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Research Article

Computational Study of Phytoconstituents in *Myxopyrum Smilacifolium Blume* against Inflammatory Mediator TNF-α

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Abstract

Secondary metabolites in plants have been used in health care for the treatment of various ailments since ancient times. The current study was carried out to investigate on phytoconstituents in *Myxopyrum smilacifolium* against an inflammatory mediator TNF-α. Ligand and protein pdbqt files were prepared and docking was done by using Autodock 4.0 and Biovia Studio Visualizer. The docking finding revealed that Myxopyroside shown -5.1 kcal/mol which is high and mere significant docking score of natural immunosuppressive capsaicin and standard drug Methylprednisolone of -4.8 kcal/mol and -5.4 kcal/mol respectively. The obtained results were proven to posses the inhibition activity against TNF-α. The evaluated pharmacokinetic parameters of the only 3 phytoconstituents obeyed Lipinski's rule of 5. Exploration of simulation studies on Myxopyroside are in need to ensure inhibition of inflammatory mediator TNF-α.

Keywords: Autodock 4.0; *Smilacifolium*; *Myxopyroside*; TNF-α; Lipinski's

Introduction

Harmful stimuli like pathogens, damaged cells, toxic substances etc., activate the immune system's response leads to Inflammation. Thereby the immune system removes injurious stimuli and initiates the process of healing [1,2]. In other words Inflammation is said as a defence mechanism [3]. Inflammatory pathways shows its impact on pathogenesis of chronic diseases, involves the inflammatory mediators and signalling pathways. An inflammatory stimulus activates intracellular signalling pathways leads to the active production of inflammatory mediators. The primary inflammatory stimuli includes cytokines such as interleukin-1β, interleukin-6, and tumour necrosis factor-α (TNF-α), IL-1 and IL-6 receptor and the TNF receptor (TNFR) [3-5].

Since ancient times, herbs played an important role in human health care as they produce several substances which exert biological activities. These substances are resultant of biogenetic pathway of secondary metabolism. These secondary metabolites exert numerous therapeutic actions [6,7]. Due to importance of the secondary metabolites, plants became the prime source for the development of new drugs [8-11]. *Myxopyrum smilacifolium Blume4* is a shrub commonly has been used in Traditional system of Medicine, even though the findings on the phyto-constituents are limited [12,13]. Hence, the present study is carried for computational study on the phyto-constituents present in *Myxopyrum smilacifolium Blume's* against inflammatory mediator.

Materials and Methods

In silico study

Receptor and ligand preparation: The PDF files of phyto-constituents of *Myxopyrum smilacifolium's* were gathered from PubChem and the protein TNF-α was obtained from Protein Data Bank (PDB ID: 2az5) at www.rcsb.org/pdb shown in Figure 1. The attributes of ligand i.e., x,y,z coordinates towards selected protein were noted by using Biovia Discovery Visualizer after removing the water molecule. Further with the help of Autodock 4.0 the PDB files of ligand and protein were converted into pdbqt files. By using commands in command prompt the docking is per-

formed. The interactions between each ligand and protein are analysed by using Biovia Discovery Visualizer. SwissADME programming is used to predict the physiochemical characteristics and pharmacokinetics of the chosen substances.

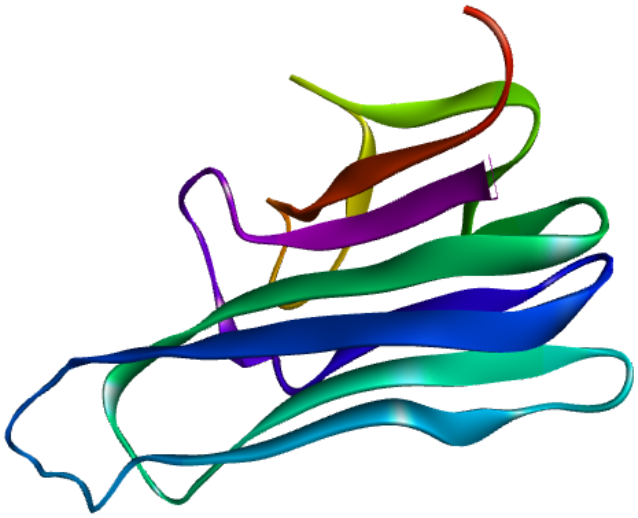

Figure 1: TNF-α (Protein ID: 2az5).

Results

Computation study of phytocompounds in *myxopyrum smilacifolium*

To investigate about phytocompounds being reasonable for anti-inflammatory property, docking score was analysed *via* binding affinity of different ligands behaviour towards the selected protein. Absorption, Distribution, Metabolism, Exertion and Toxicity of phyto constituents were predicted by using SwissADME online tool mentioned in Table 1. 2 out of 5 phytocompounds obeyed Lipinski's Rule of 5. The phyto compounds are along with their PubChem ID and the canonical smiles were represented in Table 2. Docking studies revealed that phytoconstituents *Arenarioside*, *Verbascoside*, *Myxopyroside* had docking score of -16.4 kcal/mol, -10.6 kcal/mol and -6.5 kcal/mol which showed hydrogen bonding interactions. No phyto compounds formed hydrophobic interactions. The docking score outcomes were predicted and the interactions between protein and ligand mentioned in Figure 2 and Table 3.

Table 1: *M. Smilacifolium* phyto-constituents representing Canonical Smiles.

Ligand	Pubchem ID	Canonical Smiles
Verbascoside	5281800	CC1C(C(C(C(O1)OC2C(C(OC(C2OC(=O)C=CC3=CC(=C(C=C3)O)O)CO)OCCC4=C-C(=C(C=C4)O)O)O)O)O)O
Arenarioside	6442994	CC1C(C(C(C(O1)OC2C(C(OC(C2OC(=O)C=CC3=CC(=C(C=C3)O)O)COC4C(C(C(CO4)O)O)O)OCCC5=CC(=C(C=C5)O)O)O)O)O)O
Myxopyroside	-	COC(=O)C1C(O)C(O)C2C1C(OC1OC(CO)C(O)C(O)C1O)OC=C2C(=O)OC
3-Formylindole	10256	C1=CC=C2C(=C1)C(=CN2)C=O
5-Hydroxy methyl furfural	237332	C1=C(OC(=C1)C=O)CO
Capsiacin	1548943	CC(C)C=CCCCCC(=O)NCC1=CC(=C(C=C1)O)OC
Methylpredisolone	6741	CC1CC2C3CCC(C3(CC(C2C4(C1=CC(=O)C=C4)C)O)C)(C(=O)CO)O

Table 2: Pharmacokinetic Analysis *Myxopyrum Smilacifolium* B. Phyto-compounds.

Ligands	Drug Likeness	Molar Refractivity	Consensus Log Po/W	H bond Acceptor	H Bond Donors	GI Absorption	Molecular Formula	Molecular Weight
Verbascoside	3	148.42	-0.43	15	9	Low	$C_{29}H_{36}O_{15}$	624.6
Arenarioside	3	174.84	-1.95	19	11	Low	$C_{34}H_{44}O_{19}$	756.7
Myxopyroside	2	94.62	-2.53	13	6	Low	$C_{18}H_{26}O_{13}$	450.391
3-Formylindole	0	43.69	1.72	1	1	High	$C_9H_7N_O$	145.16
5-Hydroxy methyl furfural	0	30.22	0.19	3	1	High	$C_6H_6O_3$	126.11
Capsiacin	0	90.52	3.43	3	2	High	$C_{18}H_{27}NO_3$	305.41
Methylpredisolone	0	101.87	1.94	5	3	High	$C_{22}H_{30}O_5$	374.47

Table 3: Docking Simulation between TNF-α and Phytocompounds in *Myxopyrum Smilacifolium.*

Phyto-compounds	Highest conformation Binding Energy (kcal/mole)	Hydrogen bonds
Verbascoside	-5	GLY A:121, ILE A: 97, ALA A: 96, TYR A:119
Arenarioside	-4.9	ALA A:96, LYS A:98, TYR A:119, ILE A: 118, SER A:95
Myxopyroside	-5.1	ILE A: 97, GLY A:121, SER A: 95, TYR A: 119
3-Formylindole	-3.5	TYR A: 119, ILE A: 118, ALA A:96
5-Hydroxy methyl furfural	-3.4	TYR A:119, GLY A:121, ILE A: 118
Capsiacin	-4.8	ILE A:118, PRO A:117, ALA A:96, LEU A:120, GLY A:121
Methylpredisolone	-5.4	ILE A: 97, GLY A:121, SER A:95, TYR A:119

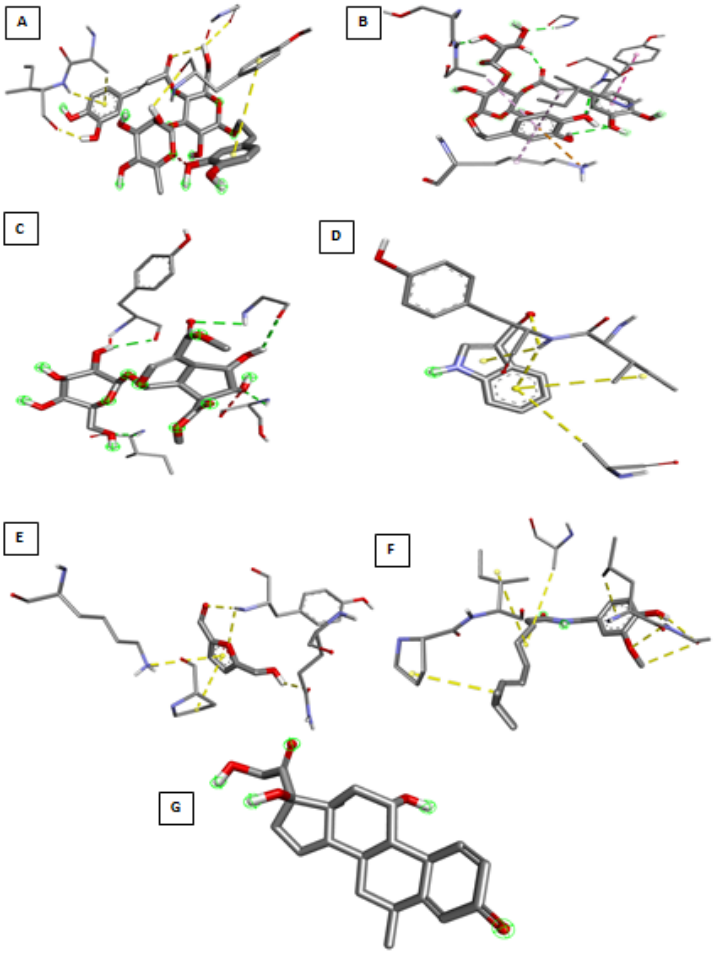

Figure 2: 3D Interactions of Ligands with receptor TNF-α A) *Verbascoside* B) *Arenarioside* C) *Myxopyroside* D) 3-Formylindole E) 5-Hydroxy methyl furfural F) Capsiacin G) Methylpredisolone.

Discussion

Findings of *myxopyroside*, a substance meant to genus Nyctanthes from single leaf of *Myxopyrum*. It was evidenced by 13C NMR spectrum for the presence of dihydroxy substituted for sythide dimethyl ester and ester derivatives [13]. Herbs have been tremendous usage from ancient times and still the natural phytochemicals exhibiting their significance in health care for the treatment of various ailments [14]. The overuse of NSAIDs brings an adverse state of disease like Myocardial Infarction [15-17]. Earlier studies were evidenced that the phyto components glycosides, polyphenols, quercetin and kaempferol inhibits the mediators TNF-α, NO, IL-1β and MCP-1 responsible for inflammation [18-21].

The docking studies disclosed a perspective interaction of stated ligands towards receptor TNF-α. The interactions of phytocomponents *Arenarioside*, *Verbascoside*, *Myxopyroside*, 3-Formylindole and 5-Hydroxy Methyl Furfural shown hydrogen bonds to GLY A:121, ALA A: 96, ILE A:118, SER A:95, TYR A:119 illustrated in Table 3. The docking score of *Arenarioside*, *Verbascoside*, *Myxopyroside*, 3-Formylindole, 5-Hydroxy Methyl Furfural is

around -5.0, -4.9, -5.1, -3.5, and 3.4, respectively. In current study the 5 ligands of *Myxopyrum smilacifolium* at the receptor TNF-α site, docking score was analysed by the use of Autodock 4.0. It has shown good docking score of about -5.1 kcal/mol between Myxpyroside and receptor TNF-α, proves that *Myxopyroside* inhibits the inflammatory mediator, evidenced by strong binding affinity with receptor. By using SwisADME tool, the pharmacokinetic study was studied for the components *Arenarioside*, *Verbascoside*, *Myxopyroside* where it revealed GI absorption is low whereas 3-Formylindole, 5-Hydroxy Methyl Furfural, 3-Formylindole GI absorption is high depicted in Table 3. *Myxopyroside* had shown high and mere equivalent to docking score around -5.1 kcal/mole when compared to reference natural phyto-constitutent Capsiacin and standard drug Methylprednisolone of about -4.8 kcal/mole and -5.4 kcal/mole.

Conclusion

Inflammatory mediators are responsible for various conditions of diseased state. Researches on phyto constituents were limited against inflammation. It can concluded that the phyto components in *Myxopyrum smilacifolium* can be explored and by modifying the SAR it may lead to finding of new moiety to treat inflammatory conditions and simultaneously the use of NSAIDs can be limited to overcome their adverse effects.

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Conflict of Interest

No conflict of interest.

References

1. R. Medzhitov, Inflammation 2010: New adventures of an old flame, Cell, 140(2010):771–776.
2. L. Ferrero-Miliani, O. Nielsen, P. Andersen, S. Girardin, Chronic inflammation: Importance of NOD2 and NALP3 in interleukin-1β generation, Clin Exp Immunol, 147(2007):227–235.
3. C. Nathan, A. Ding, Non-resolving inflammation, Cell, 140(2010):871–882.
4. C. Linlin, D. Huidan, C Hengmin, F. Jing, Z. Zhicai, et al. Inflammatory responses and inflammation-associated diseases in organs, Oncotarget, 9(2018):7204-7218.
5. B. Kaminska, MAPK signalling pathways as molecular targets for anti-inflammatory therapy from molecular mechanisms to therapeutic benefits, BBA, 1754(2005):253–262.
6. C. Locatelli, G. Nardi, M.A.D.F. Anuário, C.G. Freire, K. Schneider, et al. Anti-inflammatory activity of berry fruits in mice model of inflammation is based on oxidative stress modulation, Pharmacogn Res, 8(2016):S42–S49.
7. S.J. Virshette, M.K. Patil, A.P. Somkuwar, A review on medicinal plants used as anti-inflammatory agents, J Pharmacogn Phytochem, 8(2019):1641–1646.
8. L. Fialho, J.A. Cunha-E-Silva, A.F. Madureira, Comparative study of systemic early postoperative inflammatory response among elderly and non-elderly patients undergoing laparoscopic cholecystectomy, Rev Col Bras Cir, 45(2018):e1586.
9. D.J. Newman, Developing natural product drugs: Supply problems and how they have been overcome, Pharmacol Therapeut, 162(2015):1–9.
10. D.J. Newman, G.M. Cragg, Natural products as sources of new drugs from 1981 to 2014, J Nat Prod, 79(2016):629–661.
11. V. Arya, M.L. Arya, A review on anti-inflammatory plant barks, Int J Pharm Tech Res, 3(2011):899–908.
12. R. Kiew, The genus *Myxopyrum* L. (*Oleaceae*), Blumea, 29(1984):499-512.
13. F. Henrik, R.J. Soren, E.O. Carl, Iridoid Glucosides from *Myxopyrum smilacifolium*, J Nat Prod, 64(2001):632-633.
14. M.C. Hochberg, COX-2 selective inhibitors in the treatment of arthritis: A rheumatologist perspective, Curr Top Med Chem, 5(2005):443-448.
15. S. Gopalakrishnan, R. Rajameena, E. Vadivel, Phytochemical and pharmacognostical studies of the leaves of *myxopyrum serratulum* A.W.Hill, J Chem Pharmac Res, 4(2012):788-794.
16. A.A.M. Abdel-Aziz, K.E.H. Eltahir, Y.A.A. Siri, Synthesis, anti-inflammatory activity and cox-1/cox-2 inhibition of novel substituted cyclic imides, Part 1, Molecular docking study, Euro J Med Chem, 46(2011):1648–1655.
17. C. Patrono, B. Rocca, Nonsteroidal antiinflammatory drugs: Past, present and future, Pharm Res, 59(2009):285–289.
18. D.K. Ajay, V.P. Prashant, N.H. Uday, K.N. Rabindra, M.S. Haidarali, Anti-inflammatory and anti-arthritic activity of anthraquinone derivatives in rodents, Int J Inflam, 5(2014):1-12.
19. N. Kumar, P. Bhandari, B. Singh, A.P. Gupta, V.K. Kaul, Reversed phase-HPLC for rapid determination of polyphenols in flowers of rose species, J Sep Sci,

31(2008):262.

20. T.L. Wadsworth, T.L. McDonald, D.R. Koop, Effects of *Ginkgo biloba* extract (EGb 761) and quercetin on lipopolysaccharide-induced signaling pathways involved in the release of tumor necrosis factor-alpha, Biochem Pharmacol, 62(2001):963–974.

21. V. García-Mediavilla, I. Crespo, P.S. Collado, A. Esteller, Sánchez-Campos, et al. The anti-inflammatory flavones quercetin and kaempferol cause inhibition of inducible nitric oxide synthase, cyclooxygenase-2 and reactive C-protein, and down-regulation of the nuclear factor kappaB pathway in Chang liver cells, Eur J Pharmacol, 557(2007):221–229.