IJBPAS, August, 2020, 9(8): 1889-1896

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

MOLECULAR DOCKING OF COMPOUNDS FROM *WITHANIA SOMNIFERA* AGAINST ORAL CARCINOMA DRUG TARGETS

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Received 17th Dec. 2019; Revised 15th Jan. 2020; Accepted 16th Feb. 2020; Available online 1st Aug. 2020

https://doi.org/10.31032/IJBPAS/2020/9.8.5145

ABSTRACT

Aim: To check the compatibility between NF kappa B and active compounds of *withania somnifera*.

Materials and methods: Molecular docking simulations were performed to predict the bioactive conformations and explore the binding interactions of bioactive compounds such as withanolide analogs from *Withania somnifera* using computer aided techniques such as ACD lab chemsketch which is a ACD/ChemSketch Freeware is a drawing package that allows to draw chemical structures including organics, organometallics, polymers, and Markush structures, calculation of molecular properties (e.g., molecular weight, density, molar refractivity etc.), 2D and 3D structure cleaning and viewing, functionality for naming structures (fewer than 50 atoms and 3 rings), prediction of logP and GOLD – which is a protein ligand docking.

Result: The standard compound reversterol has a GOLD score of 29.96 and withanolide A with the GOLD score of 53.65 forms h bonds with greater activity.

Conclusion: This study concludes that Withanolide A has better h bond interaction and compatibility with NF kappa B. Futher studies is to be conducted to get a promising result against oral carcinoma.

Keywords: *Withania somnifera*, oral carcinoma, GOLD score, molecular docking, Withanolides

INTRODUCTION

Withania somnifera is a plant commonly started from the dry areas of Asian nations, for example, India, Pakistan, Afghanistan just as South Africa, and others **[1-5]**. The various restorative utilizations of *W. somnifera* are identified with the nearness of alkaloids and lactones, which can be found at various dimensions in plant parts like roots, stems, and leaves and are as one in charge of the pharmacological adaptability connected to it **[6, 7]**. Various withanolides have been acquired and portrayed in the course of recent years. This kind of steroid has pulled in noteworthy consideration from various specialists, as a result of their complex basic highlights as well as on account of their different bioactivities and potential in medication innovative work **[8-10]**. A few investigations have revealed the roots and leaves of *W. somnifera* as a more extravagant wellspring of withanolides and related mixes **[15, 16]**.

Conceivable neuroprotective impact of *Withania somnifera* root extricate against 3-nitropropionic corrosive incited social, biochemical, and mitochondrial brokenness in a creature model of Huntington's malady **[11-14]**. *Withania somnifera* home grown concentrates have appeared anticancer action thatcapacities through different pathways. In addition, the toxicological examinations uncovered that the sensible portions of *W. somnifera* are non-harmful and safe **[17-19]**.

Molecular docking is a key apparatus in auxiliary sub-atomic science and PC helped medicate plan. The objective of ligand-protein docking is to anticipate the prevalent restricting mode(s) of a ligand with a protein of known three-dimensional structure. Docking techniques look high-dimensional spaces adequately and utilize a scoring capacity that effectively positions competitor dockings. Docking can be utilized to perform virtual screening on substantial libraries of mixes, rank the outcomes, and propose auxiliary speculations of how the ligands hinder the objective, which is significant in lead enhancement **[20, 21]**.

MATERIALS AND METHODS

ACD labs Chemsketch

ACD/ChemSketch is an advanced chemical drawing tool and is the accepted interface for the industry's best NMR and molecular property predictions, nomenclature, and analytical data handling software.

ACD/ChemSketch is also available as freeware, with functionalities that are highly competitive with other popular commercial software packages. The freeware contains tools for 2D structure cleaning, 3D

optimization and viewing, In ChI generation and conversion, drawing of polymers, organometallics, and Markush structures—capabilities that are not even included in some of the commercial packages from other software producers. Also included is an IUPAC systematic naming capability for molecules with fewer than 50 atoms and 3 rings. The capabilities of ACD/ChemSketch can be further extended and customized by programming.

GOLD - Protein-Ligand Docking

GOLD is a program for calculating the docking modes of small molecules in protein binding sites and is provided as part of the *GOLD Suite*, a package of programs for structure visualization and manipulation (Hermes), for protein-ligand docking (GOLD) and for post-processing (GoldMine) and visualization of docking results. Hermes acts as a hub for many of CCDC's products, for more information please refer to the Hermes product page.

Active site of NF Kappa B

The active site of the crystal structure of NF Kappa B (PDB id: 4DN5) GLU 375A, ALA 427A , ARG 408A , ASN 520A , ASP 515A , ASP 519A , ASP 534A , CYS 533A , EDO 1006A , GLN 479A , GLU 440A , GLU 470A , GLY 407A ,ARG408A, GLY 409A , GLY 412A , GLY 536A , HIS 537A , LEU 406A , LEU 471A , LEU 472A , LEU 522A , LYS 429A , MET 469A , MG 1001A , PHE 411A , SER 410A , SER 476A , VAL 414A

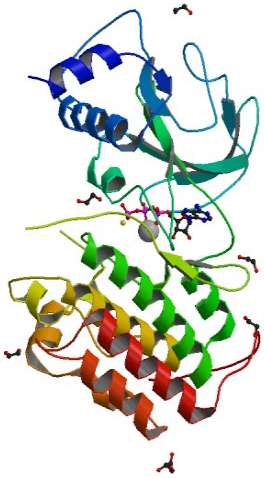

Figure 1: Crystal structure of NF kappa B

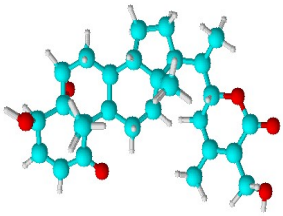

Figure 2: Structure of Withaferin A

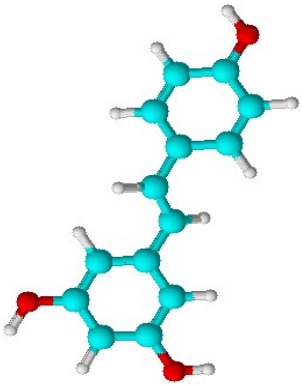

Figure 3: Revesterol

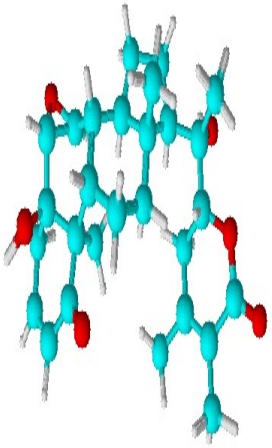

Figure 4: Withanolide A

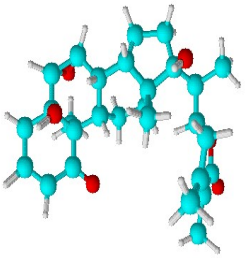

Figure 5: Withanone

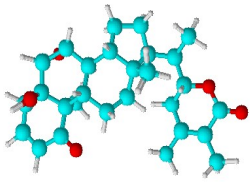

Figure 6: Withanolide B

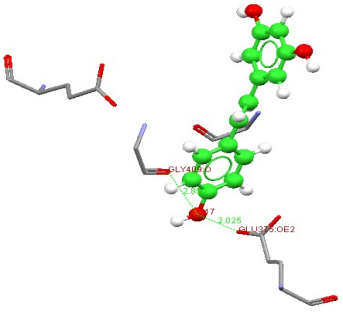

Figure 7: Resvesterol in complex with protein

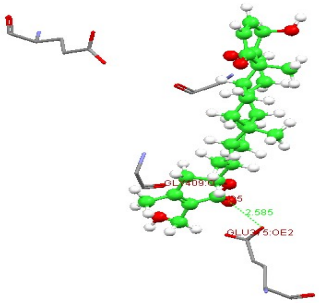

Figure 8: Withaferin a in complex with protein

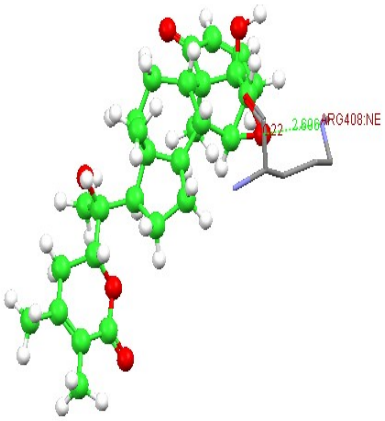

Figure 9 :withanolide a in complex with protein

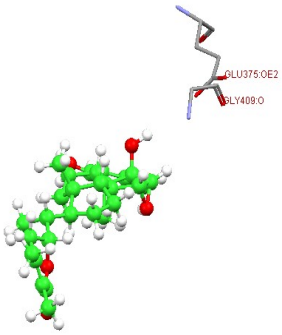

Figure 10: withanolide B in complex with protein

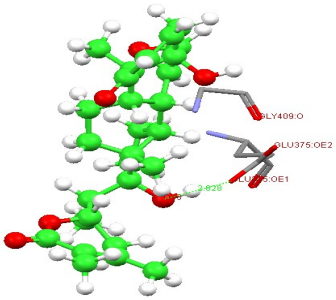

Figure 11: Withanone in complex with protein

RESULTS AND DISCUSSION

The standard compound reversterol has a GOLD score of 29.96 and withanolide A with the GOLD score of 53.65 forms hbonds with greater activity. The active compounds such as Withaferin A, Withanolide A, Withanolide B, Withanone are derived from *Withania somnifera*. On comparing the compatibility between NF kappa B and the active compounds of *W. somnifera*, Withanolide A is found to have the highest GOLD score among other compounds **(Table 1)**.

NF kappa B is a nuclear factor light chain protein complex which consists of various functions such as transcription of DNA, cytokine production, tumour cell survival and proliferation, cellular metabolism, metastasis. It plays a key role in regulating a immune response to infections. Upon activation of NF-κB has been linked to cancer, inflammatory and autoimmune diseases,

septic shock, viral infection, and improper immune development.

Studies have reported the development of a quantitative structure activity relationship (QSAR) model for the antiproliferative activity of withanolide analogs against human breast (SK-Br-3 and MCF7/BUS) cancer cell lines. It is stated that *W.Somnifera* root and leaf extracts has anticancer potential and their QSAR and molecular docking-based prediction of withanolide analogs showed that 2,3-dihydrowithaferin A-3-beta-O-sulfate, withanolide 5, withanolide A, withaferin A, CID_10413139, CID_11294368, CID_53477765, CID_135887, CID_301751 and CID_3372729 against Sk-Br-3 and CID_73621, CID_435144, CID_301751 and CID_3372729 possess a significant anticancer activity against the MCF7/BUS **[22]**.

Table 1: Docking Sores and H-Bond Formation

Ligand Name	Atom in Ligand	Atom in Protein	H-Bond Distance	Score
Resveratrol	**O17**	**GLY409:O**	**2.89**	**29.96**
	O17	**GLU375:OE2**	**2.632**	
Withaferin A	**O5**	**GLU375:OE2**	**2.585**	**10.9**
withanolide A	**O22**	**ARG408:NE**	**2.606**	**53.65**
withanolide B	**NO HBONDS**			**1.39**
Withanone	**O33**	**GLU375:OE1**	**2.828**	**48.7**

CONCLUSION

Withanolide A showed better compatibility with NF kaapa B based on GOLD Score and interaction with the active site residues in comparison with the existing drug molecules. This data provides molecular insights to the consideration of Withanolides as potential candidates against the NF Kappa B.

Acknowledgment

The authors would like to thank Saveetha Dental College, Biozone R & D for their support and able guidance.

Conflict Of Interest

NIL

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