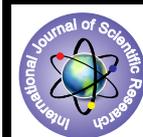


## Docking Studies of Piperine with some Drug Transporters



### Biotechnology

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### ABSTRACT

*Piperine is the standardized extract made from the fruit of Piper Nigrum (black pepper) or Piper longum L (long pepper) and is manufactured for use as a nutritional ingredient for both human and animal health. Studying the binding affinities of piperine with drug transporter molecules will give us information about iron and other micro-nutrient transport into the cell. In this paper we docked piperine with CYP450 enzymes, p-glycoprotein and ferroportin.*

### INTRODUCTION

#### PIPERINE:

Piperine is an alkaloid responsible for the pungency of black pepper and long pepper along with chavicine (isomer of piperine). Piperine is used in medicine and as an insecticide. Piperine was first hydrolysed by alkalis into a base and acid which were named as piperidine and piperic acid. Piperine has found to inhibit human CYP3A4 and P-glycoprotein, enzymes responsible for metabolism transport of xenobiotics and metabolites. In animal studies, piperine also inhibited enzymes important in drug metabolism and increase the bioavailability of various compounds. The exact mechanism of piperine's bioavailability enhancing abilities is unknown.

#### FERRITIN

Ferritin is an intracellular iron storage protein in both prokaryotes and eukaryotes and produced by all living organisms like algae, bacteria, higher plants and humans. Ferritin serves to store iron in nontoxic form and transport it to places where it is required. Free iron is toxic to cells as it acts as a catalyst in the formation of free radicals. If ferritin level is low, there is a risk for lack of iron which leads to anaemia. Low ferritin indicates hypothyroidism, vitamin C deficiency. If ferritin is high, there is excess iron or there is an inflammatory reaction which ferritin is mobilized.

#### CYTOCHROME P 450

The cytochrome P 450 is a large group of enzymes which catalyze the oxidation of organic substances. CYP's enzymes are involved in drug metabolism and bio activation and deactivate many drugs directly or by facilitated excretion from the body. Many drugs increase or decrease the activity of various CYP isoenzymes by inducing biosynthesis of isoenzyme or by inhibiting the activity of CYP. Naturally occurring compounds induce or inhibit CYP activity. For example, bioactive compounds found in pepper have been found to inhibit CYP3A4 mediated metabolism of certain medications leading to increased bioavailability. 3,4.

#### P-GLYCOPROTEIN

P-glycoprotein (permeability glycoprotein) also known as multidrug resistance protein 1 (MDR1) or ATP binding cassette sub-family member 1 (ABC1). P-glycoprotein is extensively distributed and expressed in intestinal epithelium, adrenal gland, hepatocytes, renal proximal tubular cells. ABC proteins transport various molecules across extra and intracellular membranes which includes drugs (colchicines, quinidine), chemotherapeutic agents, lipids, steroids, Xenobiotics, Peptides, Bilirubin.

In order to validate our studies, we performed in silico studies using molecular docking softwares like GLIDE, AutoDOCK 4.0 and Molegro Virtual Docker 4.1.0. Different proteins like P-glyco-

protein, Ferritin, Cytochrome P450 were docked with piperine to find whether it has any effect on Iron metabolism. The docking score was compared with other scores and best binding energy was found out.

### MATERIALS AND METHODS

Different protein compounds were taken from RCSB PDB database [www.rcsb.org](http://www.rcsb.org). The compounds are P-glycoprotein, cytochrome P450, Ferritin. These structures were downloaded from PDB website and imported into the Molecular Docking Window. The piperine molecule was taken and was drawn using the ISIS DRAW software or CHEMSKETCH software. These molecules were optimized and retrieved in pdb format for docking.

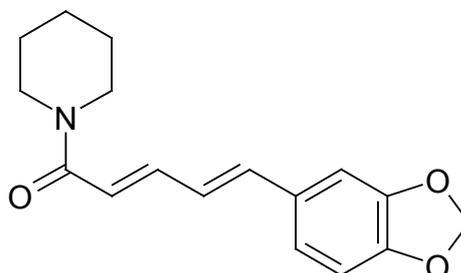


Figure 1: Piperine structure drawn using ISIS DRAW

### RESULTS AND DISCUSSION

The following scores were obtained when piperine was docked with CYP450, P-glycoprotein and Ferritin.

DOCKING OF PIPERINE WITH			
	PDB ID	MOLECULAR DOCK SCORE (Kcal/Mol)	STRUCTURE
P-GLYCOPROTEIN	3G60	-124.51	Figure2
CYTOCHROME P450	1W0E	-124.83	Figure3
FERRITIN	2FFX	-60.143	Figure4

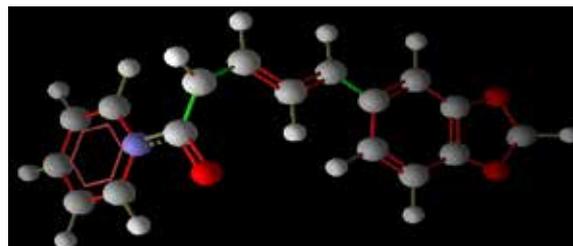


Figure2: Structure obtained from Docking of p-glycoprotein with piperine

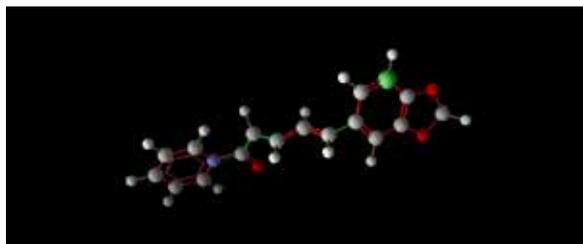


Figure3: Structure obtained from Docking of cytochrome P450 with piperine

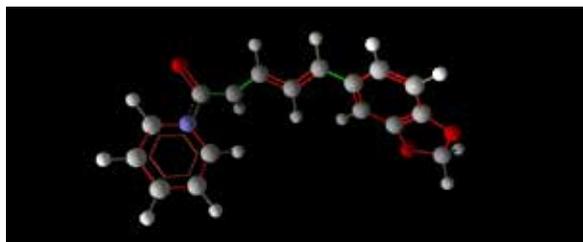


Figure4: Structure obtained from Docking of ferritin with piperine

Out of all three proteins, piperine has high impact on cytochrome P450 in terms of binding capacity

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