

In silico antimalarial bioprospecting of neem (*Azadirachta indica*) quinine-derivative alkaloids

Alfin Hidayat¹, Mamat Sugianto¹, Ali Budhi Kusuma^{1,2}, Lili Suharli¹, Adhityo Wicaksono^{3*}

Table 1. Autodock Vina's search space for three selected receptors.

Receptor (lr)4-6	Binding Site Residue	Chain	Coordinate			Dimension		
			X	Y	Z	X	Y	Z
PNP (PDB ID: 5ZNC)	His7, Arg45, Cys92, Gly93, Ser157, Tyr160, Glu182, Met183, Asp206, Trp212, Asp218	A	64.7963	63.3105	14.0424	All set to 25 Å		
DHODH (PDB ID: 6GJG)	Gly181, Cys184, His185, Phe188, Phe227, Ile263, Arg265, Val532, Met536	A	11.7281	-7.9624	-6.7855			
EMP1 (PDB ID: 6S8U)	Asn973, Asn974, Glu1098, Glu1099, Gln1103, Gly1114 (*)	A	-17.0929	-54.4949	-7.2024			

Note: For PNP and DHODH, the binding sites referred to the active sites of the proteins. As for EMP1, residues marked with (*) referred to the binding sites where the protein EMP1 binds to intercellular adhesion molecule 1 (ICAM1) polypeptide molecule.

Table 2. List of enzymes targeted by the control and studied compounds.

Compounds and their respective targets

IZP	Quinine	A	B	C	D	E
11-β-hydroxysteroid dehydrogenase 1	Mitogen-activated protein kinase kinase 12	Aldehyde dehydrogenase 1A1	Steryl-sulfatase	6-phosphofructose-2,6-bisphosphatase 3	11-β-hydroxysteroid dehydrogenase 1 (by homology)	PH domain leucine-rich repeat-containing protein phosphatase 2

Acyl-CoA desaturase	Nitric oxide synthase, inducible	Aldo-keto reductase family 1 member B10	Acyl-CoA desaturase (by homology)	6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3	Quinone reductase 2
Arachidonate 15-lipoxygenase	Phenylethanolamine N-methyltransferase	Aldehyde reductase	α -1,6-mannosylglycoprotein 2-beta-N-acetylglucosaminyltransferase	Acetyl-CoA carboxylase 1	
Elongation of very long chain fatty acids protein 6	PI3-kinase p110-α subunit	Anandamide amidohydrolase	Acyl coenzyme A:cholesterol acyltransferase 1	Aldose reductase	
Estradiol 17- β -dehydrogenase 2	S-methyl-5-thioadenosine phosphorylase	Leukocyte common antigen	Adenosine kinase	Autotaxin	
Glutaminyl-peptide cyclotransferase	Telomerase reverse transcriptase	Macrophage migration inhibitory factor	Arachidonate 12-lipoxygenase	Geranylgeranyltransferase type I	
Indoleamine 2,3-dioxygenase		Myeloperoxidase	Arachidonate 15-lipoxygenase, type II	Group IID secretory phospholipase A2	
PI3-kinase p110-α subunit		Nicotinamide phosphoribosyltransferase	Carnitine O-palmitoyltransferase 1, liver isoform	Hexokinase type IV	
PI3-kinase p110- δ subunit		Nitric oxide synthase, inducible (by homology)	Deoxycytidine kinase	Liver glycogen phosphorylase	
PI3-kinase p110- γ subunit		Poly [ADP-ribose] polymerase-1	Diacylglycerol O-acyltransferase 2	Peptidyl-prolyl cis-trans isomerase NIMA-interacting 1	
Poly [ADP-ribose] polymerase-1		Protein-glutamine γ-glutamyltransferase	Estradiol 17- β -dehydrogenase 1	Prostaglandin E synthase	
Poly [ADP-ribose] polymerase 2		Steryl-sulfatase	Estradiol 17- β -dehydrogenase 2	Protein farnesyltransferase	

Tankyrase-2	Thymidine phos- phorylase	Prostaglandin synthase	E	Squalene syn- thase (by homol- ogy)
Tankyrase-1		Isocitrate dehydro- genase [NADP] cy- toplasmic		
Thymidine phos- phorylase		Peptidyl-prolyl cis-trans isomerase FKBP5		
		Phosphoglycerate kinase 1		
		Protein- glutamine	γ-	
		glutamyltransferase		
		Protein-glutamine gamma- glutamyltransferase K		

Note: Enzymes in bold letters are the shared enzymes that target the compounds.