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Curcumin and piperin: Anti-inflammatory potential revealed in molecular docking

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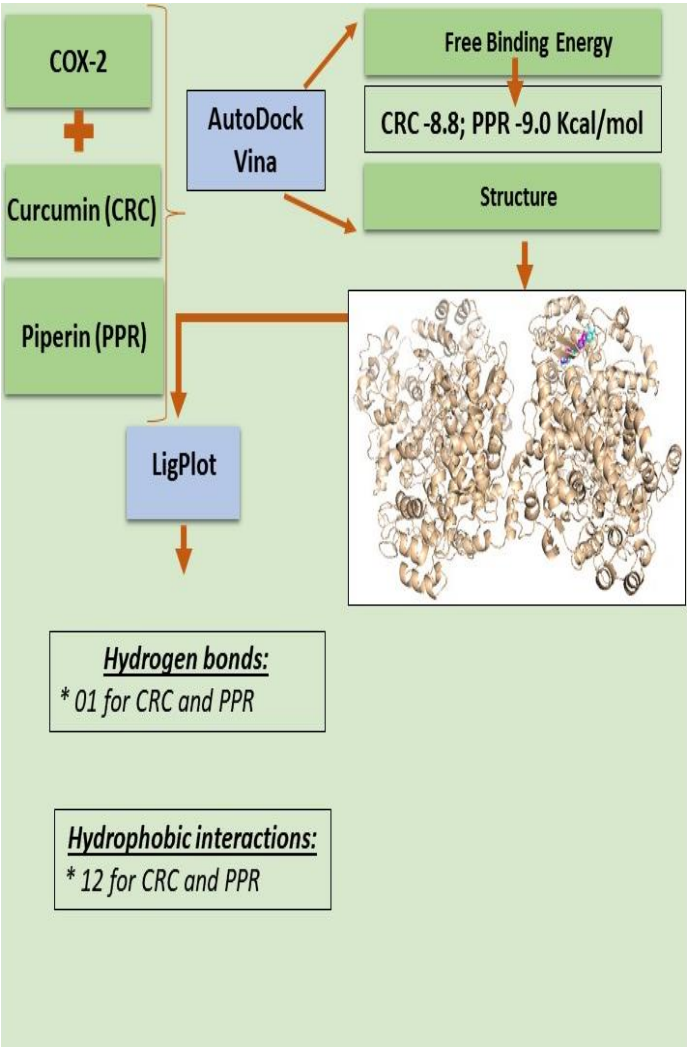
Graphical Abstract



Abstract. *Natural products comprise several medicines. The curcumin (CRC) is a constituent of the spice turmeric and part of the mixture of compounds referred to as curcuminoids. The Piperin (PPR) is the major pungent alkaloid present in the fruits of Piper nigrum L. Both have several biological activities, including anti-inflammatory. The inflammatory process is important for tissue homeostasis, however its imbalance is related to several pathologies. Cyclooxygenase-2 (COX-2) participates in the inflammatory process by converting arachidonic acid into prostaglandins (inflammatory mediators). Understanding the connection pattern, at the molecular level, of CRC and PPR with COX-2 can assist in the development of research on natural anti-inflammatories. Comparing the binding pattern of CRC and PPR with COX-2 through molecular docking was the main objective of this study. The docking simulation by AutoDock Vina demonstrated a binding energy with the COX-2 quite similar: for CRC -8.8 Kcal/mol and for PPR -9.0 Kcal/mol. In addition, the binding site at COX-2 was also similar for CRC and PPR. The number of Hydrogen bonds and hydrophobic interactions established with COX-2 was exactly the same for CRC and PPR (01 Hydrogen bond and 12 hydrophobic interaction), however the COX-2 amino acids involved in these bonds were not the*

	same. The energy patterns, location and types of binding established with COX-2 were similar for CRC and PPR, so the anti-inflammatory properties may be similar. In this sense, it would be important to continue in vitro and in vivo studies with both molecules.

Introduction

. *Natural products comprise several medicines (1). The curcumin (CRC) is a constituent of the spice turmeric and part of the mixture of compounds referred to as curcuminoids (1). The Piperin (PPR) is the major pungent alkaloid present in the fruits of Piper nigrum L (2). Both have several biological activities, including anti-inflammatory (2,3). The inflammatory process is important for tissue homeostasis, however its imbalance is related to several pathologies. A dysregulation of the inflammatory mechanisms can result in the destruction of tissues and the excessive inflammation can ultimately lead to a series of pathologies such as: fibrosis, metaplasia and cancer* (4–6). *Cyclooxygenase-2 (COX-2) participates in the inflammatory process by converting arachidonic acid into prostaglandins (inflammatory mediators)* (7). *Understanding the connection pattern, at the molecular level, of CRC and PPR with COX-2 can assist in the development of research on natural anti-inflammatories. Comparing the binding pattern of CRC and PPR with COX-2 through molecular docking was the main objective of this study.*

Materials and Methods

The COX-2 structure (receptor) was obtained from Protein Data Bank PDB (PDB ID: 1CX2) (8) *and ligands CRC and PPR were obtained from Pubchem (PubChem ID: 969516 for CRC and 638024 for PPR)* (9). *Firstly, using the UCSF chimera (available to download at http://www.cgl.ucsf.edu/chimera/download.html*) *we remove heteroatoms from the COX-2. Then, we prepare receptor and ligand input files using AutoDockTools software for AutoDockVina* (10). *To perform docking simulations, we configure grid box as: size x = 94 Å; size y = 76 Å; and size z = 124 Å; and center box coordinates are x = 42.335 Å center; y = 33.591 Å center; z = 36.078 Å; considering exhaustiveness as 500. Molecular docking simulations were performed with AutoDock Vina* (10). *The more negative FEB indicates the greater stability of ligand-receptor complex. Visual analysis of docking results was performed with PyMol (available for download https://pymol.org/2/) and for check the types of connections between molecules we used the LigPlot* (11).

Results and Discussion

The docking simulation demonstrated a binding energy with the COX-2 quite similar: for CRC -8.8 Kcal/mol and for PPR -9.0 Kcal/mol. In addition, the binding site at COX-2 was also similar for CRC and PPR (Fig, 1A). The number of Hydrogen bonds and hydrophobic interactions established with COX-2 was exactly the same for CRC and PPR (01 Hydrogen bond and 12 hydrophobic interaction), however the COX-2 amino acids involved in these bonds were not the same (Fig. 1B and C). Both molecules had already demonstrated anti-inflammatory action in previous studies (2,3). *Our study*

reinforces the anti-inflammatory character of these molecules (due to the possible blocking of COX-2) and details the interaction with COX-2 at the molecular level is similar to CRC and PPR.

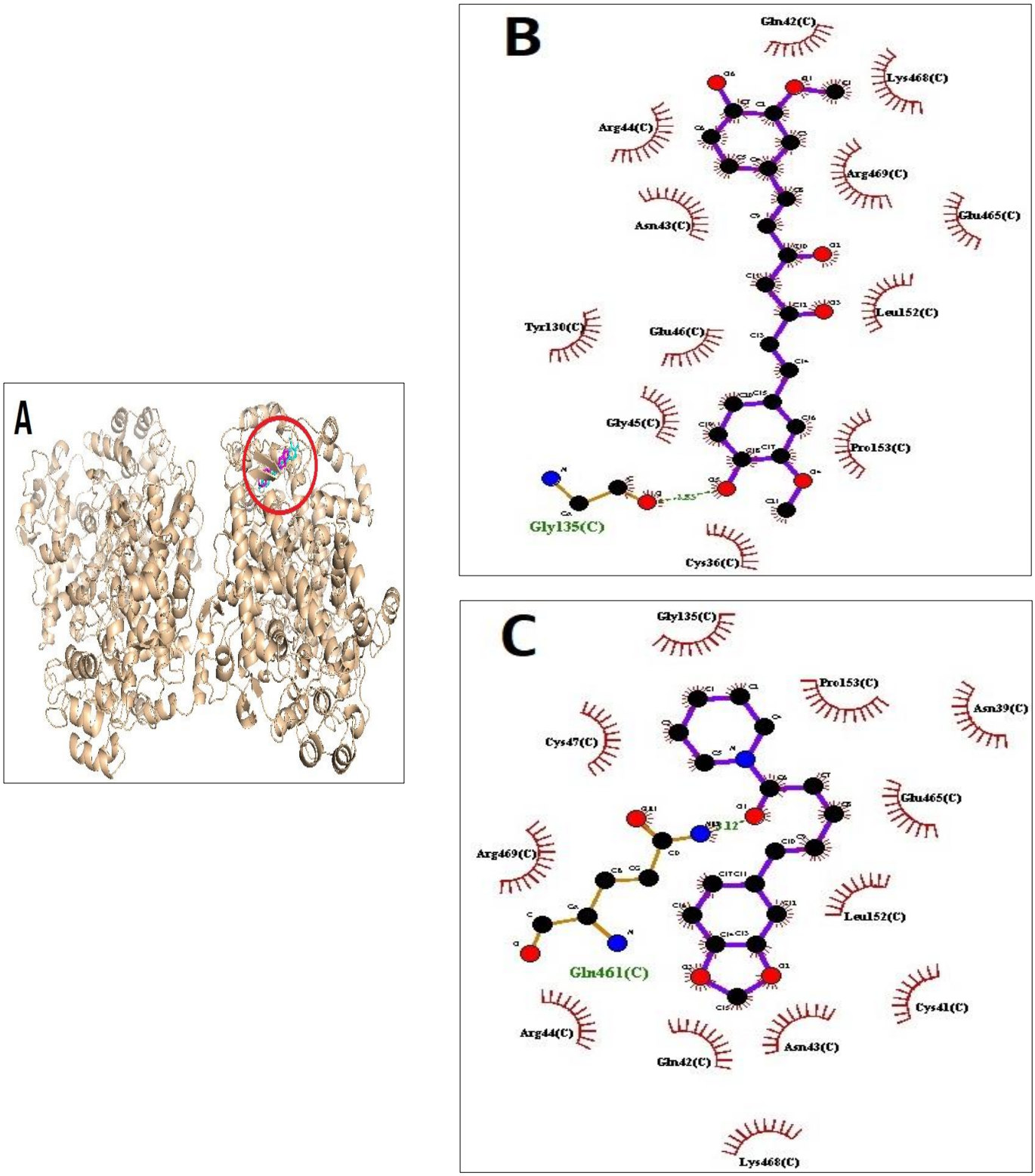


Figure 1: COX-2 (wheat color), Curcumin (cyan strokes with red circle around) and Piperin (violet strokes with red circle around) (A). COX-2 and Curcumin interaction (B). COX-2 and Piperin interaction (C). For B and C: Black, blue, red circles – COX-2 or Curcumin or Piperin atoms; Purple strokes – bonds between the atoms of Curcumin or Piperin; Orange strokes – bonds between the atoms of COX-2; Dotted green lines – Hydrogen bonds with distances (numbers) between COX-2 and Curcumin (B) or Piperin (C); Red semi-circles with lines - hydrophobic interactions.

Conclusions

The energy patterns, location and types of binding established with COX-2 were similar for CRC and PPR, so the anti-inflammatory properties may be similar. In this sense, it would be important to continue in vitro and in vivo studies with both molecules.

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