ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND LIFE SCIENCES

Published by ScienzTech Publication Journal Home Page: www.scienztech.org/ijprls

High throughput virtual screening of cyclooxygenase-2 by using database

Ravi D*, Chaitanya Kumar K, Mothilal K, Mahender K

Department of Pharmaceutics, Scient Institute of Pharmacy, Hyderabad-501506, Ibrahimpatnam, Telangana, India

Article History:

Received on: 10 Sep 2020
Revised on: 30 Sep 2020
Accepted on: 01 Oct 2020
Published on: 10 Dec 2020

Volume: 8 Issue: 2

Keywords:

databases,
renal failure,
virtual screening,
docking

ABSTRACT

COX-2 is a type of Non-steroidal mitigating drug (NSAID) that legitimately targets COX-2, a protein liable for irritation and torment. Selectivity for COX-2 decreases the danger of peptic ulceration and is the fundamental component of celecoxib, rofecoxib and different individuals from this medication class. COX-2 selectivity doesn't appear to influence other antagonistic impacts of NSAIDs (most prominently an expanded danger of renal disappointment), and a few outcomes have excited the doubt that there may be an expansion in danger for cardiovascular failure, apoplexy and stroke by a relative increment in thromboxane. The target of this investigation is to screen drug-like compounds from Zinc database and to predict the potency and activity by using Virtual Screening and Molecular Docking Study. The scope of the study extends to predict the feasibility of the compounds for Drug development. Hence, this examination expresses the significance of little particle libraries and their utilization to upgrade drug revelation measure earlier amalgamation. This way to deal with screen original mixes as COX-2 inhibitors from ZINC information base relies upon different boundaries, for example, Lipinski's standard of 5, pharmacophoric bunches appended on the ligand, size of the dataset and compound libraries among others. Additional, exertion can be stretched out to consider the receptor-ligand associations tentatively, and assessment of their organic action would help in planning mixes dependent on simulated screening strategies.

*Corresponding Author

Name: Ravi D
Phone: 9182096143
Email: dandigaravi15@gmail.com

DOI: https://doi.org/10.26452/ijprls.v8i2.1358

Production and Hosted by

ScienzTech.org

INTRODUCTION

Cyclooxygenase (COX) is a catalyst that is liable for the development of significant organic go-betweens called prostanoids, containing prostaglandins, prostacyclin and thromboxane. Pharmacological restraint of COX can give help from the side effects of aggravation and torment. Non-steroidal mitigating drugs, for example, anti-inflammatory medicine and ibuprofen, apply their belongings concluded hindrance of COX [1]. The name "prostaglandin synthase (PHS)" and "prostaglandin endoperoxide synthetase (PES)" are as yet used to allude to COX.

COX-2 particular inhibitor is a type of Non-steroidal mitigating drug (NSAID) that legitimately targets COX-2, a protein liable for irritation and torment. Selectivity for COX-2 decreases the danger of peptic ulceration and is the primary element of celecoxib, rofecoxib and different individuals from this medication class [1–3]. COX-2 selectivity doesn't appear to influence other unfriendly impacts of NSAIDs (most eminently an expanded danger of renal dis-

appointment), and a few outcomes have excited the doubt that there may be an expansion in danger for respiratory failure, apoplexy and stroke by a relative increment in thromboxane. Rofecoxib (regularly known as Vioxx) was removed from the market in 2004, given these worries [2]. Early COX-2-hindering medications, for example, Celebrex and Vioxx, were presented in 1999 and quickly turned into the most often endorsed new medications in the United States. COX-2 Inhibitors as a treatment for neuroblastomas in future [4].

Virtual screening is a computational strategy utilized in medication configuration research. It includes the fast appraisal of vast libraries of substance structures to direct the choice of likely medication applicants [3]. Advances in atomic demonstrating, combinatorial science and sub-atomic science have profoundly changed the way to deal with drug revelation in the drug business, and Virtual Screening is a result of exploration in these zones [5–8].

MATERIALS AND METHODS

Hardware environment

System configuration

- Pentium 4 - 3.20 GHz
- 512 MB of RAM
- 40 GB Hard Disk Drive
- 1 MB cache
- 1.44" Floppy Disk Drive
- 17" Color Monitor
- 128 MB AGP Card

Softwares

Operating System : LINUX EL – 5.0, Dos

Virtual Screening Software: Argus lab

Molecular Docking : AutoDock version-3.0

Visualization Tool : PyMOL

Conversion Tool : CORINA.

Databases : PDB and PubChem

PyMOL [5]

PyMOL is an open-source, client supported, atomic representation framework made by Warren Lyford DeLano and marketed by DeLano Scientific LLC, which is a private programming organization committed to making helpful apparatuses that generally converted available to logical and instructive groups [4, 9–11]. It is appropriate for delivering top-notch 3D pictures of little particles and organic macromolecules, for example, proteins. PyMOL is one of only a handful not many open source exemplification devices reachable for use in rudimentary science. The 'Py' part of the product's name mentions to the way that it broadens, and is extensible by, the Python Programming Language [12].

METHODOLOGY

Preparation of ligand [4]

At first, the hydrogens were added to all the particles in the ligand and guaranteed that their valences were finished. This was finished utilizing this subatomic demonstrating bundle (ADT). It was ensured that the iota types were right before, including hydrogens [7]. Contingent upon whether emotional or unbiased amides and carboxylates are wanted, the PH was indicated naturally.

Next, halfway nuclear responsibilities were relegated to the ligand atom. MOPAC or AMPAC was utilized to produce fractional nuclear custodies for the ligand. These customers were inscribed in 'pdbq' design, which had similar segments as a Brookhaven PDB design, yet with an additional section of fractional nuclear charge [6].

Autodock

Consecutively AutoDock Once the network maps have been set up via AutoGrid and the docking boundary document, or 'dpf', is equipped, the client is organized to run an AutoDock work [9].

The docking consequences were seen exploiting "get-docked", a PDB arranged document was made. It was designated "lig.macro.dlg.pdb" and will comprise all the cropped compliances produce via AutoDock in the "lig.macro.dlg" record.

RESULTS & DISCUSSION

The X-ray structure of COX-2, PDB ID: 6COX was selected as the template from pdb. The drug-like compounds from Zinc database were selected and submitted to virtual screening.

Molecular Docking [Figures 1 and 2] [8]

Virtual screening approaches are routinely and broadly used to diminished expense and season of medication revelation. It has been exhibited that the methodology used in this investigation is fruitful in discovering two novel COX-2 inhibitors from the ZINC information base. ZINC03832518, ZINC03782818 specifically, demonstrated high restricting liking with an Argus lab dock score of -10.6204 kcal/mol, -9.91631 kcal/mol against 6COX respectively showed in fig1 and fig2. The

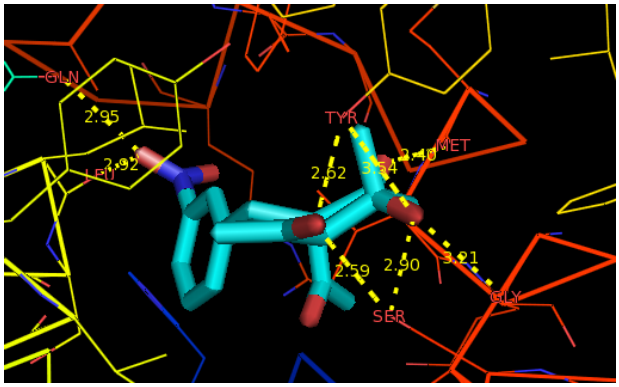

Figure 1: COX-2 complex with ZINC03832

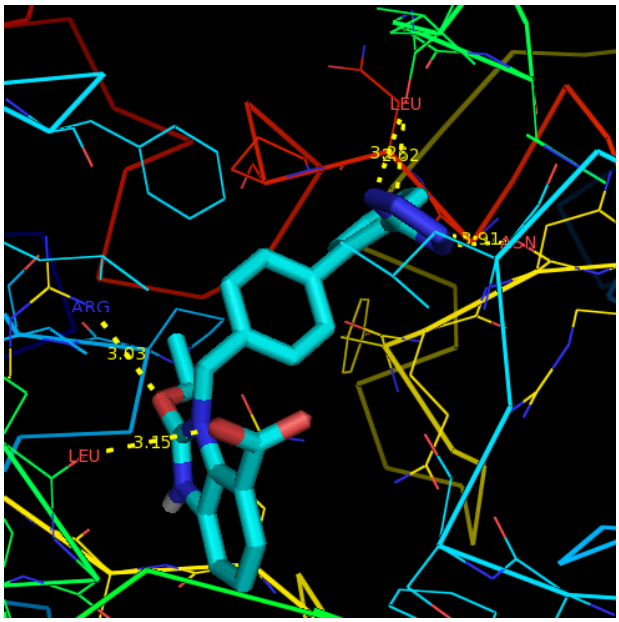

Figure 2: COX-2 complex with ZINC03782818

ligand was docked deeply within the binding pocket region forming interactions with ZINC03832518 {GLN (192) at 2.95Å, LEU (352) at 2.92 Å, MET (522) at 2.40Å, SER (530) at 2.59 Å, SER (530) at 2.90Å, GLY (526) at 3.21 Å, TYR (385) at 3.54Å and TYR (385) at 2.62 Å} and ZINC03782818 { LEU (224) at 3.15Å, ARG (376) at 3.03 Å, LEU (224) at 3.23Å, LEU (224) at 2.62 Å, and ASN (375) at 3.91Å} respectively. [12–14].

From the Virtual Screening interpretation, we confirm that the Drugs have shown best docking score (kcal/mol) from Argus lab the ZINC03832518 (-10.6204) and ZINC03782818 (-9.91631) were submitted to AutoDock to observe the interactions [[15]].

CONCLUSION

Hence, this examination expresses the significance of little particle libraries and their utilization to upgrade drug revelation measure earlier amalgamation. This way to deal with screen original mixes as COX-2 inhibitors from ZINC information base relies upon different boundaries, for example, Lipinski's standard of 5, pharmacophoric bunches appended on the ligand, size of the dataset and compound libraries among others. Additional, exertion can be stretched out to consider the receptor-ligand associations tentatively, and assessment of their organic action would help in planning mixes dependent on simulated screening strategies.

ACKNOWLEDGEMENT

The authors are thankful to all who have extended their constant support for the completion of the work.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

REFERENCES

[1] Seifert MHJ, Wolf K, Vitt D. Virtual high-throughput in silico screening. BIOSILICO. 2003;1(4):143–149. Available from: 10.1016/s1478-5382(03)02359-x.

[2] Butkiewicz M, Lowe EW, Mueller R, Mendenhall JL, Teixeira PL, Weaver CD, et al. Benchmarking ligand-based virtual high-throughput screening with the pubchem database. Molecules. 2013;Available from: https://doi.org/10.3390/molecules18010735.

[3] Tuccinardi T. Docking-Based Virtual Screening: Recent Developments. Combinatorial Chemistry & High Throughput Screening. 2009;12(3):303–314. Available from: 10.2174/138620709787581666.

[4] Plewczynski D, Hoffmann M, Grotthuss MV, Ginalski K, Rychewski L. In silico prediction of SARS protease inhibitors by virtual high throughput screening. Combinatorial Chemistry & High Throughput Screening. 2007;Available from: https://doi.org/10.1111/j.1747-0285.2007.00475.x.

[5] Baurin N, Mozziconacci JC, Arnoult E, Chavatte P, Marot C, Morin-Allory L. 2D QSAR Consensus Prediction for High-Throughput Virtual Screening. An Application to COX-2 Inhibition

Modeling and Screening of the NCI Database. Journal of Chemical Information and Computer Sciences. 2004;44(1):276–285. Available from: 10.1021/ci0341565.

[6] Sudha KN, Shakira M, Prasanthi P, Sarika N, Kumar CN, Babu PA. Virtual screening for novel COX-2 inhibitors using the ZINC database. Combinatorial Chemistry & High Throughput Screening . 2008;Available from: https://doi.org/10.6026/97320630002325.

[7] Ghasemi J, Shiri F, Pirhadi S, Heidari Z. Discovery of New Potential Antimalarial Compounds Using Virtual Screening of ZINC Database. Combinatorial Chemistry & High Throughput Screening. 2015;18(2):227–234. Available from: 10.2174/1386207318666141229123705.

[8] Plewczynski D, von Grotthuss M, Spieser SH, Rychewski L, Wyrwicz L, Ginalski K, et al. Target Specific Compound Identification Using a Support Vector Machine. Combinatorial Chemistry & High Throughput Screening. 2007;10(3):189–196. Available from: 10.2174/138620707780126705.

[9] Guner O, Clement O, Kurogi Y. Pharmacophore Modeling and Three Dimensional Database Searching for Drug Design Using Catalyst: Recent Advances. Current Medicinal Chemistry. 2012;.

[10] Kirchmair J, Ristic S, Eder K, Markt P, Wolber G, Laggner C, et al. Fast and Efficient in Silico 3D Screening: Toward Maximum Computational Efficiency of Pharmacophore-Based and Shape-Based Approaches. Journal of Chemical Information and Modeling. 2007;47(6):2182–2196. Available from: 10.1021/ci700024q.

[11] Swamidass SJ, Azencott CA, Lin TW, Gramajo H, Tsai SC, Baldi P. Influence Relevance Voting: An Accurate And Interpretable Virtual High Throughput Screening Method. Journal of Chemical Information and Modeling. 2009;49(4):756–766. Available from: 10.1021/ci8004379.

[12] Korth M. Large-scale virtual high-throughput screening for the identification of new battery electrolyte solvents: evaluation of electronic structure theory methods. Phys Chem Chem Phys. 2014;16(17):7919–7926. Available from: 10.1039/c4cp00547c.

[13] Harper G, Bravi GS, Pickett SD, Hussain J, Green DVS. The Reduced Graph Descriptor in Virtual Screening and Data-Driven Clustering of High-Throughput Screening Data. Journal of Chemical Information and Computer Sciences. 2004;44(6):2145–2156. Available from: 10.1021/ci049860f.

[14] Bullock C, Cornia N, Jacob R, Remm A, Peavey T, Weekes K, et al. DockoMatic 2.0: High Throughput Inverse Virtual Screening and Homology Modeling. Journal of Chemical Information and Modeling. 2013;53(8):2161–2170. Available from: 10.1021/ci400047w.

[15] Vangrevelinghe E, Zimmermann K, Schoepfer J, Portmann R, Fabbro D, Furet P. Discovery of a Potent and Selective Protein Kinase CK2 Inhibitor by High-Throughput Docking. Journal of Medicinal Chemistry. 2003;46(13):2656–2662. Available from: 10.1021/jm030827e.

ABOUT AUTHORS

Ravi D

Department of Pharmaceutics, Scient Institute of Pharmacy, Hyderabad-501506, Ibrahimpatnam, Telangana, India.

Cite this article: D Ravi, Kumar K Chaitanya, K Mothilal, K Mahender. **High throughput virtual screening of cyclooxygenase-2 by using database**. Int. J Pharm. Res. Life Sci. 2020; 8(2): 97-100.

ScienZTech