Molecular docking studies of natural phenolic acids ellagic and chlorogenic acid with enzyme Cyclooxygenase-2

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ABSTRACT

Cyclooxygenase (COX)-2 is a pro-inflammatory immediate early response enzyme, chronically up-regulated in several pathological conditions. COX-1 and COX-2 are two isoforms of the key enzymes used in the synthesis of prostaglandins, the major mediator of inflammation and pain. Cytokines, growth factor and other stimuli induce COX-2 during the inflammation response. COX-2 selective and non-selective drugs are associated with side effects. Natural phenolic compounds are safe resorts to alleviate the symptoms of inflammation with negligible toxicity. In the present work, molecular docking of Ellagic acid and chlorogenic acid with COX-2 enzyme has been carried out with the help of AutoDock Vina 1_1.2 suite. The structure of COX-2 (PDB ID: 3LN1) used in this study is available at protein data bank (http://www.rcsb.org). During the docking experiment, water molecules and heteroatoms have been removed, while the hydrogen atoms were added at appropriate geometry groups. The COX-2 was ionized as required at the physiological pH and its protonated form was used for the final docking experiment. Chlorogenic acid was found to be more effective inhibitor of COX-2 enzyme with binding affinity of -8.5 kcal/mole as compared to clinically prescribed drug Celecoxib (-7.4 kcal/mol). Ellagic acid showed low efficacy.

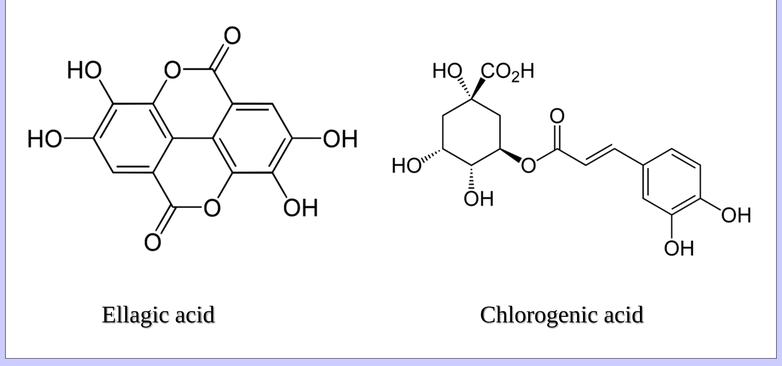
Experimental Procedures

METHODS

The pdb file of cyclooxygenase-2 (PDB ID: 3LN1) was downloaded from protein data bank [1]. All the hetero-atom and water molecules and unnecessary hydrogen atoms in the downloaded protein structure prior to docking have been removed. The .pdb files of receptor and ligands were changed into .pdbqt format prior to final docking and docking parameters for blind docking were set [2]. The grid was fixed at 24, 20, and 22 along with the X, Y, and Z axis with 0.5 Å of grid spacing. The centre of the grid was set to 30.576, -28.11, and -6.261 Å. The most energetically favourable conformation was selected for further analysis.

Reference:

1. Wang, J.L., Limburg, D., Graneto, M.J., Springer, J., Hamper, J.R.B., Liao, S., Pawlitz, J.L., Kurumbail, R.G., Maziasz, T., Talley, J.J. and Kiefer, J.R., 2010. The novel benzopyran class of selective cyclooxygenase-2 inhibitors. Part 2: the second clinical candidate having a shorter and favorable human half-life. Bioorganic & medicinal chemistry letters, 20(23), pp.7159-7163.
2. N. Kumar, S. Gupta, T.C. Yadav, V. Pruthi, P.K. Varadwaj, N. Goel, “Extrapolation of phenolic compounds as multi-target agents against cancer and inflammation”, J. Biomol. Struct. Dyn. (ID: 1481457)



INTRODUCTION

Ellagic acid is a natural phenol antioxidant found in numerous fruits and vegetables. The antiproliferative and antioxidant properties of ellagic acid have prompted research into its potential health benefits. Ellagic acid is the dilactone of hexahydroxydiphenic acid. Chlorogenic acid (CGA) is the ester of caffeic acid and (−)-quinic acid, functioning as an intermediate in lignin biosynthesis. The term "chlorogenic acids" refers to a related polyphenol family of esters, including hydroxycinnamic acids (caffeic acid, ferulic acid and p-coumaric acid) with quinic acid.

RESULTS

Compounds	Docking Score (Kcal/mol)
Ellagic acid	- 6.97
Chlorogenic acid	- 8.5
Celecoxib	- 7.4

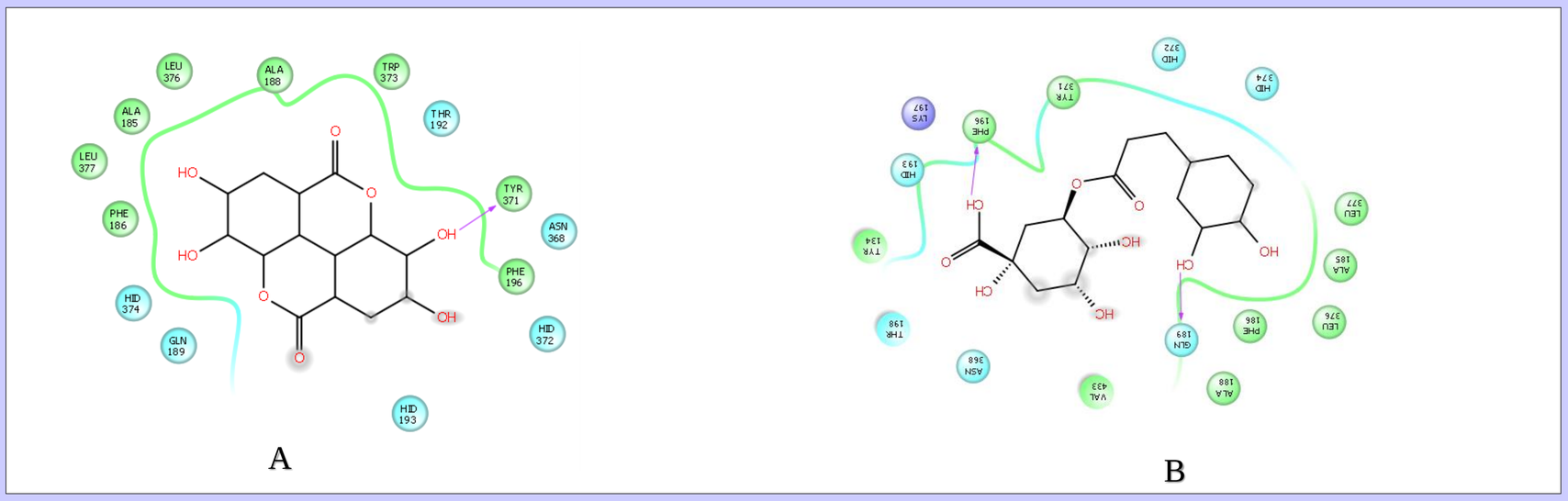


Figure 1: 2D representation of the interaction between the best pose found for Ellagic acid (A) and Chlorogenic acid (B) with COX-2 enzyme (PDB ID: 3LN1).

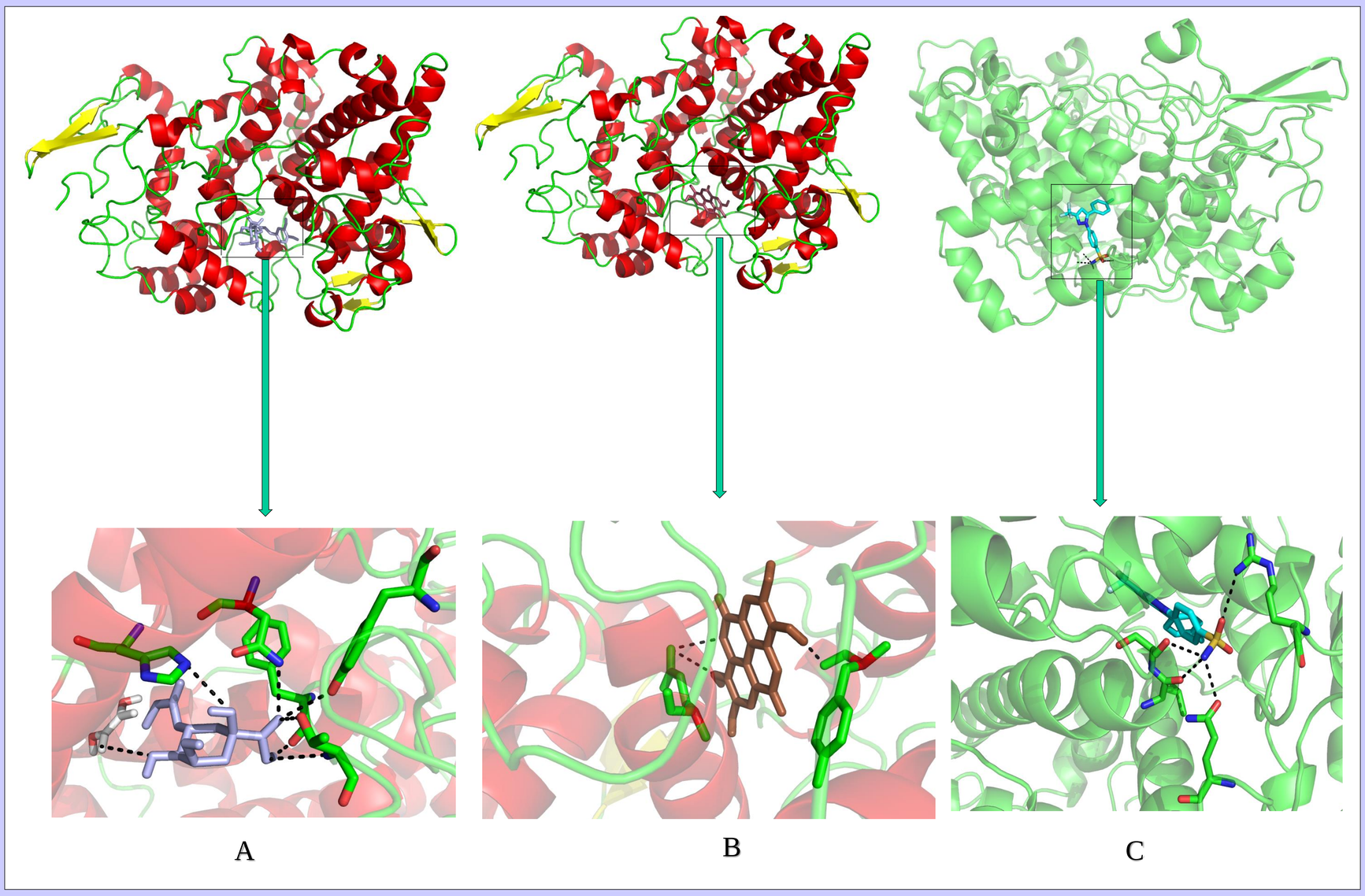


Figure 2: 3D representation of the interaction between the best pose found for Ellagic acid (A) and Chlorogenic acid (B) and Celecoxib (C) with COX-2 enzyme (PDB ID: 3LN1).

CONCLUSIONS

Among both the compounds Chlorogenic acid showed the best docking score towards the inflammatory enzyme cyclooxygenase-2. However *in-vitro* and *in-vivo* experimental studies need to identify the COX-2 enzyme inhibitory activity of selected phenolic acids .

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