Uttar Pradesh Journal of Zoology

Volume 44, Issue 10, Page 21-36, 2023; Article no.UPJOZ.2581
ISSN: 0256-971X (P)

Comparitive Study of Hibiscatin with Quercetin and Lutonarin with Rutin by Using Docking Studies

Sowjanya Kattupalli [a++*], Kamepalli Krishnaveni [a#], Ravilanke Venkata Sai [b], Dharna Ramya Sri [b], J. Nuthana Yaswanth [b], Mallela Surya Narayana [b], Prathuru Sandhya [b] and Potti Srinivas [b]

[a] Nirmala College of Pharmacy, Atmakur (Vil), Mangalagiri (Mandal), Guntur (Dist), Andhra Pradesh, India.
[b] Bachelor of Pharmacy, Nirmala College of Pharmacy, Atmakur (Vil), Mangalagiri (Mandal), Guntur (Dist), Andhra Pradesh, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.56557/UPJOZ/2023/v44i103500

Editor(s):
(1) Prof. Juan Carlos Troiano, University of Buenos Aires, Argentina.
Reviewers:
(1) Harishchander Anandaram, Amrita Vishwa Vidyapeetham, India.
(2) S. Bharanidharan, Panimalar Engineering College, India.

Review Article

Received: 14/03/2023
Accepted: 19/05/2023
Published: 31/05/2023

ABSTRACT

Hordeum Vulgare Young barley leaves were used to extract lutonarin. Reactive oxygen species removal has been linked to the presence of lutonarin in plants, particularly in leaves. Hibiscatin is a new flavonoid glycoside obtained from *Hibiscus Plantifolius*. EMDOCK is a graphical –automatic

[++] Associate Professor;
[#] Assistant Professor;
**Corresponding author: Email: ksowjanya.1504@gmail.com;*

drug design system for docking, screening, and analysis. It's also a programme for calculating ligand shape and orientation concerning the protein's active site. The molecular interactions of Hibiscatin, Lutonarin, Rutin, and Quercetin with anti-oxidant proteins like Catalase (1DGF), Glutathione Reductase (3DK4), and Superoxide Dismutase (5YTO) were studied using Insilco docking simulations (Patel A. K. *et al*., 2022) The ligands' 2D structure was created and stored in mol format using BIOVIA Draw Software. The ligand structures were optimised and reduced using Avogadro software. The macromolecules were cleansed of water residues and Gasteiger charges were added using Dock Prep in UCF Chimera [1].

Keywords: Hibiscatin; lutonarin; quercetin; rutin; docking.

1. INTRODUCTION

Herbal plants are the oldest known health care products that have been used by people all over the world as natural remedies. However, according to the Department of Health, medicinal herbs are used for primary healthcare by 80 per cent of the worldwide people [2-5]. With the emergence of synthetic medications, medicinal plants' utility has waned in modern times, particularly in industrialized Western countries. After all, in less developed countries, the use of readily available, reasonably priced herbal remedies coexisted alongside those of more advanced pharmaceuticals. Herbal remedies have recently regained popularity due to their shown efficacy and lack of side effects [6]. The biological activity is mainly caused by active molecules created during secondary metabolism. Up until the development of iatrochemistry in the 16th century, plants were used to treat illness and prevent it [7-9].

Plants have been isolated/derivative for the past 50 years, revolutionizing modern medicinal treatment. The therapeutic characteristics of these chemical components are similar to those of plant and animal medications [10-16]. The World Health Organization encourages the use of medicinal biologics in nationwide health services because they are easily accessible at a cost that is affordable to the average person, and they have been thoroughly evaluated [17,18].

Bioactive chemicals are often detected using sophisticated bioassays and bioassay-guided fractionation of medicinal herbs utilized by traditional healers, according to research. As a result, several new medically significant molecules have been isolated. Due to the dedicated efforts of researchers, a huge number of strong medications, therapeutic leads, and many new pharmacologically active ingredients have been produced from herbal drugs [19].

The unending search for happiness will last till he takes his last breath; this search has led him down countless pathways, both known and unknown. Man has been plagued with the disease since the beginning of his existence. Drugs are as old as disease, and the search for solutions to counteract them is probably as old as well [20]. Humans are more susceptible to sickness, and they have long sought to alleviate their pain from injury or disease by utilising the plants that grow around them. The plant, known as "The sleeping giant of drug discovery," is now the world's primary supplier of pharmaceuticals [21,22].

Plants have long been associated with the history of medications, and plant products are widely used in ethnomedicine and traditional medical systems [20]. Over the last three decades, the number of medicinally valuable plants has exploded. Multinational medicine corporations and research institutes are looking for new drugs and lead compounds in the unexplored abundance of the plant kingdom. The study of traditional remedies, mostly of botanical origin, on which the vast medical care is still provided to a large proportion of the worldwide people [23].

According to the World Health Organization, plant-based medicine is used by 3.5 billion people in poor nations for primary health care. Because of the following factors, there has been a global upsurge plant-based medications are gaining popularity.

i. High-priced synthetic medications
ii. Synthetic medications made from non-renewable basic raw resources
iii. Chemical industries contribute to environmental contamination.
iv. Public acceptance of plant-based drugs as well as a patient tolerance and a lengthy history of use
v. Plant drugs from renewable sources

vi. In environmentally friendly conditions cultivation and processing of drugs
vii. The majority of new lead molecules are obtained from plants

Herbal remedies are beneficial; even though it is used to treat many diseases often require further research in light of modern science [24].

In India's largely rural and tribal villages, some 7500 plants are used in indigenous health practices. Out of these, over 4000 plants of real medicinal value are either little known or completely unknown to the general public. A thorough examination and documenting of plants utilized in local health traditions, as well as a medicinal assessment of these plants and their taxonomic relations, can lead to the discovery of priceless plant medications for a variety of ailments [25-29].

Despite enormous progress in the identification of novel therapeutic chemicals, the current medical system fails to provide appropriate medications for a wide range of diseases [30]. Hepatic illnesses, viral infections, AIDS, rheumatic ailments, and other medications are among them. The symptomatic alleviation provided by existing treatment medicines may not affect the curative process, increasing the likelihood of relapse and the risk of adverse effects. Because the majority of people suffer from hepatic disorders and inflammatory conditions of known and unknown origin, the creation of hepatoprotective medications is a prominent focus of research in the field of natural product research.

The literature review conducted as part of the proposed work suggests that chemical compounds found in the stem of *Hibiscus plantifolius* and the leaves of *Hordeum vulgare* have antioxidant [26].

anti-diabetic, and hepatoprotective properties. The activities that have been identified from various portions of these plants are due to chemical elements such as flavonoids, steroids, terpenoids, and quinones [31] Plants used in this study have no scientific evidence of anti-diabetic or hepatoprotective effects. The screening of phytochemicals and pharmacological activity of the chosen species may provide important information and material for improved management of free radical generation, liver toxicity, and hyperglycemia.

SELECTION OF PLANTS

Hibiscus plantifolius ***Hordeum Vulgare***

Constituents Present in *H. plantiifolius*

Many active compounds from ***H. plantiifolius***, include **Hibiscatin**, friedoolean-14-en-3-yl acetate, Nimbosterol, campestral, stigmasterol, cholesteryl alcohol, ergosterol, fats, and Anhydrous citric acid, tartrate and ethanedioic acid, levulose, dextrose, cellulose, polyphenols and polyphenol glycosides have been identified. An active compound from ***H. vulgare*** contains a variety of vitamins, minerals and polyphenol compounds, including flavone C glycosides, saponarins and **lutonarin**. C-glycosyl flavones and O-glycosyl -C-glycosyl flavones distinguish between Di-O- glycosyl flavones and O-diglycosyl -flavonens. Most of them are first described in barley. Saponarin (Isovitexin-7-O-glucoside), **Lutonarin** (Isoorientin-7-O-glucoside) and Isoscoparin-7-O-glucoside derivatives make up the majority of the detected compounds. Several acylated derivatives, namely, 7-O-[6-acyl]-glucosides and 7-O-[6-acyl]-glc-4-glucosides of isovitexin, isoorientin and isoscoparin are also described (Ferreres F et al., 2008).

Reported Activity:

Study of Saravanan et al. [32] showed that the *H. platanifolius* showed a concentration-dependent removal effect on hydrogen peroxide, and had the properties of metal chelation and reducing power. The flavonoid content was 57 ± 5.4 mg g^{-1} and the phenol content was 289.5 ± 5 mg g^{-1}. The ethanolic and aqueous thermal extracts of *H. platanifolius* were found to be effective in this investigation and have excellent antioxidant, hypoglycemic, and lipid-lowering effects.

Yu YM et al. [33] the antioxidative and dyslipidemia of *Hordeum Vulgare* were investigated in a rabbit model of arterial sclerosis. The results showed that 30% suppression of hyperlipidemia arterial sclerosis by barley leaves was associated with a decrease in plasma lipids and an increase in antioxidant

capacity. These findings imply that the antioxidant and lipid-lowering effects of BL may help prevent cardiovascular diseases such as atherosclerosis [34]

PROCEDURE:

- Malunavar et al. [1] utilised the iGEMDOCK version 2.1 software (http://gemdock.life.nctu.edu.tw/dock/) for docking simulations to analyse binding mode and interactions for the synthesised compounds.
- The synthesised compounds were subjected to docking simulations to determine binding mechanisms and interactions. The iGEMDOCK version 2.1 software (http://gemdock.life.nctu.edu.tw/dock/) was used (Malunavar *et al*., 2022). G
- EMDOCK is a graphical –automatic drug design system for docking, screening, and analysis. It's also a programme for calculating ligand shape and orientation concerning the protein's active site.
- The molecular interactions of Hibiscatin, Lutonarin, Rutin, and Quercetin with anti-oxidant proteins like Catalase (1DGF), Glutathione Reductase (3DK4), and Superoxide Dismutase (5YTO) were studied using Insilco docking simulations (Patel A. K. et al. 2022) The ligands' 2D structure was created and stored in mol format using BIOVIA Draw Software. The ligand structures were optimised and reduced using Avogadro software. The macromolecules were cleansed of water residues and Gasteiger charges were added using Dock Prep in UCF Chimera [1].
- Ligand interactions were displayed using Biovia's Discovery Visualizer. For the typical docking approach, a reliable docking method was used. The scoring function was used to evaluate the best docking solutions. Combining van der Waal's, hydrogen bonding, and electro statistic energies, it calculates fitness. To determine the interactions between the ligand and the target protein, a post docking interaction profile analysis of optimal poses was performed [1].
- The ligands' 2D structure was sketched in BIOVIA Draw programme and stored in mol format. Avogadro software was used to optimise and reduce the ligand structures. Water residues were removed from the macromolecules, and Gasteiger charges were added using Dock Prep in UCF Chimera [1].
- Discovery Visualizer was used to visualising and analyse ligand interactions (Biovia). A stable docking approach was chosen and a standard docking protocol was followed. The best docking solutions were examined using the scoring function..By combining van der Waal's, hydrogen bonding, and electro statistic energies, the scoring function estimates fitness. To determine the interactions between the ligand and the target protein, a post docking interaction profile analysis of optimal poses was performed

Docking interactions of molecules with antioxidant proteins

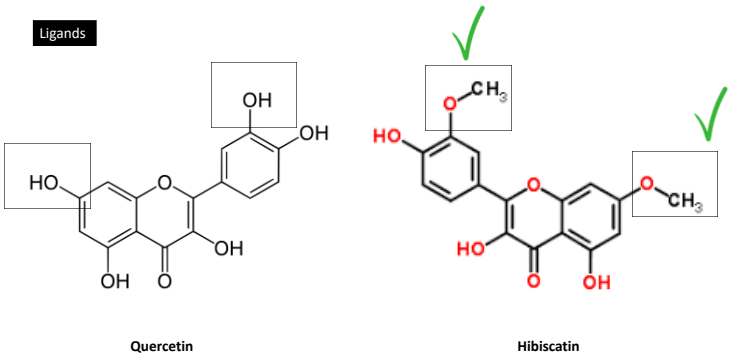

Fig. 1. Ligands of Quercetin and Hibiscatin

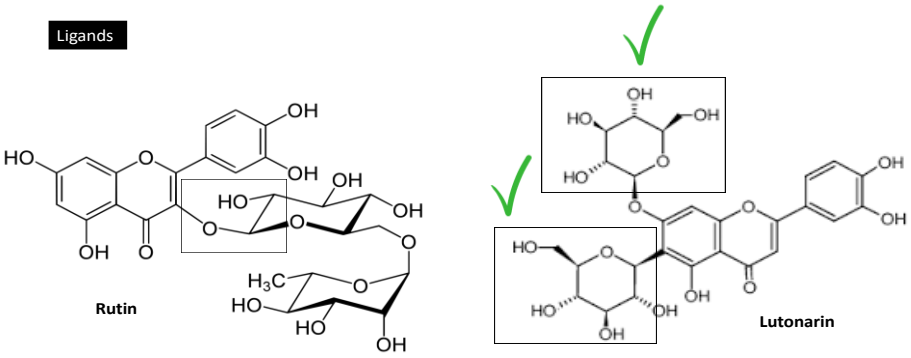

Fig. 2. Ligands of rutin and lutonarin

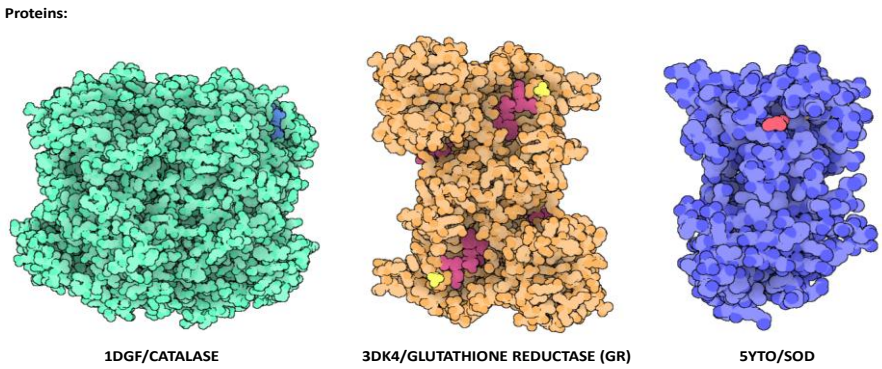

Fig. 3. Proteins

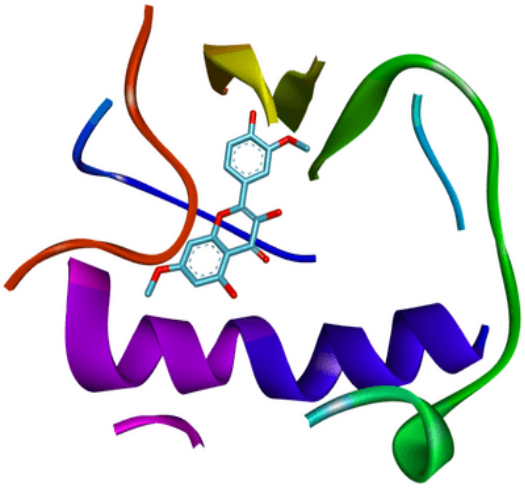

Fig. 4. Hibiscatin- catalase

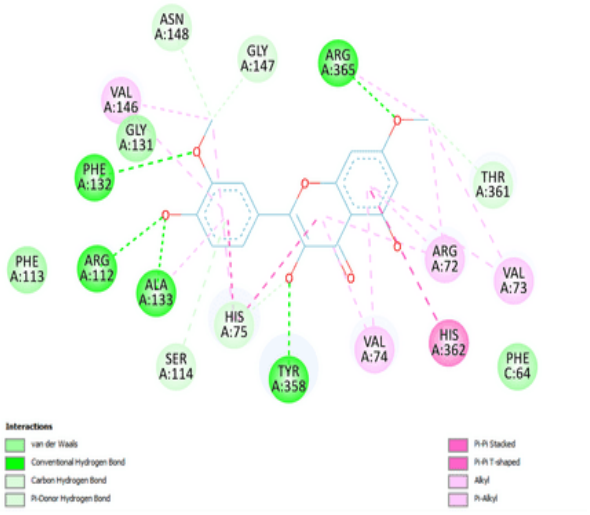

Fig. 5. Hibiscatin- catalase 2D

Fig. 6. Quercetin- catalase

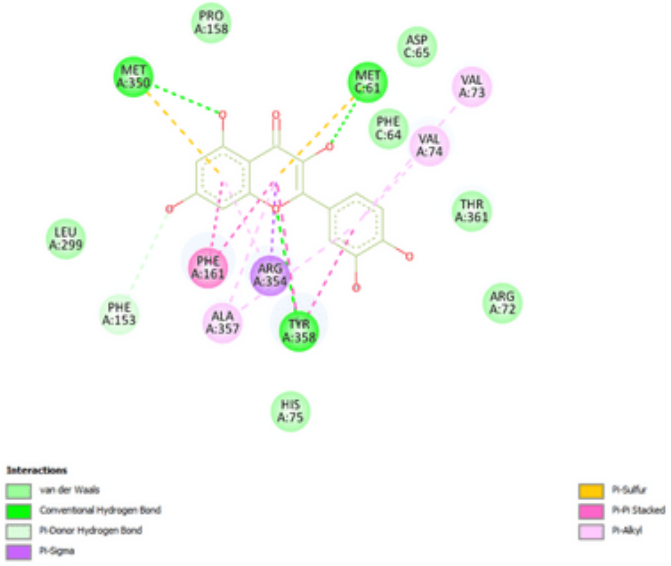

Fig. 7. Quercetin- Catalase 2D

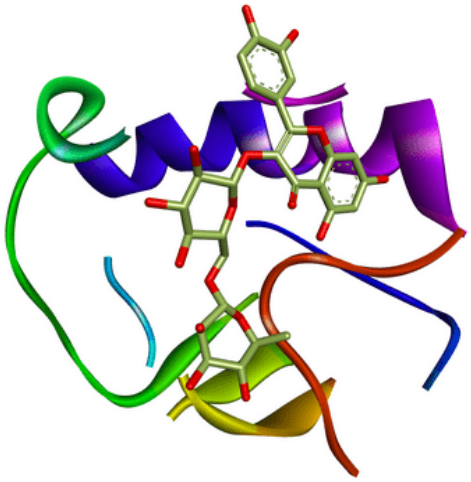

Fig. 8. Rutin- catalase

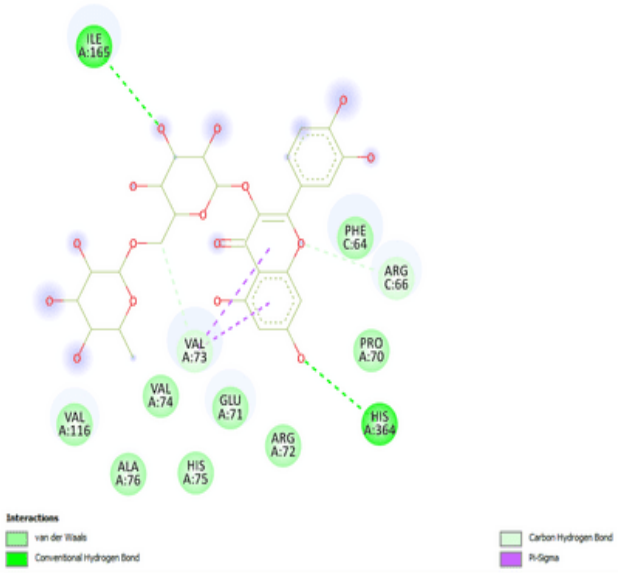

Fig. 9. Rutin- Catalase 2D

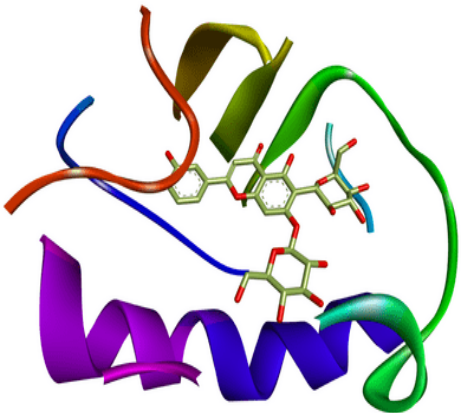

Fig. 10. Lutonarin- catalase

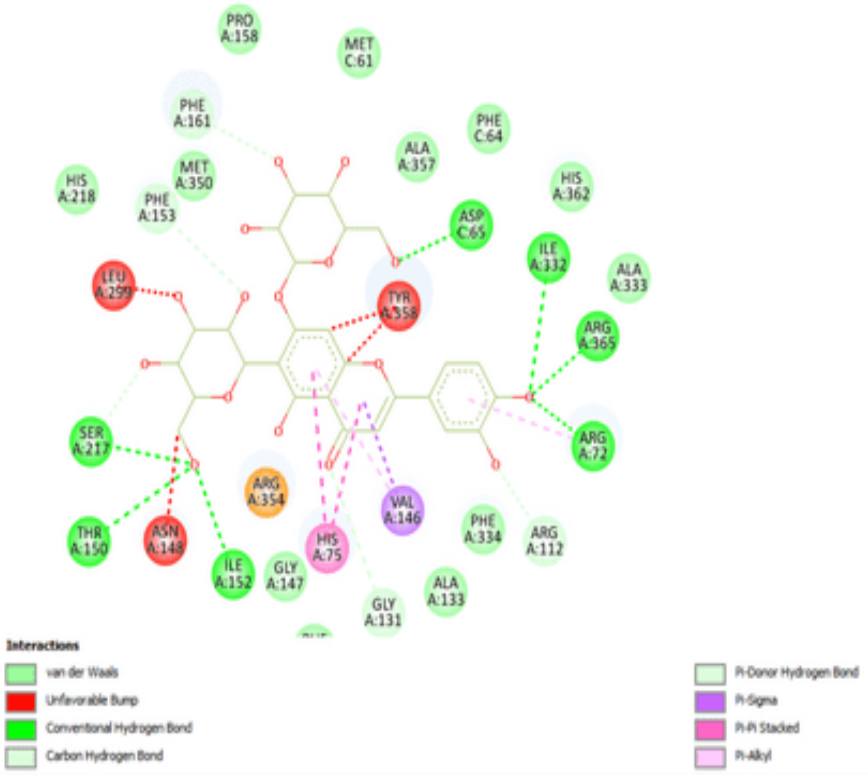

Fig. 11. Lutonarin- Catalase 2D

Molecular docking interaction with catalase:

The structurally similar Hibiscatin and Quercetin had a good binding energy profile compared to the Lutonarin and Rutin compounds. The binding energy of Hibiscatin and Quercetin are - 124 and -108.95 K.cal/mol respectively. Both –OCH3 and -OH substituents in Hibiscatin and –OH substituents in Quercetin are responsible for the majority of Hydrogen bond interactions with the active site amino acid residues in the Catalase protein. Due to the complicated nature of the Lutonarin and Rutin, they have steric hindrance and clashes with the active site pocket and thus they have lower binding energy with Catalase.

Molecular Docking Interactions with Glutathione Reductase:

Among the compounds docked with the Glutathione Reductase Lutonarin (-93.82 K.cal/mol) and Rutin (-88.79 K.cal/mol) had a good binding profile compared to the Hibiscatin and Quercetin compounds. The –C=O and the –OH groups are involved in the interaction with the active site ‘amino acid residues in both Lutonarin and Rutin compounds.

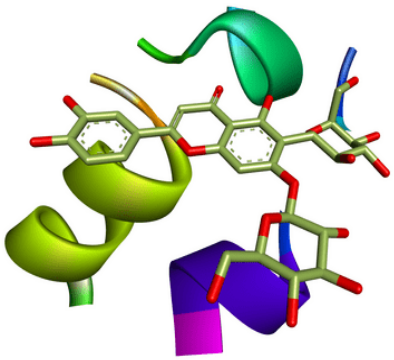

Fig. 12. Lutonarin-GSH

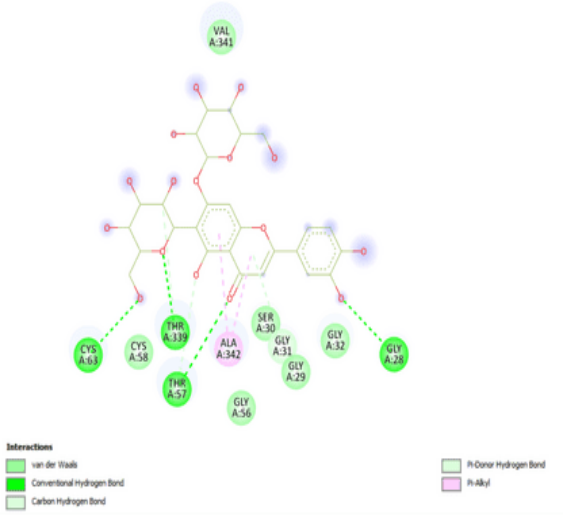

Fig. 13. Lutonarin-GSH 2D

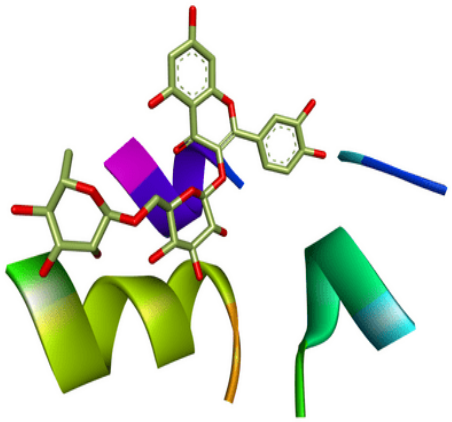

Fig. 14. Rutin-GSH

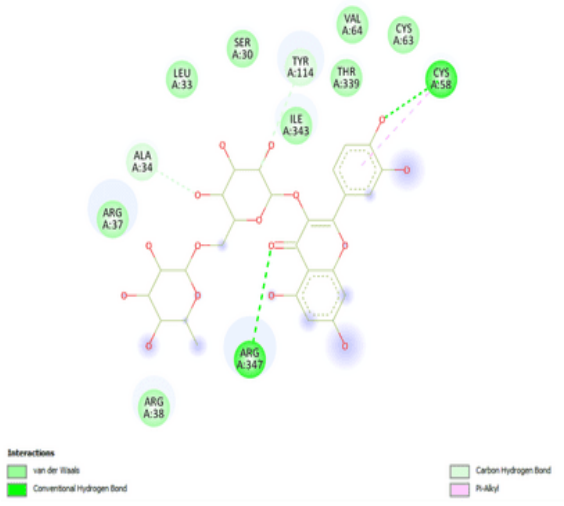

Fig. 15. Rutin-GSH 2D

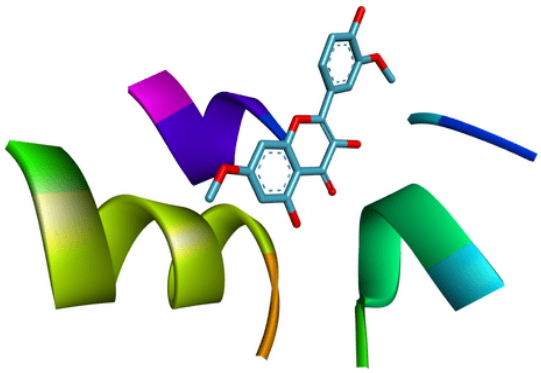

Fig. 16. Hibiscatin-GSH

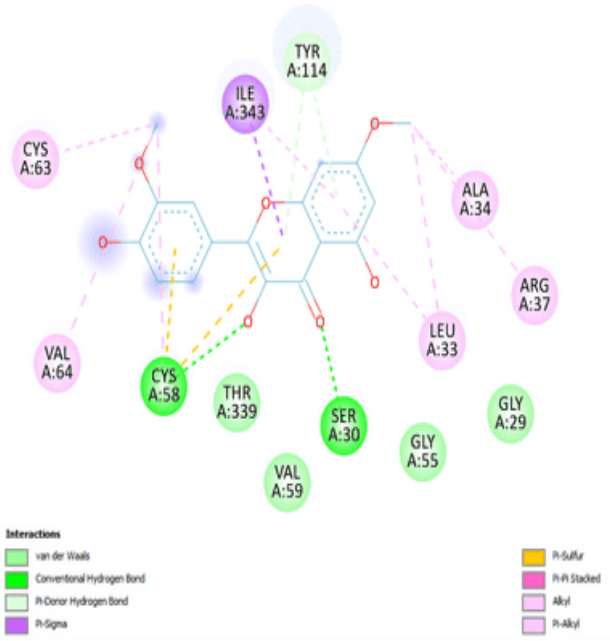

Fig. 17. Hibiscatin-GSH 2D

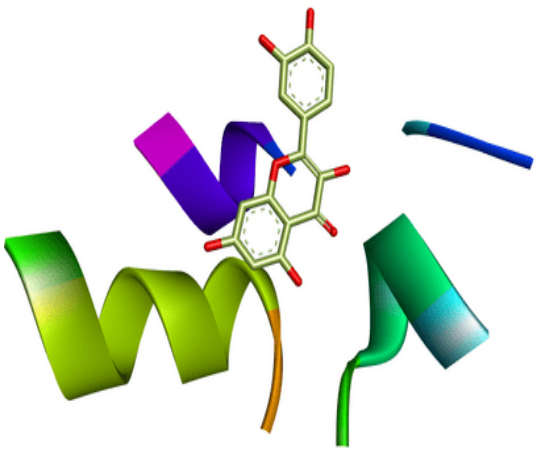

Fig. 18. Quercetin-GSH

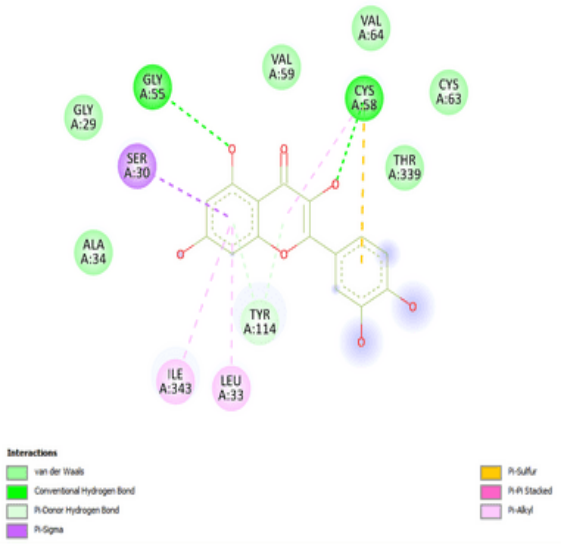

Fig. 19. Quercetin -GSH 2D

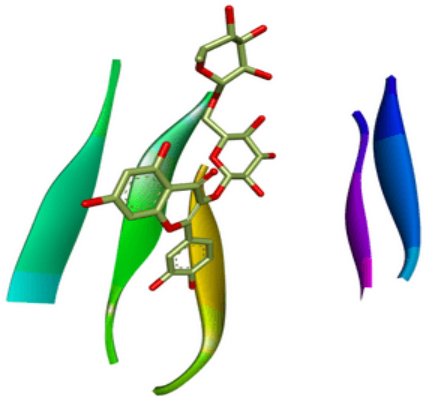

Fig. 20. Rutin- SOD

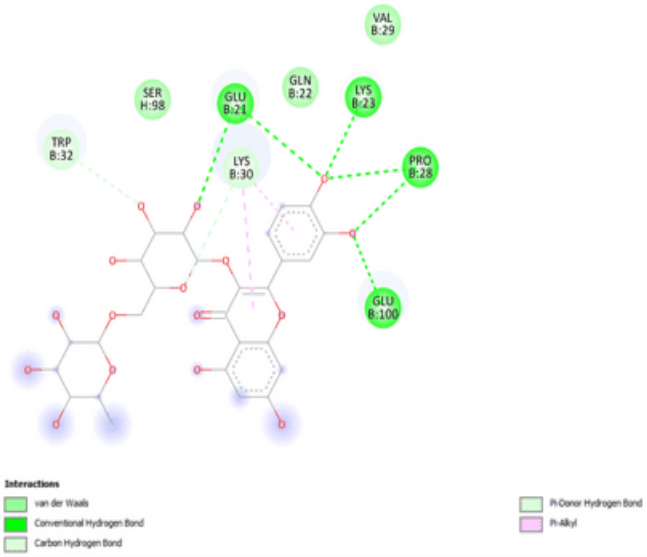

Fig. 21. Rutin- SOD 2D

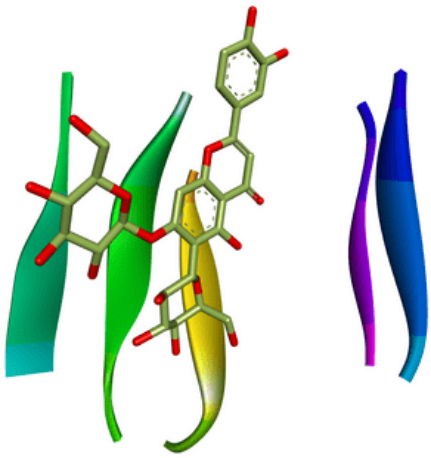

Fig. 22. Lutonarin- SOD

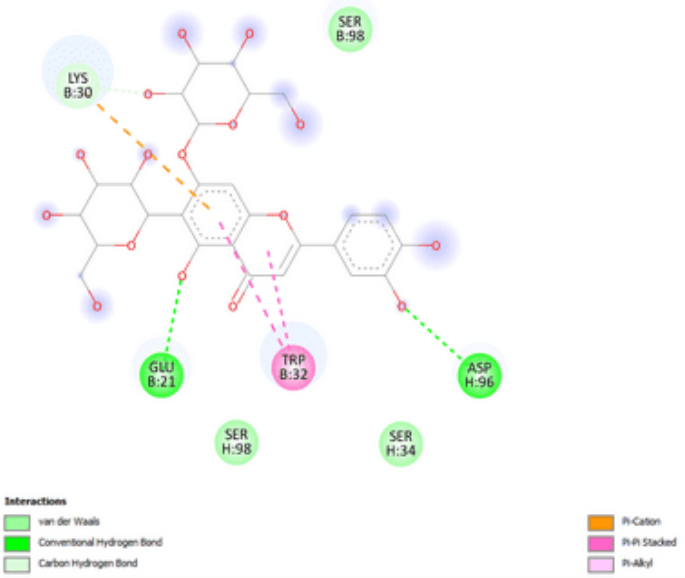

Fig. 23. Lutonarin- SOD 2D

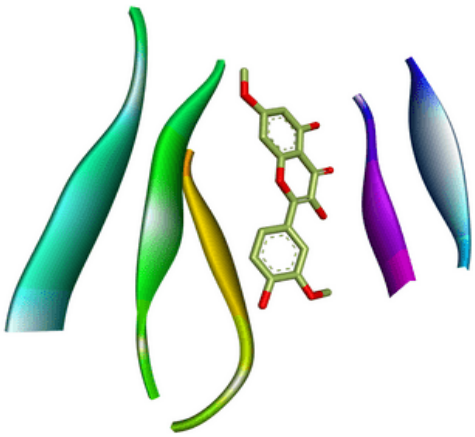

Fig. 24. Hibiscatin-SOD

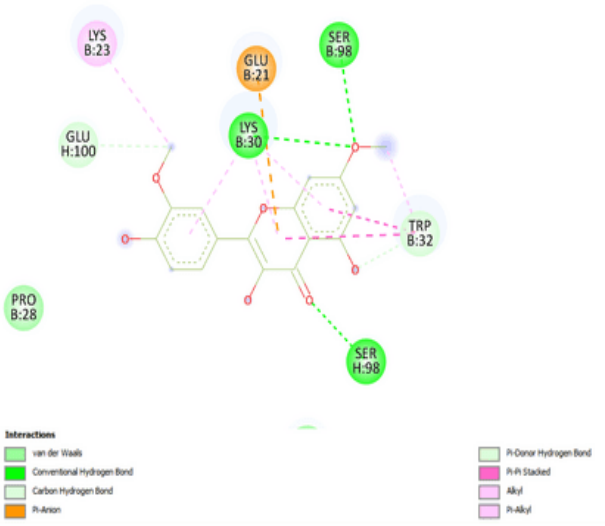

Fig. 25. Hibiscatin-SOD 2D

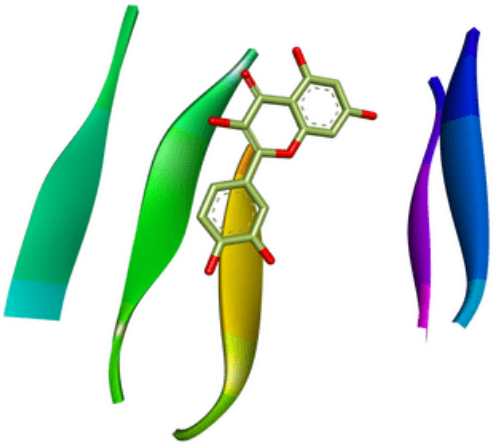

Fig. 26. Quercetin- SOD

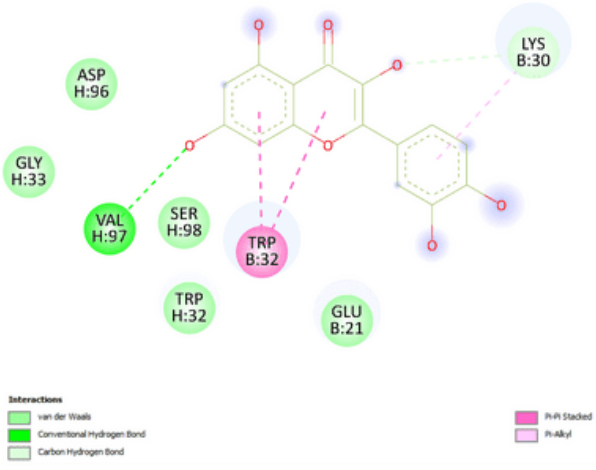

Fig. 27. Quercetin- SOD 2D

Table 1. Energies of Catalase, Glutathione, SOD

Binding Energy K.cal/mol	Catalase	Glutathione Reductase (GSH)	SOD
Hibiscatin	-124	-83.32	-105.68
Lutonarin	-90.7	-93.82	-108.61
Quercetin	-108.95	-70.95	-88.07
Rutin	-83.38	-88.79	-116.67

Molecular docking interactions with superoxide dismutase:

Rutin had very good binding energy with SOD (-116.67 K.cal/mol) followed by Lutonarin (- 108.61 K.cal/mol). They both are structurally similar compared to Hibiscatin and Quercetin. Hibiscatin also had a better binding profile (-105.68 K.cal/mol) with SOD. The peripheral –OH substituents are involved in the interactions in both Rutin and Lutonarin compounds with the active site residues of SOD protein.

2. DISCUSSION

In the present study, docking studies of hibiscatin which is obtained from Hibiscus Plantifolius and Lutonarin obtained from Hordeum Vulgare was evaluated. The binding energies of Hibiscatin, Lutonarin, Quercetin and Rutin were studied and compared with the antioxidant enzymes Catalase, Glutathione Reductase and Super oxide dismutase. The binding energies and comparisons were tabulated. The structurally similar Hibiscatin and Quercetin had a good binding energy profile with catalase compared to the Lutonarin and Rutin compounds. Among the compounds docked with the Glutathione Reductase Lutonarin and Rutin had good binding profiles compared to the Hibiscatin and Quercetin compounds. Rutin had very good binding energy with SOD followed by Lutonarin. They both are structurally similar compared to Hibiscatin and Quercetin. Hibiscatin also had a better binding profile with SOD. A good binding profile was observed for Rutin, Lutonarin, Hibiscatin, and Quercetin.

3. CONCLUSION

By using these docking studies comparative studies has been done for the chemical constituents obtained from palnt sources. Based on this, the structurally similar Hibiscatin, Quercetin Lutonarin, and Rutin has good binding energy profiles which are compared with the antioxidant enzymes Catalase, Glutathione Reductase and Super oxide dismutase.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Malunavar SS, Prabhala P, Sutar SM, Kapavarapu R, Mittal MK, Kalkhambkar RG. Molecular modeling and In vitro antimicrobial evaluation of some 2-Aryl-Benzoxazoles/ Benzothiazole analogues containing alkyl, alkenyl and alkynyl linkages. Chemical Data Collections. 2022; 39:100876.
2. Valko MMHCM, Morris H,. Cronin MTD. Metals, toxicity and oxidative stress. Current medicinal chemistry. 2005; 12(10):1161-1208.
3. Valko Marian CJB, Rhodes Jan Moncol, Izakovic M.M, Milan Mazur. Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chemico-biological interactions. 2006;160(1):1-40.
4. Vogel H. Gerhard Günter Müller, Jürgen Sandow, Bernward A Schölkens. Drug discovery and evaluation: pharmacological assays. Edited by H. Gerhard Vogel, and Wolfgang H. Vogel. Berlin: springer. 1997;2.
5. Walston J, Xue Q, Semba RD, Ferrucci L, Cappola AR, Ricks M, Guralnik J, Fried LP. Serum antioxidants, inflammation, and total mortality in older women. American Journal of Epidemiology. 2006;163(1):18-26.
6. Zimmet Paul, Alberti KGMM, Jonathan Shaw. Global and societal implications of the diabetes epidemic. Nature. 2001; 414(6865):782-787.
7. Yu, Ya-Mei, Chien-Hsi Wu, Yueh-He Tseng, Chingmin E Tsai, Weng-Cheng Chang. Antioxidative and hypolipidemic effects of barley leaf essence in a rabbit model of atherosclerosis. Japanese Journal of Pharmacology. 2002;89(2): 142-148.

8. Nourooz-Zadeh, Jaffar, Jarad Tajaddini-Sarmadi, Eddie Ling KL, Simon P Wolff. Low-density lipoprotein is the major carrier of lipid hydroperoxides in plasma. Relevance to determination of total plasma lipid hydroperoxide concentrations. Biochemical Journal. 1996;313(3): 781-786.
9. Zimmerman. Hepatotoxicity HJ. The adverse effect of drugs and other chemicals on the liver. New York. 1978;3-10.
10. Definition WHO. Diagnosis and classification of diabetes mellitus and its complications: Report of a WHO consultation; 1999.
11. Willcox Joye K, Sarah L Ash, George L Catignani. Antioxidants and prevention of chronic disease. Critical reviews in food science and nutrition. 2004;44(4): 275-295.
12. Riley William J. Insulin dependent diabetes mellitus, an autoimmune disorder?. Clinical immunology and immunopathology. 1989; 53(2):S92-S98.
13. Yamaura Katsunori, Noriyuki Nakayama, Maki Shimada, Yuanyuan Bi, Hideki Fukata, Koichi Ueno. Antidepressant-like effects of young green barley leaf (*Hordeum vulgare* L.) in the mouse forced swimming test. Pharmacognosy Research. 2012;4(1):22.
14. Tripathi Yamini B., Savita Chaurasia, Ekta Tripathi, Anil Upadhyay, Dubey GP. Bacopa monniera Linn. as an antioxidant: mechanism of action. Indian Journal of Experimental Biology 1996;34(6):523-526.
15. Bhendes YM. General pathology and pathology of systems, S. G. Deodhare, 6th edition Popular Prakashan, Mumbai. 2002;277.
16. Young IS, Woodside JV. Antioxidants in health and disease. Journal of clinical pathology. 2001;54(3):176-186.
17. Ceruti PA. Oxy-radicals and tumour promotion. Science. 1994;344:862-3.
18. Lee J, Koo N, Min DB. Reactive oxygen species, aging, and antioxidative nutraceuticals. Comprehensive reviews in food science and food safety. 2004; 3(1):21-33.
19. Kumar GS, Jayaveera KN. A textbook of pharmacognosy and phytochemistry. S. Chand Publishing; 2014.
20. Ames BN, Shigenaga MK, Hagen TM. Oxidants, antioxidants, and the degenerative diseases of aging proceedings of the National Academy of Sciences. 1993;90(17):7915-22.
21. Rajan S, Gokila M, Jency P, Brindha P, Sujatha RK. Antioxidant and phytochemical properties of Aegle marmelos fruit pulp. Int J Curr Pharm Res. 2011;3(2):65-70.
22. Ardestani A, Yazdanparast R. Antioxidant and free radical scavenging potential of *Achillea santolina* extracts. Food chemistry. 2007;104(1):21-9.
23. Dean RT, Gieseg S, Davies MJ. Reactive species and their accumulation on radical-damaged proteins Trends in biochemical sciences. 1993;18(11):437-41.
24. Blois MS. Antioxidant determinations by the use of a stable free radical. nature. 1958;181(4617):1199-200.
25. Ananth A, Rajan S. Antibacterial and phytochemical investigation of datura stramonium leaf extract against clinical wound samples. European J Biomed and Pharmaceutical Sciences. 2015;2(2):281-294.
26. Jonathan Y. Aust J Basic Appl Sci. 2009; 3(4):3975-9.
27. Blazovics A, Lugasi A, Szentmihalyi K. Acta Biol Szegediensis. 2003;47:99-102.
28. Gülçın İ, Oktay M, Kıreçcı E, Küfrevıoğlu Öİ. Screening of antioxidant and antimicrobial activities of anise (*Pimpinella anisum* L.) seed extracts. Food Chem. 2003;83(3):371-82.
29. Riceevans CA, Miller NJ, Bolwell PG, Bramley PM, Pridham JB, Free. Rad Re. 1995;22:375-83.
30. Watson R, Revenga C, Kura Y. Fishing gear associated with global marine catches: I. Database development. Fisheries Research. 2006;79(1-2):97-102.
31. Gülçın I, Oktay M, Kıreçcı E, Küfrevıoğlu Öİ. Screening of antioxidant and antimicrobial activities of anise (*Pimpinella anisum* L.) seed extracts. Food chemistry. 2003;83(3):371-82.
32. Saravanan D, Lakshmi IA, Gobinath M, Kumar BG, Priya S, Syamala E, Rahamathbee K. Potential antioxidant, hypoglycemic and hypolipidemic effect of leaves of Hibiscus platanifolius Linn. International Journal of Pharmaceutical Sciences and Drug Research. 2011; 3(3):236-40.
33. Yu YM, Chang WC, Chang CT, Hsieh CL, Tsai CE. Effects of young barley leaf extract and antioxidative vitamins on LDL oxidation and free radical scavenging

activities in type 2 diabetes. Diabetes & metabolism. 2002;28(2):107-14.

34. Yamaura K, Doi R, Suwa E, Ueno K. Repeated application of glucocorticoids exacerbate pruritus via inhibition of prostaglandin D2 production of mast cells in a murine model of allergic contact dermatitis. The Journal of toxicological sciences. 2012;37(6): 1127-34.