ZITA MEDICAL MANAGEMENT

www.hsmc.gr/en/pharmakeftiki-journal/

PHARMAKEFTIKI, 37, 2S, 2025 | 181-184 RESEARCH

https://doi.org/10.60988/p.v37i2S.183

In silico docking and target prediction of stigmasterol extracted from *Chrysanthemum hortorum*

Hawraa Kareem Al-yassery[1,*], Abbas H. Abdulsada[2]

[1]Department of Pharmacognosy and Medicinal Plants, College of Pharmacy, University of Babylon, Hillah, Iraq
[2]Department of Pharmaceutical Chemistry, College of Pharmacy, University of Babylon, Hillah, Iraq

KEY WORDS:
MOE software; *in silico* study; hPXR; 7N4V; 7AXK

ARTICLE INFO:
Received: December 28, 2024
Revised: January 09, 2025
Accepted: January 31, 2025
Available online: October 10, 2025

ABSTRACT

This *in silico* study explores the therapeutic potential of stigmasterol (a phytosterol identified in *Chrysanthemum hortorum via* gas chromatography mass spectrometry; GC-MS) through computational docking against 14 proteins predicted using SwissTargetPrediction. These proteins, implicated in various cancers and metabolic pathways, were retrieved from the Protein Data Bank (PDB) and were analysed using the Molecular Operating Environment (MOE) software. Stigmasterol exhibited high binding affinities with key targets, notably 7N4V (Niemann-Pick C1-like 1; NPC1L1) and 7AXK (the ligand-binding domain of the human pregnane X receptor; hPXR), with ΔG values of -9.2442 and -9.0119 kcal/mol, respectively. Hydrophobic interactions involving residues such as TRP, TYR, PHE, and ILE enhanced ligand stability, while water-mediated contacts (particularly those observed in 4EY7 and 2ZNN) contributed to binding specificity. These findings suggest stigmasterol's potential to modulate cancer-associated pathways, especially those of hormone-sensitive cancers, by influencing cholesterol metabolism and nuclear receptor signalling.

*** CORRESPONDING AUTHOR:**
Hawraa Kareem Al-yassery, Department of Pharmacognosy and Medicinal Plants, College of Pharmacy, University of Babylon, Hillah, Iraq; e-mail: pha384.hawraa.kareem@uobabylon.edu.iq

1. Introduction

Developed nations are increasingly integrating conventional clinical practices with the use of herbal medicines and remedies, resulting in growing reliance on these treatment strategies. Numerous pharmaceuticals have been developed and derived from plants in industrialized countries. Approximately 70% to 95% of the global population relies on traditional medicine as their primary form of healthcare. *Chrysanthemum hortorum*, a member of the Asteraceae family, is

PHARMAKEFTIKI, 37, 2S, 2025 | 181-184

Table 1. Molecular docking results obtained using the Molecular Operating Environment (MOE) software. Target proteins include: 1Q1M (protein tyrosine phosphatase 1B), 2ZNN (human PPAR alpha ligand-binding domain), 2ZNQ (human PPAR delta ligand-binding domain), 4C49 (reactive loop-cleaved human corticosteroid-binding globulin; CBG), 4EY7 (recombinant human acetylcholinesterase), 4YVX (aldo-keto reductase family 1 member C3), 6ESY (human butyrylcholinesterase), 6HJ2 (human pregnane X receptor; hPXR), 6IIU (human thromboxane A_2 receptor), 6K9H (human liver X receptor beta; LXR-β), 6Q2W (human retinoic acid receptor-related orphan receptor gamma; RORγ LBD), 7AXK (ligand-binding domain of the human pregnane X receptor; hPXR), 7CX3 (taprenepag), and 7N4V (cholesterol-bound human Niemann-Pick C1-like 1; NPC1L1). Other abbreviations used: ALA, alanine; ARG, arginine; CYS, cysteine; GLY, glycine; HIS, histidine; HOH, water; IEU, placeholder for ILE or LEU; ILE, isoleucine; LEU, leucine; LYS, lysine; MET, methionine; PHE, phenylalanine; RMSD, root mean square deviation in binding; TRP, tryptophan; TYR, tyrosine; VAL, valine.

Proteins	**ΔG** (kcal/mol)	**RMSD** (Å)	**HOH**	**Amino acids included in H-bonding**	**Amino acids included in short contacts**
4EY7	-6.2767	2.0025	HOH_{952} (2x)	-	TRP_{286}, PHE_{338}, TYR_{341}, TYR_{337}, TYR_{124}, TRP_{86}
4YVX	-7.3928	1.0548	-	-	PHE_{306}, HIS_{117}, PHE_{311}, TRP_{86}, TRP_{227}, TYR_{24}, TYR_{55}, LEU_{268}, TYR_{216}
6ESY	-7.1311	1.5331	-	GLY_{197}	TYR_{332}, GLY_{439}, TRP_{82}, HIS_{438}
7N4V	-9.2442	1.3738	-	-	VAL_{697}, ILE_{1234}, VAL_{701}, PHE_{1239}, LEU_{234}, ILE_{698}, TRP_{383}, PHE_{772}, IEU_{871}, TYR_{1102}, LEU_{621}, ALA_{876}, ILE_{625}, VAL_{1166}
4C49	-6.7286	1.5322	-	ARG_{260}	ARG_{260}, TRP_{371}, HIS_{368}, PHE_{366}, ILE_{263}
7AXK	-9.0119	1.5027	-	ARG_{410} (2x)	ARG_{410} (2x)
6K9H	-6.4266	1.4434	-	-	PHE_{349}, IEU_{313}, ILE_{353}, MET_{312}, PHE_{340}, ILE_{327}, PHE_{354}, IEU_{345}, ILE_{350}, ILE_{309}, HIS_{435}, LEU_{442}, VAL_{439}, ALA_{275}, TRP_{457}, PHE_{349}
6Q2W	-7.3919	1.3449	-	-	MET_{365}, VAL_{376}, ILE_{397}, PHE_{388}, LEU_{391}, ILE_{400}, TRP_{317}, MET_{3588}, LEU_{396}, CYS_{320}, PHE_{378}, LEO_{324}
6HJ2	-7.5185	1.4055	-	-	ILE_{414}, LEU_{411}, LEU_{209}, MET_{243}, VAL_{211}, MET_{246}, TYR_{306}, MET_{323}, TRP_{299}, PHE_{288}, HIS_{407}, PHE_{251}, PHE_{429}, PHE_{429}, PHE_{281}, CYS_{284}
2ZNN	-7.6006	1.8405	HOH_{1004}	-	VAL_{255}, CYS_{275}, ILE_{354}, PHE_{318}, LEU_{321}, MET_{355}, MET_{330}, CYS_{276}, VAL_{332}, ILE_{339}, ILE_{272}, ALA_{333}, LEU_{250}, LEU_{254}, LEU_{247}, ALA_{250}, ILE_{241}
2ZNQ	-5.6081	1.6253	-	CYS_{285}	VAL_{341}, LEU_{353}, VAL_{348}, VAL_{281}, ARG_{284}, LYS_{367}, PHE_{327}, HIS_{449}
7CX3	-8.4296	1.4498	-	-	MET_{116}, ILE_{309}, ILE_{85}, MET_{31}, ARG_{302}, VAL_{89}
1Q1M	-6.43447	1.7784	-	ARG_{24}, GLY_{259}	VAL_{49}, LYS_{120}, TYR_{46}, PHE_{182}, ALA_{217}
6IIU	-5.3068	1.4327	-	-	ALA_{158}, LEU_{161}, LEU_{76}, TRP_{157}

widely cultivated as a cut flower and potted plant[1]. The genus *Chrysanthemum* comprises approximately 37 species, predominantly distributed across East Asia, including China, Korea, Japan, and Siberian Russia[2]. *Chrysanthemum* L. has long been valued in traditional medicine for its associations with health and longevity. Decoctions of *Chrysanthemum* are known to reduce blood pressure, improve coronary circulation, regulate myocardial function, lower low-density lipoprotein (LDL) cholesterol, exert an-

PHARMAKEFTIKI, 37, 2S, 2025 | 181-184

titoxic and anticancer effects, and support the autonomic nervous system. Phytochemical evaluation of *Chrysanthemum hortorum* Bailey has revealed the presence of essential oils, organic acids, and phenolic compounds such as flavonoids, hydroxycinnamic acids, and tannins, which contribute to its medicinal profile[3]. Additional studies have confirmed the presence of phytosterols (including sitosterol, stigmasterol, and campesterol), thereby further substantiating its therapeutic potential[4,5]. The present study investigates the molecular docking of stigmasterol with 14 selected proteins identified through SwissTargetPrediction.

2. Methodology

Whole plants of *Chrysanthemum hortorum* (including leaves, stems, and roots) were collected from the Babylon Nursery Plantation. A total of 100 g of powdered plant material was macerated in n-hexane for 48 h, and were subsequently filtered. The filtrate was evaporated in order to obtain the hexane extract, which was then analysed using gas chromatography mass spectrometry (GC-MS) for compound identification[6].

The study focused on the molecular docking of stigmasterol with 14 proteins (4EY7, 4YVX, 6ESY, 7N4V, 4C49, 7AXK, 6K9H, 6Q2W, 6HJ2, 2ZNN, 2ZNQ, 7CX3, 1Q1M, and 6IIU) selected based on their relevance to stigmasterol's anticipated biological activity, particularly in cancer and metabolic pathways. The three-dimensional structure of stigmasterol was retrieved from the PubChem database, was geometrically optimized, and was assigned atomic charges in order to comply with the docking protocol requirements.

Crystal structures of the target proteins were obtained from the Protein Data Bank (PDB). Proteins were protonated, missing hydrogen atoms were added, bond orders were corrected, and suitable protonation states were assigned in order to simulate physiological conditions. Docking studies were conducted by using the Molecular Operating Environment (MOE) software, with attention given to binding interactions between stigmasterol and the active sites of the target proteins. Binding affinities and interaction types (such as hydrogen bonding and hydrophobic contacts) were analysed in order to assess the stability and energetics of the ligand-protein complexes. This methodological approach enabled a systematic evaluation of stigmasterol's interactions with target proteins, providing insights into its potential therapeutic mechanisms across disease pathways.

3. Results and Discussion

The undertaken structural analysis of the n-hexane extract confirmed the presence of stigmasterol. Molecular docking revealed significant interactions between stigmasterol and the selected proteins from SwissTargetPrediction, underscoring its therapeutic potential. Notably, proteins such as 7N4V (Niemann-Pick C1-like 1; NPC1L1) and 7AXK (ligand-binding domain of the human pregnane X receptor; hPXR) demonstrated high binding affinities, with ΔG v0,3alues of -9.2442 and -9.0119 kcal/mol, respectively. These results suggest robust and stable ligand-protein interactions, which may be critical in modulating cancer-associated pathways.

Hydrophobic interactions involving residues such as TRP, TYR, PHE, and ILE were observed; these seem to enhance ligand stability, especially in targets such as 6HJ2 (hPXR) and 7CX3 (Taprenepag). Additionally, water-mediated interactions – particularly in 4EY7 (acetylcholinesterase) – contributed to binding specificity. Proteins such as NPC1L1 and hPXR were emphasized for their roles in cholesterol metabolism and nuclear receptor signalling, both of which are commonly dysregulated in cancer[7,8].

These findings are consistent with earlier studies indicating that stigmasterol may influence cholesterol uptake and nuclear receptor pathways, thereby suggesting promising therapeutic avenues for hormone-sensitive malignancies.

4. Conclusion

Stigmasterol demonstrated strong binding affinities with key protein targets, highlighting its potential as a therapeutic agent in cancer and metabolic dis-

PHARMAKEFTIKI, 37, 2S, 2025 | 181-184

orders. Its interactions with proteins such as hPXR and NPC1L1 suggest a role in modulating cholesterol metabolism and hormone-sensitive signalling pathways, warranting further pharmacological investigation.

Acknowledgements

We extend our sincere gratitude to the College of Pharmacy of the University of Babylon for providing the facilities and support that enabled this research.

Conflicts of interest

None exist.

ORCIDs

0009-0001-0591-5424 (H.K. Al-yassery); 0000-00020,3-7621-0245 (A.H. Abdulsada)

References

1. Al-Taha H.A.A., Mazine L.H.M. Impact of osmotic stress peg and sucrose on callus growth and adventitious micro shoots regeneration of *Chrysanthemum hortorum* hort. cv. dwarf in *in vitro* condition. *Plant Arch.* 20(s2), 347–352, 2020.
2. Ma Y.P., Zhao L., Zhang W.J., Zhang Y.H., Xing X., Duan X.X., *et al.* Origins of cultivars of *Chrysanthemum*: evidence from the chloroplast genome and nuclear LFY gene. *J. Syst. Evol.* 58, 925–944, 2020. DOI: 10.1111/jse.12682
3. Marchyshyn S., Polonets O., Tkachuk N., Nakonechna S., Harnyk M., Yurkiv V. Study of antimicrobial effect of *Chrysanthemum hortorum* Bailey pectoral variety flowers and leaves. *Pharmacol. Online* 3, 1957–1965, 2021.
4. Biswas P.K., Paul K.B., Henderson J.H.M. Effect of *Chrysanthemum* plant extract on flower initiation in short-day plants. *Physiol. Plant.* 19, 875–882, 1966. DOI: 10.1111/j.1399-3054.1966.tb07077.x
5. Choi J.M., Lee E.O., Lee H.J., Kim K.H., Ahn K.S., Shim B.S., *et al.* Identification of campesterol from *Chrysanthemum coronarium* L. and its antiangiogenic activities. *Phytother. Res.* 21(10), 954–959, 2007. DOI: 10.1002/ptr.2189
6. Al-yassery H.K., Kadhim E.J. Isolation and characterization of a tetrahydroprotoberberine alkaloid from *Crassula ovata*. *Rev. Clin. Pharmacol. Pharmacokinet. Int. Ed.* 38(s2), 101–104, 2024. DOI: 10.61873/IJZC4054
7. Redinger R.N. Nuclear receptors in cholesterol catabolism: molecular biology of the enterohepatic circulation of bile salts and its role in cholesterol homeostasis. *J. Lab. Clin. Med.* 142(1), 7–20, 2003. DOI: 10.1016/S0022-2143(03)00088-X
8. Ramalingam P.S., Elangovan S., Mekala J.R., Arumugam S. Liver X receptors (LXRs) in cancer – an Eagle's view on molecular insights and therapeutic opportunities. *Front. Cell Dev. Biol.* 12, 1386102, 2024. DOI: 10.3389/fcell.2024.1386102

HOW TO CITE:
Al-yassery H.K., Abdulsada A.H. *In silico* docking and target prediction of stigmasterol extracted from *Chrysanthemum hortorum*. *Pharmakeftiki* 37(2s), 181-184, 2025. https://doi.org/10.60988/p.v37i2S.183