1: Whole plant *of Cichorium intybus.* Fig.2: Root of *Cichorium intybus.*

Ethnobotanical Uses

In the past people used *Cichorium intybus* in traditional medicine for its hepatoprotective active and appetite stimulant. The leaves were used to heal wounds and skin problems. The roots were used to cure jaundice and liver diseases. Roasted roots can be used as a substitute for coffee. In medicine *Cichorium intybus* is used to treat diabetes and gastrointestinal disorders. The seed of *Cichorium intybus* have traditional been used for the liver disordes of their hepatoprotective bioactive phytochemicals. This activity is attributed to the presence of bioactive phytochemical. Chicory seeds, also known as *Cichorium intybus* seeds are useful for people, with liver disorders because they help the liver.[9] Cichorium intybus exhibits an antiviralactivity. It exhibits antiviral properties by activating plant defense mechanisms and improve the resistance against viral infection.[10] Cichorium intybus extracts possess significant wound healing property.[11]

Phytochemical Review

Phytochemical Studies have revealed that *Cichorium intybus* has phytochemical/bioactive compounds including carbohydrates, sesquiterpene lactones, flavonoids, alkaloids, tannins, coumarins, vitamins and minerals. The major bioactive compound identified in *Cichorium intybus* are inulin, lactucin, lactucopicrin, cichoric acid, chlorogenic acid, caffeic acid, quercetin and kaempferol derivatives.[6,3]

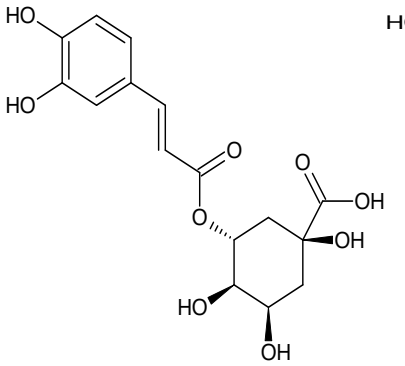

Fig.3: Chlorogenic Acid.

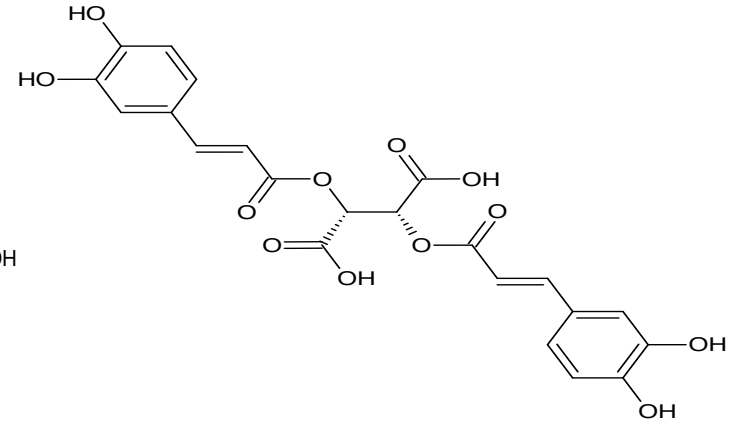

Fig.4: Cichoric Acid.

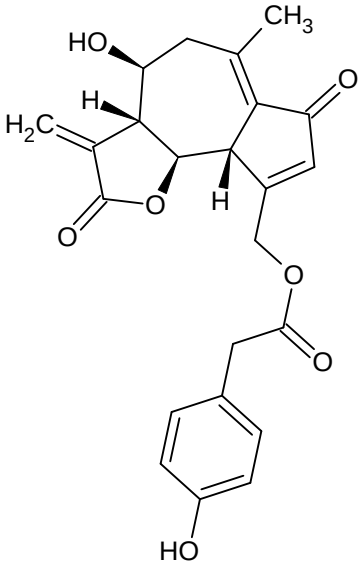

Fig.4: lactucopicrin.

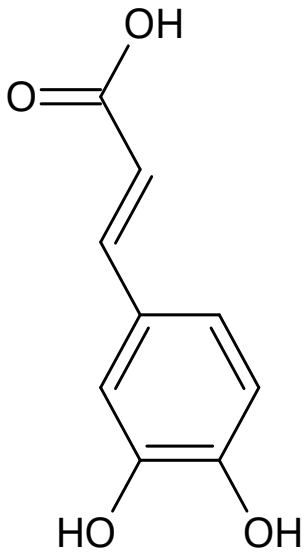

Fig.5: caffeic acid.

Chicory is rich in polyphenols and antioxidants

Environmental factors, such as water stress, significantly influence the phytochemical composition of chicory. Cultivation of chicory can enhance its antioxidant properties and help promote sustainable agricultural approaches.[12] Chicory is in rich phenolic compounds and bioactivity, supporting its use as a medicinal plant and functional food.[13] The *Cichorium intybus* plant has different varieties and they all have unique phytochemical profiles, including chicoric acid, chlorogenic acid and monocaffeoyl tartaric acid. Red chicory varieties additionally contain anthocyanins.[14] Cichorium leaves have strong antioxidant and bioactive compounds (Flavonoids, Phenolic compounds, Tannins, Alkaloids, Saponins, glycosides) The leaves contain minerals such as Potassium(K), Calcium(Ca), Magnesium(Mg), Iron(Fe), Zinc(Zn), Sodium(Na).[15]

Pharmacological Properties

Many pharmacological studies have demonstrated that *Cichorium intybus* has effects, including anti-inflammation, hepatoprotective, antidiabetic, anticancer and antimicrobial.[2,3] These effects are mainly because of the compounds, flavonoids, sesquiterpene lactones and inulin in *Cichorium intybus*.[16] *Cichorium intybus* has shown beneficial effects on blood glucose and lipid metabolism, thereby reducing blood glucose and serum cholesterol levels. It has traditionally been used as a medicinal plant for the management of diabetes mellitus.[17] Medicinal plants rich in flavonoids and other phytochemicals showed significant antidiabetic activity through improving insulin sensitivity, glucose metabolism, oxidative stress and protection of pancreatic β-cells. These mechanisms result in improved glycemic control and provide help in the management of diabetes mellitus.[18] *Cichorium intybus exhibits* hepatoprotective properties. *Cichorium intybus* also has antidiabetes, antimicrobial, and anticancer properties.[19] Flavonoids and phenolic compounds present in *Cichorium intybus* stong posses antioxitant activity and contribute to cardiovascular protection by reducing oxidative stress and preventing cellular damage.[20] The *Cichorium intybus* fruit extract has hepatoprotective activity against 4-tert-octyphenol, this was induce the liver injury in male rats. After the treatment, reduced elevated liver enzymes, improved antioxidant level, and minimised histopathological.[21] Chicory root has a polysaccharide. It has a hepatoprotective effect[22] developed functionalized iron oxide nanoparticles. Used *Cichorium intybus* extract for this. To manage anaemia through the skin.[23] Chicory leaves have a significant phytochemical that has a hepatoprotective effect, and the antioxidants help to reduce liver damage by heavy metals.[24]

Clinical Study

Clinical Trial: Chicory Supplementation In Nafld Patients

There was a study on people with NAFLD. This is a condition characterised by excessive fat accumulation in the liver. The participants in the absence of significant alcohol consumption. The participants received *Cichorium intybus* supplementation to evaluate its hepatoprotective activity. The researchers assessed liver enzyme levels and lipid profile parameters. The findings suggested that chicory may improve liver function and lipid metabolism in NAFLD. More studies are needed to ensure chicory is safe and effective for NAFLD patients[25] *Cichorium intybus* improves liver enzymes and lipid metabolism in people with liver disease. Further large-scale, well-designed clinical trials are required. We need research on *Cichorium intybus* to confirm that it is safe and effective for people with liver disease.

Clinical Trial: *Cichorium Intybus* On Liver Enzymes In Burn Patient

Another study was done on burn patients. They took *Cichorium intybus*, also known as chicory. The patients and doctors did not know who was getting chicory. The researchers checked liver enzymes in the blood to see how well the liver was working. It looks like chicory helped protect the liver from burn damage and improved its function. More studies are needed to confirm this for burn patients taking chicory.[26]

Hepatoprotective Activity

The leaves and seeds of *C. Intybus* are often used in medicine to protect the liver.[27,28] This plant is one of the ingredients in Liv-52, an Indian tonic for liver health. A study on patients with cirrhosis showed that taking Liv-52 reduced liver enzymes and improved liver function. It also reduced swelling in the stomach. Improved overall liver health.[29] Another herbal mix, Jigrine contains C. Intybus leaves. Was tested on rats with liver damage. The results showed that Jigrine reduced liver enzymes and increased antioxidants in the blood and liver. It also prevented liver damage and reduced inflammation.[30] The seeds of C. Intybus were studied for their ability to protect the liver against damage from chemicals. The extract from the seeds reduced liver damage and death rate in mice. It also decreased liver enzymes. Improved liver health.*C. Intybus* extracts were given to rats with liver damage. The results showed a decrease in liver enzymes. The liver also showed no accumulation. The extracts were also tested on rat liver cells. The results showed that they reduced liver damage. A study on the seed extract of *C. Intybus* showed that it was effective in reducing accumulation in liver cells.[31] It also increased the breakdown of triglycerides. The extract was also tested on rats with liver damage and the results showed a significant decrease in fat accumulation and fibrosis.[32] The liver-protecting effects of *C. Intybus* are thought to be due to its ability to prevent damage from radicals. A study on the leaf extract showed that it prevented damage to DNA from radicals. The results showed a dose- decrease in DNA damage.[33] *C. Intybus* seems to be a plant, in protecting the liver. *C. Intybus* has been shown to protect the liver in studies. The plant *C. Intybus* has health benefits.

Mechanism of Hepatoprotective

Cichorium intybus exhibits hepatoprotective activity. It does this by reducing oxidative stress. It also increases the activity of enzymes, including SOD and GSH. This extract decreases lipid peroxidation, which is measured by MDA levels. Additionally, it improves liver function by lowering ALT and AST levels in liver injury models. *Cichorium intybus* extract is

beneficial for liver health. It achieves this through its properties. The extract manages liver injury. *Cichorium intybus* plays a role in reducing liver damage.[34]

C. Intybus helps reduce the liver injury biomarkers like ALT and AST. It also decreases the pro-inflammatory mediators TNF-α and NO. It also restores antioxidant status by increasing the activities of antioxidant enzymes such as GSH and SOD, thereby inhibiting lipid peroxidation. Chicory supplements decrease the oxidant stress that damages our liver and keep the liver tissue safe by making our antioxidant defence systems work properly again. Chicory supplementation is protecting our liver from damage.[35,36]

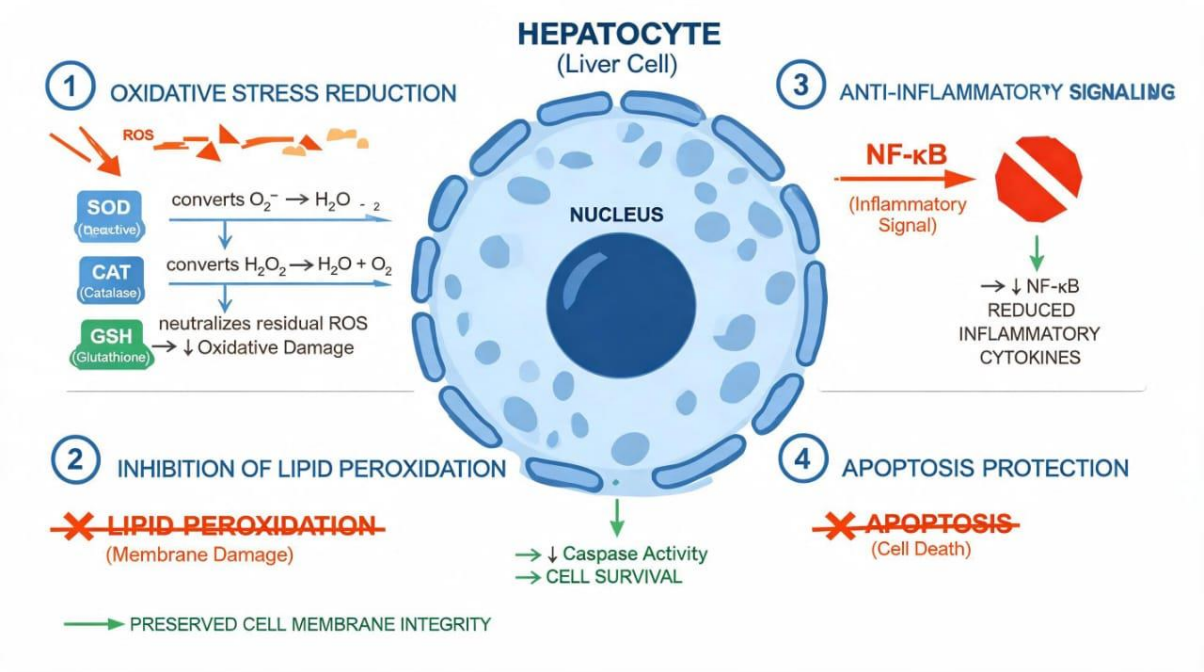

Fig.6: A Schematic diagram represents mechanism of hepatoprotective action for *Cichorium intybus.*

***Insilico* Molecular Docking studies.**

Target Enzymes	BINDING AFFINITY (KJ/Mol)					
	Chicoric acid	Chlorogenic acid	Ursodeoxy cholicAcid	N-Acetyl O-cysteine	Metadoxine	Bifendate
8BHE	-9.7	-8.4	-9.5	-5.0	-5.5	-7.6
5LDO	-8.4	-8.4	-7.1	-4.8	-5.7	-7.0
2R3X	-9.3	-8.9	-9.7	-4.9	-5.8	-7.3
3NXU	-7.8	-7.2	-9.2	-4.8	-5.5	-6.7
4IQK	-9.4	-9.1	-9.7	-4.8	-6.4	-7.6
2C6U	-6.4	-7.1	-7.9	-4.3	-5.4	-5.8
2H14	-9.4	-9.6	-7.1	-4.9	-6.6	-7.6

The study of how chicoric acid and chlorogenic acid bind to certain targets in the liver showed that they both have a good connection to these targets. The scores for how they bind ranged from -6.4 to -9.7 kcal/mol, which means they have a strong interaction with the proteins. Chicoric acid was the best at binding to the targets. It had the connection to target 8BHE with a score of -9.7 kcal/mol, which is similar to the score of a drug called ursodeoxycholic acid. Chicoric acid also bound well to targets 4IQK, 2H14 and 2R3X, which shows it has an interaction with many proteins that help protect the liver.

Chlorogenic acid also had results. It bound best to target 2H14 with a score of -9.6 kcal/mol. Also bound well to targets 4IQK and 2R3X. Its score for target 5LDO was the same as chicoric acid, which means it has a similar ability to interact with this target. The standard drugs were also tested. Ursodeoxycholic acid had binding to targets 2R3X and 4IQK and also bound well to targets 8BHE and 3NXU. These results are consistent with its known ability to help protect the liver. On the hand a drug called N-acetylcysteine did not bind as well to the proteins. Its scores ranged from -4.3 to -5.0 kcal/mol. Another drug, Metadoxine, had binding, and Bifendate had intermediate binding. Overall the study showed that chicoric acid and chlorogenic acid which are found in *Cichorium intybus* have a connection to the targets than N-acetylcysteine, Metadoxine and Bifendate. In some cases, the scores for acid and chlorogenic acid were similar to those of ursodeoxycholic acid, which suggests that these natural compounds may play a big role in helping to protect the liver.

The study on chicoric acid shows that it is a promising part of *Cichorium intybus*. Chicoric acid is really good at binding to the things that help protect the liver. Chlorogenic acid is also very good at this with 2H14 and 4IQK. The scores for these chemicals are as good as or even better than some medicines that are already used to protect the liver. This means that chicoric acid and chlorogenic acid might be why *Cichorium intybus* is good for the liver. We need to do more tests to make sure this is true. We should use computer simulations and real life studies to confirm what we found out about chicoric acid and chlorogenic acid.

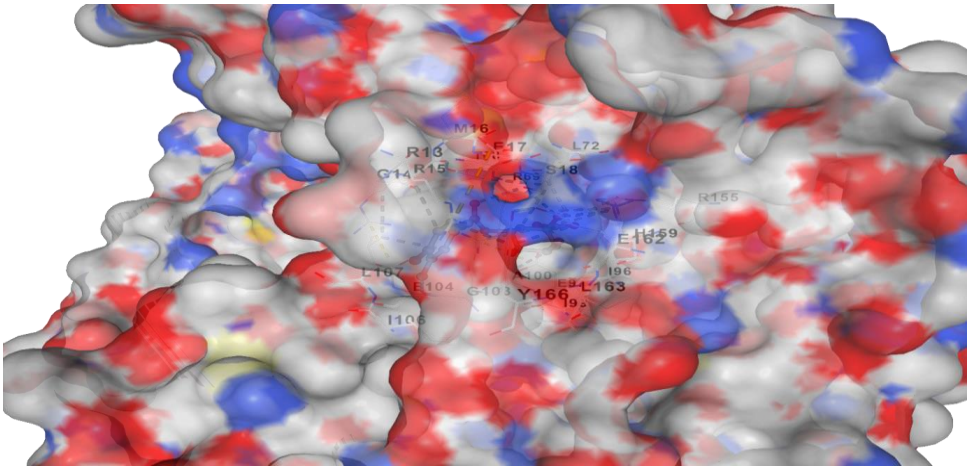

Fig.8: Repersent the binding affinity of chlorogenic acid in 8BHE Target enzymes.

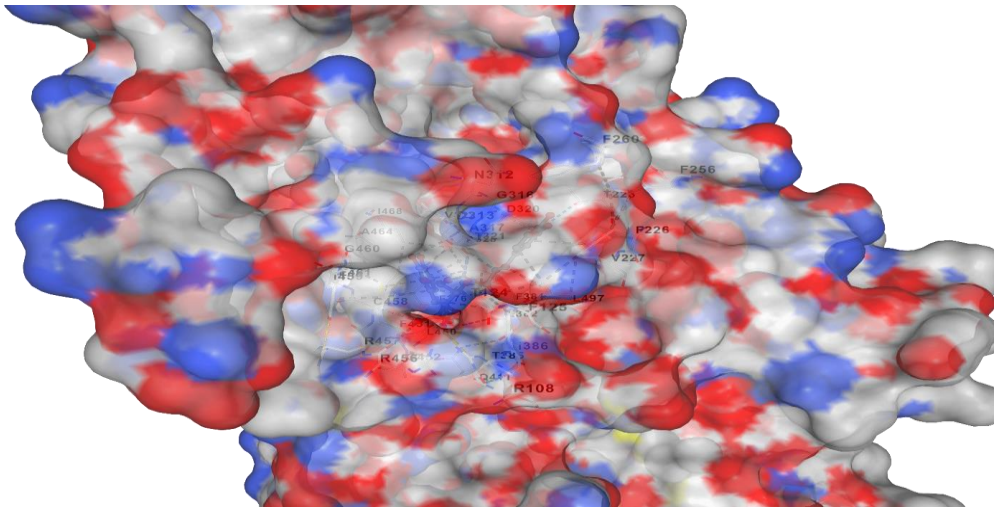

Fig.9: Represent the binding affinity of chicoric acid in 2H14 Target enzymes.

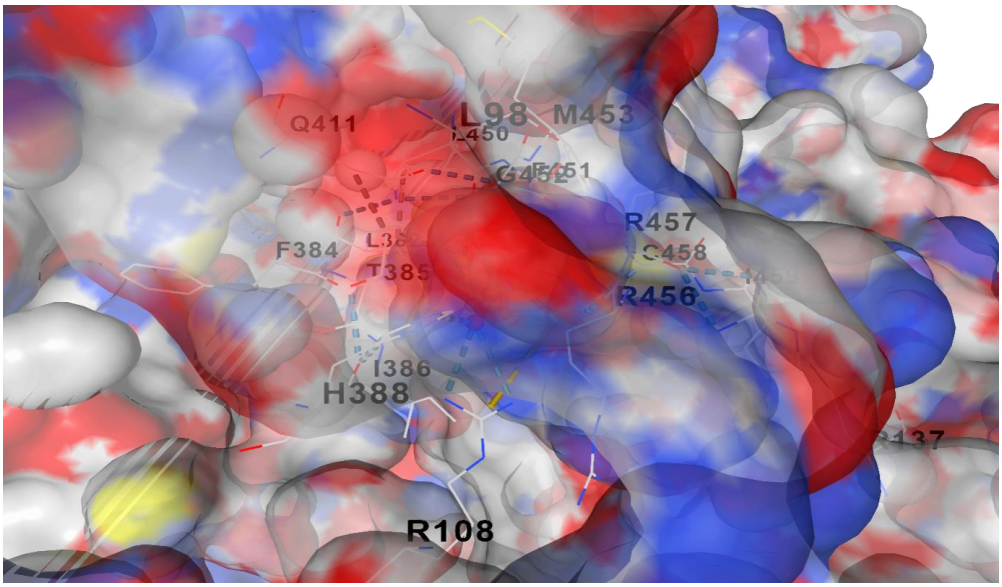

Fig.10: Represent the binding affinity of N-Acetylcystein in 41QK Target enzymes.

CONCLUSION

Cichorium intybus L. is a valuable medicinal plant, showing significant phytochemical diversity and multiple pharmacological properties. Its antioxidant, anti-inflammatory, antidiabetic, antimicrobial and hepatoprotective activities are attributed to the presence of bioactive compounds such as inulin, phenolic acids, flavonoids and sesquiterpene lactones. Its potential role in the management of various health conditions, especially liver disorders, is supported by traditional uses and scientific investigations. *Cichorium intybus* hepatoprotective activity is mainly related to the reduction of oxidative stress, enhancement of antioxidant defence systems, inhibition of lipid peroxidation, and regulation of inflammatory pathways. Molecular docking studies revealed that compounds like chicoric acid and chlorogenic acid might be important contributors to liver-protective effects by interacting with important therapeutic targets.

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