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Research Article

VIRTUAL SCREENING FOR IDENTIFICATION OF POTENT ANTI-ASTHMATIC COMPOUNDS EXTRACTED FROM *THYME* PLANT: *IN-SILICO* APPROACH

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ABSTRACT

Nowadays, asthma is a significant disease in developed and developing countries. Its chronic inflammatory lung disease. It can cause repeated symptoms such as cough, wheezing and difficulty breathing. The protein Interleukin-13 (IL-13) known as a pleiotropic type 2 cytokine that has a role in the pathogenesis of asthma. *Thyme* (*Thymus vulgaris* L.) is a name that covers both genus and species were most widely used for many centuries as a culinary herb, flavouring agent and herbal medicine for the treatment of asthma as well as various disorders of the respiratory tract, this plant is indigenous in the Mediterranean region, in Northwest Africa. Objective: In this study, molecular docking-based virtual screening of compounds reported its existence in *Thymus vulgaris*, were performed against asthma protein IL-13. The active site was determined by Site-Hound-web: server, the amino acids in the binding pocket of 1IJZ protein are Ala: 9, Glu: 12, Glu: 15, Glu: 16, Leu: 13, Asn: 19, Lys: 62, Arg: 65, Met: 66, Gly: 70 and Phe: 70 Results: Free energy of binding (FEB) showed that six compounds Ursolic acid, 6-Hydroxyluteolin, Quercetin, Taxifolin, Genkwanin, Rosmarinic acid showed the best binding affinity (-7.3, -6.3, -6.2, -6.2, -6.2 and -4.6 kcal/mol. In conclusion, this study identifies that the obtained compound present in the *Thyme* vulgaris responsible for the treatment of asthma. The result will help to use specific compounds that could be an asthma inhibitor among many compounds presented in *Thyme* vulgaris plant that used as an asthma drug.

Keywords: Virtual screening, *Thyme*, molecular docking, Asthma disease, Interleukin-13

INTRODUCTION

In several areas globally, the burden of asthma increases noticeably, the change in asthma epidemiology, as well as the clinical spectrum, also became a global concern. People of all ages affected by asthma, which was classified as a health problem. Additionally, to the increase of asthma in several geographic areas, also increase in the number of cases that are difficult and fatal. Moreover, there are confounding associations and relationship between asthma and environmental tobacco smoke exposure, tobacco smoking, air pollution, infections and infestations, Since the 1970s the Incidence of asthma has increased significantly, In the year 2010, worldwide 300 million people were affected [1]. .The asthma treatment usually is prevented troublesome and chronic symptoms, maintain the normal activity levels, normalize pulmonary function and improve the health-related quality of life [2,]. Asthma considered closely related to increased production of various cytokines, adhesion molecules and inflammatory mediators [3,4]contains many flavonoids, luteolin, lutein, thymonin, phenolic antioxidants, naringenin and pigenin. Among herbs, the fresh *Thyme* has one of the highest antioxidant levels. It is rich in both minerals and vitamins which are essential for optimum health. For the *Thyme* leaves consider one of the most abundant sources of calcium, iron, potassium, magnesium, manganese and selenium [5] .The *Thyme* plant extracts have been used in the traditional medicine for treating many respiratory diseases such as asthma and bronchitis [6] for the treatment of many other pathologies because of several properties such as antiviral, antimicrobial, antifungal, antioxidative, antiseptic and antispasmodic [7,8] .

Virtual screening (VS) is a method that widely used to find the virtual hit of compounds among a batch of compounds, where a variety of studies shown successful results [9,10]. Many reports in the past few years indicated that virtual screening techniques demonstrated to be effective in term of making qualitative predictions that distinguished the active and non-active compounds [11,12]. The primary goal of virtual screening is the reduces the budget, time and the coast of the lab experiments as the compound that needs to tested are selected depend on f exhibited values of drug-receptor interaction together with it is *in vivo* pharmacodynamic behaviors [13] . In the current paper, I virtually screened thirty-three compounds that isolated from the *Thyme* plant that has anti-asthmatic activity, to identify the hit compounds those are responsible for the treatment of Asthma disease other than the whole extract of the *Thyme* plant, by using molecular docking against the asthma protein target.

MATERIALS AND METHODS

Ligand preparation

The structure of compounds isolated from *Thymes* plant was obtained from published literature and two standard control compound structures, were sketched using ChemDraw 2008, and the energy minimization of the ligands was carried out using (HyperChem Professional) [14] and then saved in pdb format.

Protein preparation

The crystal structure of human IL-13 (PDB ID: 1IJZ) [15] was obtained from Protein Data Bank (www.rcsb.org), the crystal structure consist of the chain (A) was used Fig.1. The co-factor and water molecules were removed, and hydrogen was added using AutoDockTools (ADT) [16] .

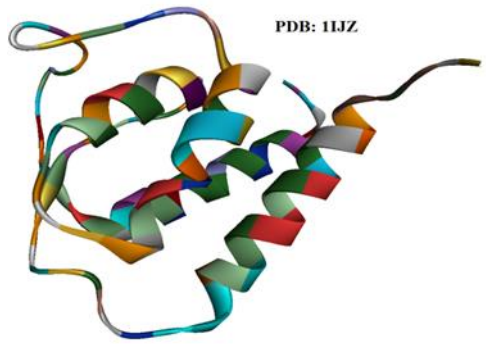


Fig. 1 Schematic diagram of the 3D structure PDB: 1IJZ of the IL-13 protein

Molecular docking

The Autodock Vina [17] was used to perform virtual screening, and all the needed file were prepared. The protein converted from pdb to pdbqt using ADT, The size of grid box with dimensional 60, 60, 60 for x, y, z coordinates in Å, were centred on the binding site of the enzyme; the ligand file converted from mol2 to pdbqt using raccoon. Confi.txt file created including all the necessary information needed to conduct the virtual screening. Other configurations were considered the default. The result of virtual screening was observed as the free energy of binding (FEB) the selected docking pose visualized using Discovery studio version 6.

Active site prediction

Site-Hound-web: server for binding site identification [18] was used to prediction of the active site of the protein, where the PDB file of the target protein uploaded to the server, and it showed the binding site present in the protein, then the amino acids residues that involved in the binding site were selected.

RESULTS AND DISCUSSION

The purpose of this study was to evaluate the binding interactions between the compounds from the *Thyme* plant and Anti-asthma protein by performing molecular docking simulation with autodock Vina. Reliable conformations of the compounds within the active site were attained to gain structural and functional insight into the mechanism of inhibition. Results of molecular docking indicated that all the selected compounds fitted inside the active pocket of the target protein showed different orientations with the amino acids residues. The Thirty-two reported compounds in *thyme* plant were obtained from various publications. These compounds identified and isolated from the *Thyme* plant with the aid of different analytical techniques (High-Performance Liquid Chromatography (HPLC), Reversed-phase HPLC and mass detection LC-MSD, Gas chromatography-mass spectrometry analysis (GC-MS) [19-25]. Molecular docking calculation of the selected compounds screened within the binding site of the asthma protein 1IJZ using Autodock Vina. Finally, the best 6 compounds (as shown in Fig.2) that exhibited the lowest binding energy of the protein-ligand complex were chosen. The name and the structure of the compounds used were tabulated in Table 1.

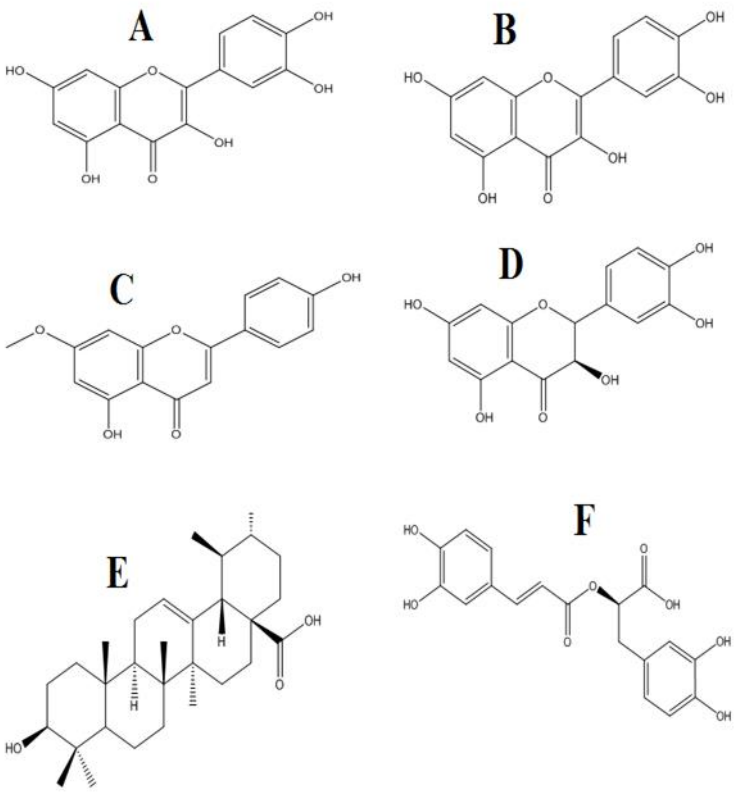
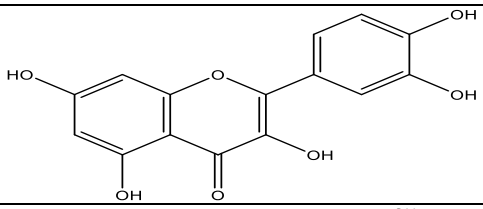
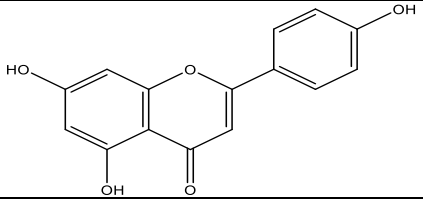
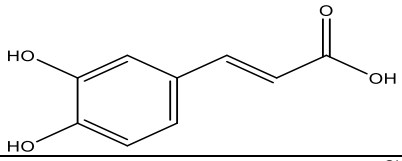
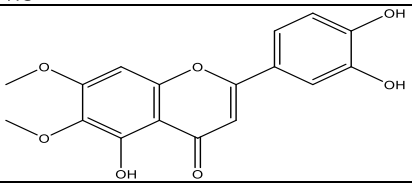
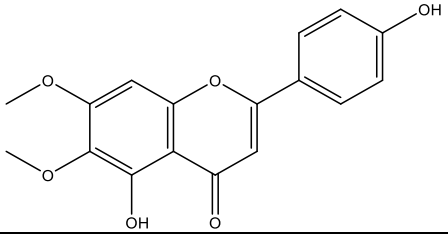
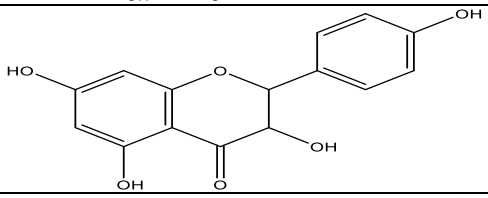
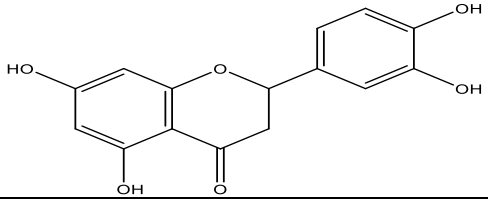
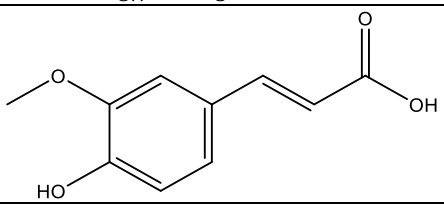
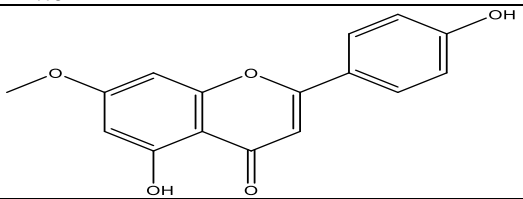
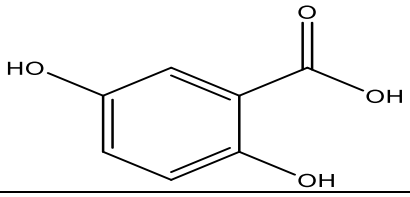
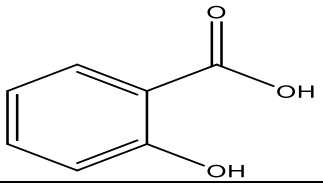
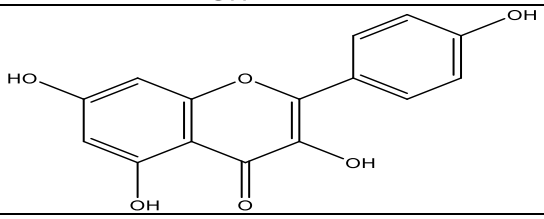
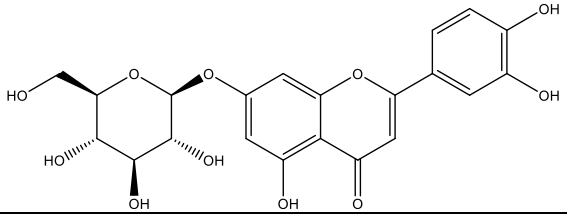
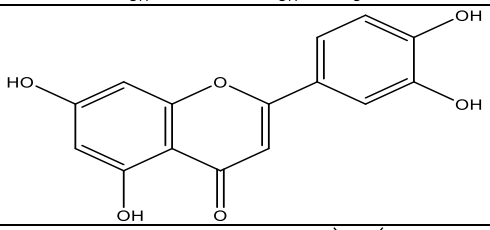
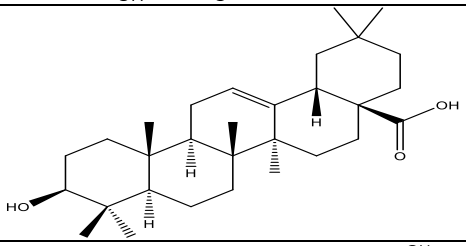
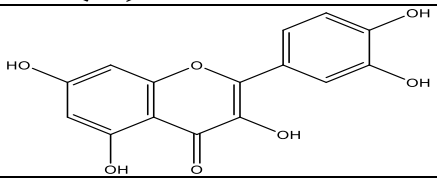
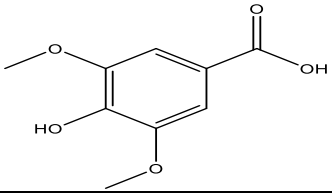
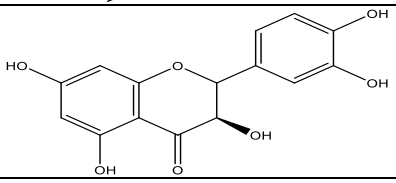
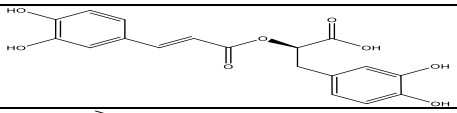
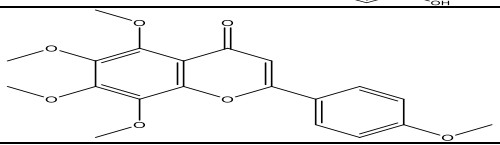
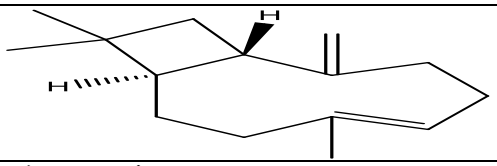
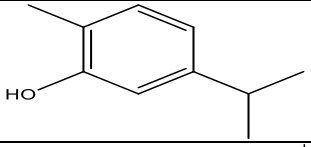
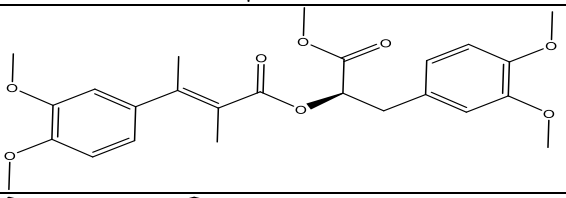
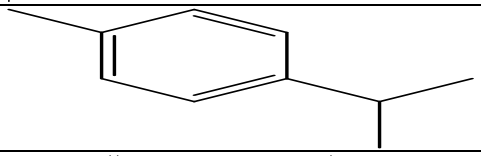
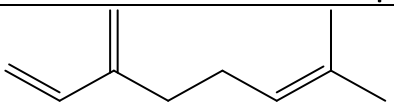
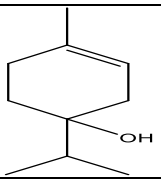
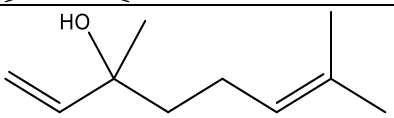
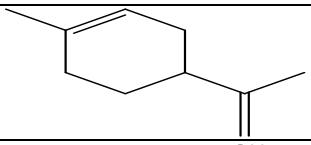
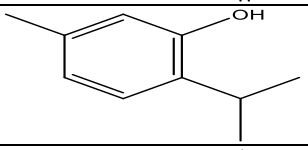
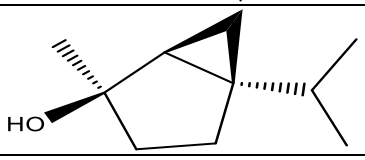


Fig. 2 Structure of the best 6 compounds (A) 6-Hydroxyluteolin, (B) Quercetin, (C) Genkwanin (D) Taxifolin, (E) Ursolic acid and (F) Rosmarinic acid.

Table 1. Compounds of Isolated from *thyme* plants

No	Name of the compounds	FEB	Chemical Structure
Compound isolated from plant			
1	6-Hydroxyluteolin	-6.3	
3	Apigenin	-6.1	
4	Caffeic acid	-5.0	
6	Cirsiliol	-6.1	
7	Cirsimaritin	-6.2	
8	Dihydrokaempferol	-6.1	
9	Eriodictyol	-6.0	
10	Ferulic acid	-5.1	
11	Genkwanin	-6.2	

12	Gentisic acid	-4.1	
13	Hydroxybenzoic acid	-4.4	
14	Kaempferol	-6.1	
15	Luteolin 7-O-β-D-glucoside	-5.3	
16	Luteolin	-6.1	
17	Oleanolic acid	-5.8	
18	Quercetin	-6.2	
19	Syringic acid	-4.5	
20	Taxifolin	-6.2	

21	Ursolic acid	-7.3	
22	Xanthomicrol	-5.9,	
Compounds extracted from essential oil			
1	Beta-Caryophyllene	-4.9	
2	Carvacrol	-4.7	
3	Rosmarinic acid	-4.6	
4	*P*-Cymene	-4.6	
5	Myrcene	-4.5	
6	Terpinen-4-ol	-4.4	
7	Linalool	-4.4	
8	Limonene	-4.4	
9	Thymol	-4.2	
10	Sabinene hydrate	-4.2	

The results obtained from docking simulation indicate that the compounds used entirely interacted at the active pocket with the essential amino acid residues such as Ala: 9, Glu: 12, Glu: 15, Glu: 16, Leu: 13, Asn: 19, Lys: 62, Arg: 65, Met: 66, Gly: 70 and Phe: 70 (as shown in Fig.3).

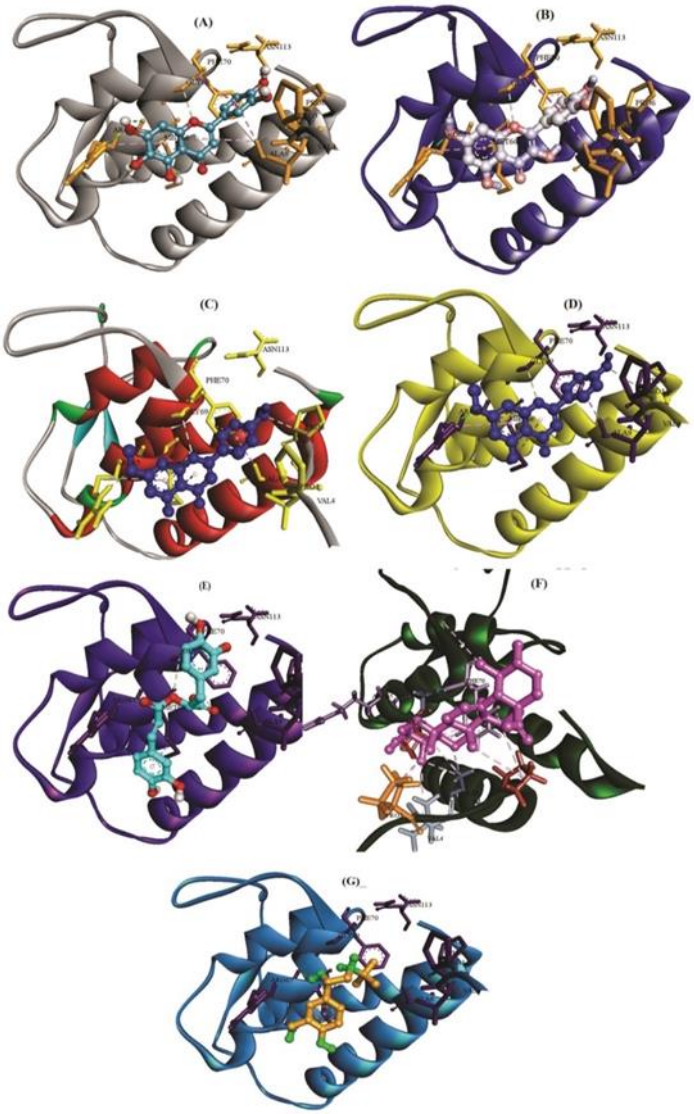


Fig.3 Show 3D of ligand interactions of the 6 candidates showing hydrogen-bond and hydrophobic interactions. (A) 6-Hydroxyluteolin, (B) Ursolic acid (C) Quercetin, (D) Genkwanin (E) Taxifolin, (F) Rosmarinic acid and (G) Salbutamol.

The observed docking results between the target protein and the compounds were manually examined and found that extensive interactions were formed with the amino acids that compose the active site. The interpretation of the docking results revealed that all of the six compounds positioned at the same location inside the active pocket of the target protein, as shown in Fig.4.

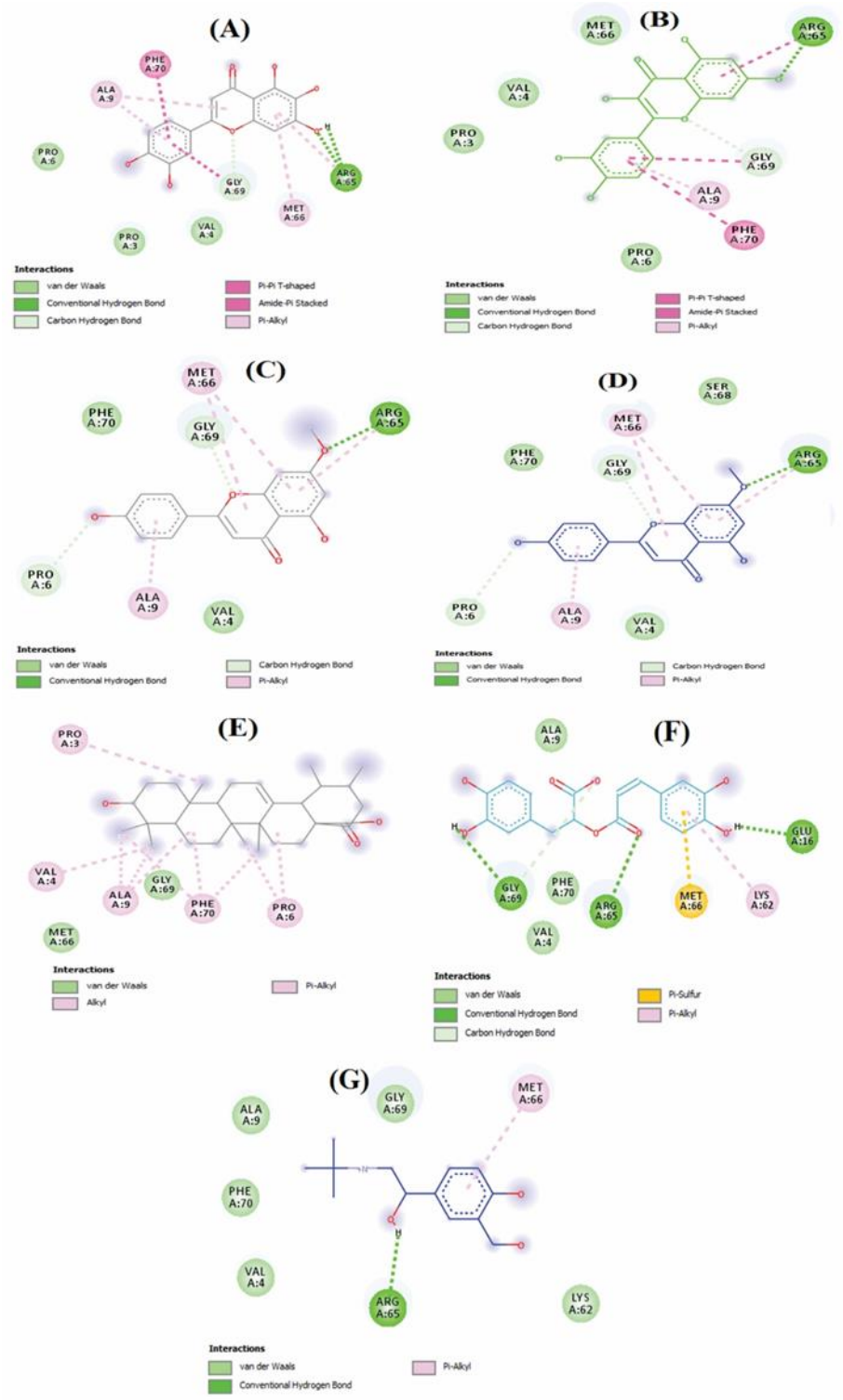


Fig.4. Show the 2D ligand interactions of the 6 candidates showing hydrogen-bond and hydrophobic interactions. (A) 6-Hydroxyluteolin, (B) Ursolic acid (C) Quercetin, (D) Genkwanin (E) Taxifolin, (F) Rosmarinic acid (G) Salbutamol

The interactions of the selected compounds were similar to that exhibited by the standard drug Salbutamol; therefore this similarity suggested that these specific compounds used in this study, among many other compounds found in *Thyme*, could be responsible for the treatment of asthma. The FEB results from virtual screening were at the range -7.2 to -4.9 kcal/mol for active compounds while inactive compounds were observed at the range -4.2 kcal/mol and higher. These compounds exhibited good binding affinities with the receptor. The binding pose of each of them was evaluated and reported as types of interactions such as H-bond, hydrophobic interaction, PI-alkyl, PI-PI- Tshaped, Amide-p shaped, and van deer walls between the compounds and the protein interactions, (detailed in Table 2).

Table 2. Molecular docking analysis between the compounds and target protein

No	Compound	Van deer walls	Hydrophobic interactions	PI-PI-Tshaped	Amide-p shaped	PI-alkyl	H-Bond	Carbon H-Bond
1	Ursolic acid	Met :66 Gly :69 Pro :3	Aal :9 Val:4 Gly:69 Phe :70 Pro :6			Pro :3 Val :4 Aal :9 Pro: 6 Phe:70		
2	6- Hydroxyluteolin	Pro :6 Pro :3 Val :4	Val :4 Phe:70 Gly:69 Met :66 Pro :3	Phe:70	Gly :69	Met :66 Ala :9 Arg :65	Arg :65	Gly :69
3	Quersitin	Pro :3 Met :66 Val :4 Pro :6	Met :66 Gly :69 Phe:7 Val :4	Phe :70 Phe :70	Phe:70 Gly:69	Ala A:9	Arg A:65	Gly :69
4	Taxifolint	Met :66 Pro :3 Pro :6	Met :66 Phe :70 Gly:69	Arg :65 Phe :70	Arg A:65 Phe A:70	Ala A:9	Val :4	69 Gly:A Gly:69
5	Genkwanin	Phe :70 Val :4	Phe A:70 Val A:4 Gly:69 Aal A:9			Met A:66 Arg A:65 Aal A:9	Arg A:65	Gly A:69
6	Rosmarinic acid	Aal :9	Lys A:62 Arg:65 Gly:69 Met:66			Lys A:62	Arg :65 Gly :69 Glu :16	
7	Salbutamol	Phe :70 Val :4 Gly :69 Lys:62 Met:66				Met A:66	Arg A:65	

The analysis of the results showed extensive interactions and correlation types with the amino acid residues found in the binding pocket, indicating the effectiveness of the compounds towards asthma. The selection of the best compounds depending on the Lipinski role of five (Lipinski, 2004), where all the compounds have (i) number of hydrogen acceptor less than 10, (ii) number of hydrogen donor less than 5, (iii) MW less than 500 (iv) log P less than 5 and do not violate Lipinski role of five as shown in (shown in Table 3). The results of interactions of the ligands with essential residues of the IL-3 protein revealed that all the ligands bonded to the residues in the binding pocket, as shown in Fig.5.

Table 3: Drug-likeness properties of the best compounds.

No	Compound	LogP	H-bond donors	H-bond acceptors	Molecular weight(g/mol)
1	6-Hydroxyluteolin	1.17	5	7	302
2	Ursolic acid	6.79	1	3	455
3	Quercetin	1.68	5	7	302
4	Taxifolin	1.5	5	7	304
5	Genkwanin	3	2	5	284
6	Rosmarinic acid	1.63	4	8	359

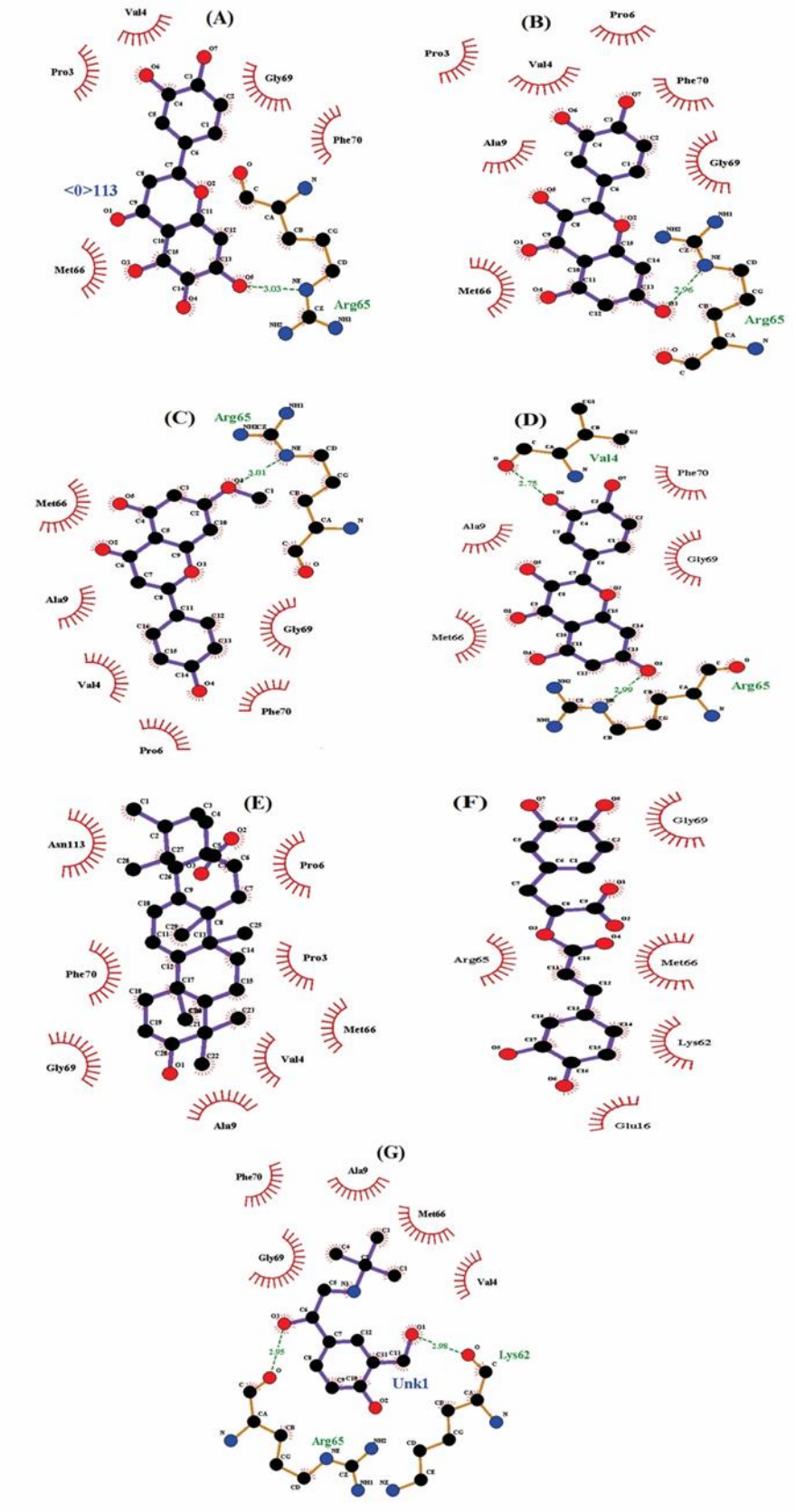


Fig.5 Show Ligplot of schematic ligand interactions of the 6 candidates showing hydrogen-bond and hydrophobic interactions. (A) 6-Hydroxyluteolin, (B) Ursolic acid (C) Quercetin, (D) Genkwanin (E) Taxifolin, (F) Rosmarinic acid and Salbutamol.

Ursolic acid is known as a triterpenoid compound found in many plants. It used in medicinal herbs and human diet and possessed an anti-allergic activity [26,27]. This compound was found to show van deer walls interaction with active site amino acid residues Met:66 Gly:69 and the PI-alkyl interaction with Pro:3 Val :4 Ala :9 Pro :6 Phe: 70, in addition, hydrophobic interaction also exhibited with the residues Ala: 9 Val: 4 Gly:69, Phe: 70 Pro:6. 6-Hydroxyluteolin compound was found to show many interactions, hydrogen bond was formed with Arg :65, Likewise, Amide-p shaped interaction with Gly:69 formed, also found to interact with Met :66, Ala :9, Arg:65 through PI-alkyl, in addition, Van deer walls interaction exhibited with the amino acids Pro:6, Pro:3, Val:4 as well as PI-PI- T-shaped with Phe:70. The third compound, Quercetin, is one of the essential flavonoids that have a chemical effect [28]. This compound interacted with amino acids in the active site, it form Hydrogen bond with the amino acid Arg: 65, in addition, found to show Van deer walls interactions with the amino acids Pro:3, Met: 66, Val: 4, Pro: 6, likewise An Amide-p-shaped interaction exhibited between the compound and the amino acid Phe:70. Carbon H-bond interaction noticed with the Phe: 70, and finally, a PI-PI-T-shaped interaction with amino acids Arg: 65, Phe: 70 formed. The compound, Taxifolin, was the fourth most active compound against the asthma protein. The binding energy obtained was -6.20 kcal/mol. Different interactions exhibited between this compound and the target protein, similar to the previous one. H-bond formed interaction with the amino acid Val: 4. Also, carbon H-Bond formed with amino acids Gly: 69. Van der Waals interactions also displayed with Met: 66, Pro :3, Pro: 6. P-alkyl bonds brought interaction with Ala: 9 and finally, the Amide-p shaped bond formed with Arg: 65, Phe: 70. Genkwanin is as a flavonoid has anti-tumour and anti-oxidant activities 29. In this study, the compound has shown many interactions with the asthma protein, which exhibited the effectiveness at the binding site of the protein, where the value of the FEB was -6.2 kcal/mol. This compound was found to show one hydrogen bond with Arg: 65, which enhances the stability of the compound in the active site. Van deer Walls interactions showed with the protein thought Phe:70, Val:4 amino acids, another interaction Pi-alkyl formed with the amino acids Met: 66 and Aal: 9, in addition, Hydrophobic interaction, was noticed between this compound and amino acids in the binding site Phe: 70 Val: 4 Gly:69 and Aal:9. Rosmarinic acid is a polyphenolic compound found in Thymus vulgaris and many other herbal plants, has anti-inflammatory activity, it is used to treat asthma and allergic disorders 30,31,32,. Although this compound showed FEB -4.6 kcal/mol higher than the other selected compound, it exhibited many interactions with amino acids at the active binding site. Three hydrogen bonds were formed with Gly:69, Arg: 65, Glu:16, these interactions enhance the stability of this compound in the active site of the protein. Pi-alkyl interaction was found to form one interaction with amino acid Lys: 62, in addition, van der Waals interaction, noticed between this compound and the protein amino acids Ala: 9, Val:4, Phe: 65, Likewise Hydrophobic interaction shown with Lys:62, Arg: 65, Gly:69 Met: 66. Ligplot (as shown in Fig. 5) demonstrated that all the selected ligands interacted with the essential amino acid residues in the binding pocket. Therefore interactions contribute significantly to the stability of compounds within the binding site of the protein and thus enhance the activity of these compounds against the disease.

CONCLUSION

Asthma considered as one of the menacing respiratory diseases that affecting children as well as adults, this disease characterised by chronic airway inflammation. There is the growing use of virtual screening in the field of discovery and development of new drugs from a plant. In this approach molecular docking and virtual screening were performed, the analysis of the obtained molecular interactions enabled to identify some compounds Ursolic acid, 6-Hydroxyluteolin, Quercetin, Taxifolin, Genkwanin, Rosmarinic acid that may be responsible for treating asthma rather than using the whole thyme plant extract. The best six compounds in this study do not violate the Lipinski rule of five to be an orally active drug and consider as a clean lead like molecules. The modification of these compounds may lead to novel drug candidates. Also, further investigations need to be carried out with the help of this in-silico approach to producing more potent and effective drugs. *In vitro* and *in vivo* studies to validate these compounds must be taken into consideration to complete this work.

REFERENCES

1. Aggarwal AN, Chaudhry K, Chhabra SK, Souza GA., Gupta D., Jindal S.K et al. Prevalence and risk factors for bronchial asthma in Indian adults: a multicentre study. Indian J. Chest Dis. Allied Sci and Allied Sciences 2006; 48(1): 13
2. Kabesch M. and Adcock IM. Epigenetics in asthma and COPD. Biochimie, 2012; 94(11): 2231-2241.
3. Pawankar R. Epithelial cells as immunoregulators in allergic airway diseases. Curr Opin Allergy Clin Immunol 2002; 2(1):1-5.
4. Barnes PJ. Cytokines as mediators of chronic asthma. Am. J. Respir. Crit. Care Med 1994; 150 (5 Pt 2): S42-9.
5. Sharangi AB and Guha S. Wonders of leafy spices: Medicinal properties ensuring Human Health. Sci Interl 2013; (9): 312-317.
6. Alonso JR. Tratado de fitomedicina: bases clínicas y farmacológicas. Isis Ediciones 1998.
7. Soliman KM and Badeaa RI. Effect of oil extracted from some medicinal plants on different mycotoxigenic fungi. Food Chem. Toxicol, 2002; 40(11): 1669-1675.
8. Bukovská, A., Cikoš, Š., Juhás, Š., Il'ková, G., Rehák, P. and Koppel, J. Effects of a combination of thyme and oregano essential oils on TNBS-induced colitis in mice. Mediat inflamm 2007; 2007.
9. Abdulsalam AAA. In-silico virtual screening and ADMET study to find novel neuraminidase N1 inhibitors extended to the 150-cavityJ. Appl. Pharm. Sci 2017; 7(05): 024-033.
10. Oprea, TI. and Matter, H. Integrating virtual screening in lead discovery. Curr Opin Chem Biol 2004; 8(4): 349-358.
11. Chang TT, Sun MF, Chen HY, Tsai FJ, Fisher M, Lin JG et al. Screening from the world's largest TCM database against H1N1 virus. J. Biomol. Struct. Dyn 2011; 28(5): 773-786.
12. Lin CH, Chang TT, Sun MF, Chen HY, Tsai FJ, Chang KL et al. Potent inhibitor design against H1N1 swine influenza: structure-based and molecular dynamics analysis for M2 inhibitors from traditional Chinese medicine database. J. Biomol. Struct. Dyn 2011; 28(4): 471-482.
13. Kitchen DB, Decornez H , Furr, J.R. and Bajorath, J.,. Docking and scoring in virtual screening for drug discovery: methods and applications. Nat Rev Drug Discov 2004; 3(11): 935.
14. HyperChem(TM) Professional 7.51, Hypercube, Inc., 1115 NW 4th Street, Gainesville, Florida 32601, USA.
15. Moy FJ, Diblasio E, Wilhelm, J. and Powers, R. Solution structure of human IL-13 and implication for receptor binding. J. Mol. Biol 2001; 310(1): 219-230.
16. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS and Olson AJ. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. J. Comput. Chem 2009; 30(16): 2785-2791.

17. Trott O. and Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading J. Comput. Chem 2010; 31(2): 455-461.
18. Hernandez M, Ghersi D and Sanchez R. SITEHOUND-web: a server for ligand binding site identification in protein structures. Nucleic Acids Res 2009; 37(suppl_2): W413-W416.
19. Varga E, Bardocz A, Belak A, Maraz A, Boros B, Felinger A, et al. Antimicrobial activity and chemical composition of thyme essential oils and the polyphenolic content of different thymus extracts. Thymus 2015; 63(3).
20. Salehzadeh A, Hashemi Doulabi, MS, Sohrabnia B. and Jalali A. The effect of thyme (*Thymus vulgaris*) extract on the expression of nor A efflux pump gene in clinical strains of Staphylococcus aureus. J Genet Resour 2018; 4(1): 26-36.
21. Ruiz-Navajas, Y, Viuda-Martos M, Sendra E, Perez-Alvarez JA. and Fernández-López, J. Chemical characterization and antibacterial activity of *Thymus moroderi* and Thymus piperella essential oils, two Thymus endemic species from southeast of Spain. Food Control 2012; 27(2): 294-299.
22. Kivilompolo M. and Hyötyläinen T. Comprehensive two-dimensional liquid chromatography in analysis of Lamiaceae herbs: characterisation and quantification of antioxidant phenolic acids. J chromatogr A 2007; 1145(1-2): 155-164.
23. Stahl-Biskup, E., Venskutonis, RP. Thyme. In: Peter KV. (Ed.), Handbook of Herbs and Spices. second ed. Cambridge, UK, Woodhead Publishing, Abington, 2012 : 499–525.
24. Ekoh SN, Akubugwo, E.I., Ude, V.C. and Edwin, N. Anti-hyperglycemic and anti-hyperlipidemic effect of spices (*Thymus vulgaris, Murraya koenigii, Ocimum gratissimum* and *Piper guineense*) in alloxan-induced diabetic rats. Int J Biol Sci 2014; 4(2), pp.179-87.
25. Prasanth Reddy V, Ravi Vital K, Varsha P.V. and Satyam S. Review on *Thymus vulgaris* traditional uses and pharmacological properties. Med. Aromat Plants 2014; 3: 164.
26. Banno N, Akihisa T, Tokuda H, Yasukawa K, Higashihara H, Ukiya M, et al. Triterpene acids from the leaves of Perilla frutescens and their anti-inflammatory and antitumor-promoting effects. Biosci Biotechnol Biochem 2004 ; 68(1): 85-90.
27. Furtado RA, Rodrigues EP, Araujo FR, Oliveira WL, Furtado MA, Castro MB et al. Ursolic acid and oleanolic acid suppress preneoplastic lesions induced by 1, 2-dimethylhydrazine in rat colon. Toxicol. Pathol 2008; 36(4): 576-580.
28. Maalik A, Khan FA, Mumtaz A, Mehmood A, Azhar S, Atif M, et al. Pharmacological applications of quercetin and its derivatives: a short review. trop j pharm res 2004; 13(9): 1561-1566.
29. Shu Y, Liang Y, Liang Z, Zhao X, Zhu X, Feng W, Liang et al. Studies on a simple and efficient method for large-scale preparation of genkwanin from daphne genkwa sieb. et zucc. using normal-phase flash chromatography. J Liq Chromatogr Relat Technol 2014; 37(6): 773-785.
30. Stansbury J. Rosmarinic acid as a novel agent in the treatment of allergies and asthma. J. Restor. Med 2014; 3(1): 121-126.
31. Liang Z, Nie H, Xu Y, Peng J, Zeng Y, Wei Y, Wen X, Qiu J, Zhong W, Deng X. and He, J. Therapeutic effects of rosmarinic acid on airway responses in a murine model of asthma. Int Immuno pharmacol 2016; 41: 90-97.
32. Gedikoğlu A, Sökmen M. and Çivit A. Evaluation of Thymus vulgaris and Thymbra spicata essential oils and plant extracts for chemical composition, antioxidant, and antimicrobial properties. Food Sci Nutr 2019; 7(5): 1704-1714.

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