An *in silico* study of the antiplasmodial and anti-inflammatory potentials of compounds derived *Anogeissus leiocarpus*

Afolayan Funmilayo I. D.*, Abdulkareem Mujidat, Ijidakinro Sekemi

Cell Biology and Genetics Unit, Department of Zoology, University of Ibadan

SUMMARY

New antimalarials can be developed to inhibit key physiological pathways essential for malaria parasite survival and can also be complemented by anti-inflammatory approach.

The compounds present in acetone leaf and stem bark extracts of *Anogeissus leiocarpus* were identified by gas chromatography-mass spectrometry analysis and assessed for their potentials as antimalarial and anti-inflammatory agents, using *in silico* methods.

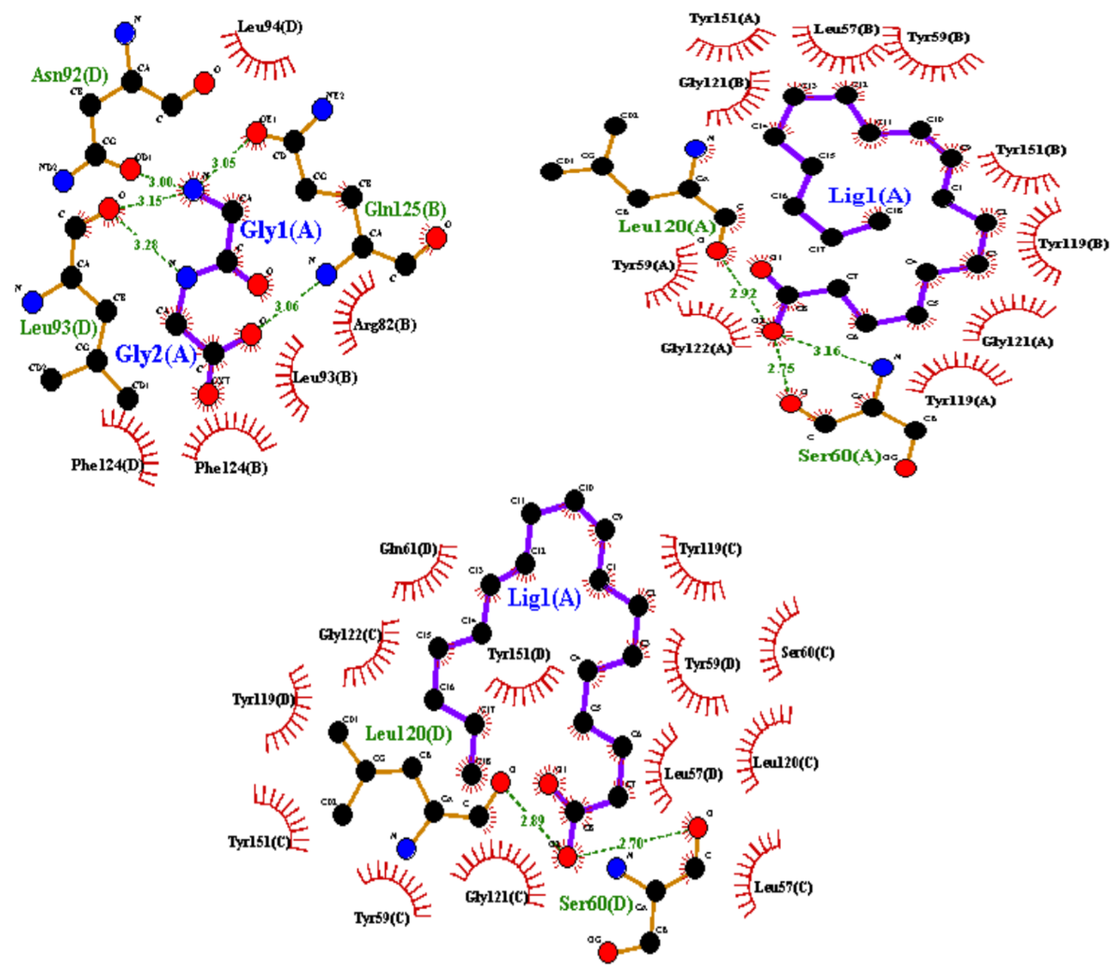
RESULTS

Table 1: Docking outcomes of compounds from *Anogeissus leiocarpus* stem bark and controls with the targets

Compound name	ΔG (kcal/mol)					
	PfDHFR	PfENR	PfHT1	IFN-γ	TNF-α	IL-12
Oleic Acid	−8.92	−8.91	−8.59	−8.25	−8.08	−7.73
Cyclopropaneoctanal, 2-octyl-	−8.91	−8.75	−8.68	−8.25	−8.20	−7.38
Octadec-9-enoic acid	−8.71	−8.95	−8.76	−8.58	−8.08	−7.51
n-Hexadecanoic acid	−8.66	−8.66	−8.39	−8.21	−7.58	−7.45
Tetradecanoic acid	−8.23	−8.20	−7.95	−7.89	−7.48	−7.31
N-Glycylglycine	−7.27	−7.80	−8.23	−7.27	−7.82	−8.72
Heptanoic acid	−6.82	−6.96	−6.67	−6.72	−6.45	−6.29
Propanedioic acid, propyl-	−6.59	−6.88	−6.47	−6.34	−6.33	−7.03
Piperidine, 1-nitroso-	−6.30	−6.13	−6.26	−5.97	−6.04	−6.32
Pentanoic acid	−6.19	−6.31	−6.15	−6.25	−5.94	−6.85
Controls	Pyrimethamine (−7.51)	Triclosan (−7.52)	Artemisinin (−7.67)	Olsalazine (−8.21)	Thalidomide (−6.80)	Tapinarof (−7.53)

Table 2: Interaction of the best docked compounds of *Anogeissus leiocarpus* stem bark with the plasmodial target

Compound name	ΔG (kcal/mol)					
	PfDHFR	PfENR	PfHT1	IFN-γ	TNF-α	IL-12
Phytol, acetate	−9.60	−9.04	−9.38	−9.02	−8.51	−7.90
Phytol	−9.10	−8.79	−8.94	−8.68	−8.16	−7.40
9,12-Octadecadienoic acid (Z,Z)-	−8.92	−9.12	−8.53	−8.28	−7.96	−7.64
n-Hexadecanoic acid	−8.73	−8.62	−8.37	−8.07	−7.55	−7.60
2-Pentadecanone, 6,10,14-trimethyl	−8.63	−8.61	−8.52	−7.99	−7.89	−7.41
Methyl 8,11,14-heptadecatrienoate	−8.42	−8.14	−8.54	−8.10	−7.76	−7.22
6-Heptadecyne, 1-chloro-	−8.32	−8.06	−8.41	−8.17	−7.79	−7.45
Tetradecanoic acid	−8.25	−8.18	−8.02	−8.27	−7.39	−7.38
Tridecanoic acid	−8.05	−8.10	−7.56	−7.74	−7.22	−7.16
1-Methoxy-3-(2-hydroxyethyl)nonane	−7.70	−7.46	−7.50	−7.12	−7.03	−6.91
Ethanone, 1-[4-Methoxy-3-(4-methylphenoxy)phenyl]-	−7.68	−7.60	−7.52	−7.24	−7.04	−7.17
2(4H)-Benzofuranone, 5,6,7,7a-tetrahydro-4,4,7a-trimethyl-	−7.05	−7.00	−6.91	−6.62	−6.86	−6.89
dl-Menthol	−6.93	−6.72	−6.83	−6.58	−6.63	−6.35
Bicyclo[5.2.0]nonane, 1,7-dimethyl-, cis-	−6.86	−6.70	−6.81	−6.53	−6.71	−6.22
Bicyclo[3.1.1]heptane, 2,6,6-trimethyl-, [1R-(1.alpha.,2.beta.,5.alpha.)]-	−6.68	−6.59	−6.60	−6.27	−6.52	−6.19
Phenol, 2-amino-4-methoxy-	−6.55	−6.60	−6.36	−6.38	−6.31	−6.34
Ethanol, 2-butoxy-	−6.45	−6.44	−6.43	−6.30	−6.08	−6.82
1,2,3-Benzenetriol	−6.30	−6.57	−6.41	−6.25	−6.37	−6.98
2-Cyclopenten-1-one, 2-methyl-	−6.05	−5.93	−5.69	−5.91	−5.67	−6.20
Reference drug	Pyrimethamine (−7.51)	Triclosan (−7.52)	Artemisinin (−7.67)	Olsalazine (−8.21)	Thalidomide (−6.80)	Tapinarof (−7.53)



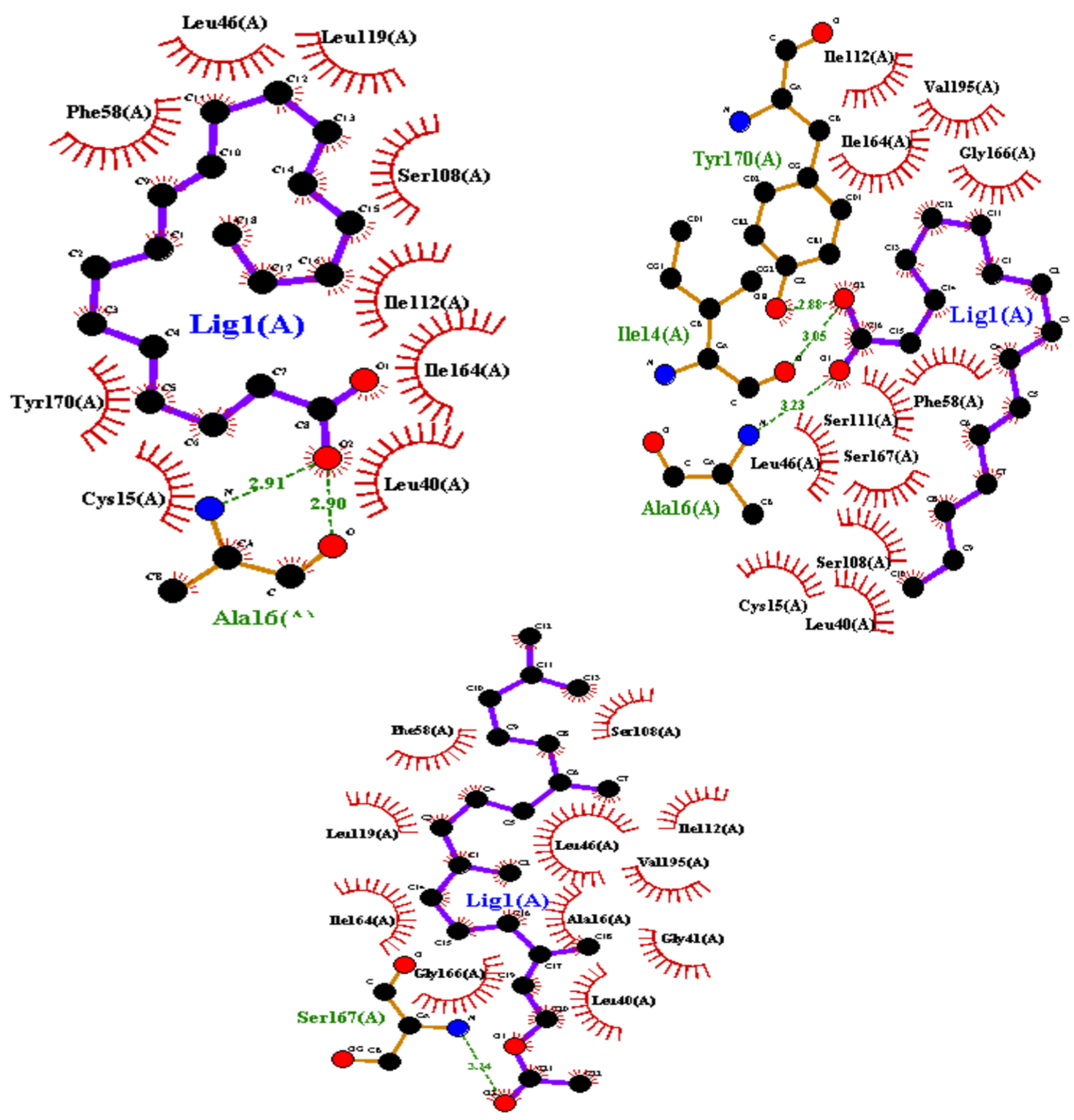


Figure 1: The interactions of (a) Oleic acid (b) n-Hexadecanoic acid and (c) Phytol, acetate with PfDHFR. The atoms of the compounds are connected with purple lines, the residues involved in hydrogen bond are written in green (bond length shown with green dashed line).

Fig. 2: The interaction of (a) N-Glycylglycine (b) Octadec-9-enoic acid and (c) 9,12-Octadecadienoic acid (Z,Z)- with TNF-α. The atoms of the compounds are connected with purple lines; the residues involved in hydrogen bond are in green (bond length shown with green dashed line). The residues involved in hydrophobic interactions are in black and indicated with red sign.

Conclusion

Lead compounds identified are oleic acid; cyclopropaneoctanal, 2-octyl-; octadec-9-enoic acid; n-Hexadecanoic acid; tetradecanoic acid; N-Glycylglycine; phytol, acetate; phytol and 9,12-Octadecadienoic acid (Z,Z)-. These compounds bind by hydrogen bonds and hydrophobic interactions to key amino acid residues at the active site of the targets.

The compounds demonstrated acceptable ADMET profiles and are predicted to be drug-like. With the binding interaction demonstrated by these lead compounds, it can be concluded that they are potential inhibitors that can be developed as antimalarial and anti-inflammatory agents.

Funmilayo Afolayan
fidifede@gmail.com