Supplemental Materials

Exploration of Chemical Diversity and Antitrypanosomal Activity of Some Red Sea-Derived Actinomycetes Using the OSMAC Approach Supported by LC-MS-Based Metabolomics and Molecular Modeling

Noha M. Gamaleldin [1,2,†], Walid Bakeer [3,†], Ahmed M. Sayed [4], Yara I. Shamikh [5,6], Ahmed O. El-Gendy [3], Hossam M. Hassan [7], Hannes Horn [8], Usama Ramadan Abdelmohsen [9,10,*] and Wael N. Hozzein [11,*]

[1] Department of Microbiology, Faculty of Pharmacy, The British University in Egypt (BUE), Cairo 11837, Egypt; noha.gamaleldin@bue.edu.eg
[2] Center for Drug Research and Development, Faculty of Pharmacy, The British University in Egypt (BUE), Cairo 11837, Egypt
[3] Department of Microbiology, Faculty of Pharmacy, Beni-Suef University, Beni-Suef 62514, Egypt; waleed.ismail@nub.edu.eg (W.B.); walidbakeer@pharm.bsu.edu.eg.
[4] Department of Pharmacognosy, Faculty of Pharmacy, Nahda University, Beni-Suef 62513, Egypt; Ahmed.Mohamed.Sayed@nub.edu.eg
[5] Department of Microbiology & Immunology, Faculty of Pharmacy, Nahda University, Beni-Suef 62513, Egypt; yara.shamikh@nub.edu.eg
[6] Virology Department, Egyptian Center for Research and Regenerative Medicine (ECRRM), 11517, Egypt
[7] Department of Pharmacognosy, Faculty of Pharmacy, Beni-Suef University, Beni-Suef 62514, Egypt; hossam.mokhtar@nub.edu.eg
[8] Independent Researcher, 69126 Heidelberg, Germany; hannes.horn@ch.tum.de
[9] Department of Pharmacognosy, Faculty of Pharmacy, Minia University, Minia 61519, Egypt
[10] Department of Pharmacognosy, Faculty of Pharmacy, Deraya University, New Minia 61111, Egypt
[11] Botany and Microbiology Department, Faculty of Science, Beni-Suef University, Beni-Suef 62514, Egypt
* Correspondence: usama.ramadan@mu.edu.eg (U.R.A.); Wael.Hozzein@science.bsu.edu.eg (W.N.H.)
† These authors contributed equally to this work.

Table S1. Panel of *Trypanosoma brucei* targets used for Autodock-Vina calculations.

Target Name	PDB code	Grid box (Å)
Trypanothione reductase (TR)	2WPF	X= -22.80, Y= -30.72, Z= 60.90
Triosephosphate isomerase (TIM)	1AG1	X= 46.05, Y= 16.79, Z= -10.89
Farnesyl diphosphate synthase (FDS)	2P1C	X= 69.01, Y= 37.02, Z= -2.02
Rhodesain	6EXQ	X= -8.23, Y= 2.3, Z= 11
Ornithine decarboxylase (OD)	1NJJ	X= 20.23, Y= 2.17, Z= 59.78
Sterol 14-alpha demethylase (AD)	3GW9	X= 22.62, Y=38.17, Z= 31.44
HSP90	3OPD	X= -1.36, Y= 16.61, Z= 12.12
Dihydrofolate reductase (DFR)	3QFX	X= -11.38, Y= 31.95, Z= 9.8
Nucleoside 2-deoxyribosyltransferase (NDT)	2F64	X= -27.17, Y= 1.97, Z= -20.94
Rhodesiense adenosine kinase (RAK)	2XTB	X= 18.39, Y= -28.42, Z= 6.5

Table S2. Binding energy scores (kcal/mol) resulted from the docking of OPLS-DA-derived metabolites against the known *T. brucei* molecular targets. Compounds got scores < -8 kcal/mol were categorized as top-scoring hits.

Targets	**(2)**	**(3)**	**(10)**	**(11)**	**(14)**	**(16)**	**(26)**	**(28)**
(TR)	**-8.7**	**-10.6**	-4.4	-4.2	-5.3	-6.8	**-8.9**	-5.6
(TIM)	-5.7	-5.9	-4.2	-5.3	-4.6	-6.5	-7.2	-4.9
(FDS)	**-8.6**	**-9.8**	-5.8	-5.4	-7.4	**-8.8**	**-9.1**	-6.1
Rhodesain	-7.4	-3.2	**-8.7**	**-8.9**	-4.2	-5.6	-6.0	-2.3
(OD)	-6.8	-5.9	-.6.3	-6.0	-6.7	-5.4	-4.9	-6.2
(AD)	-4.8	-5.2	-4.0	-5.3	-6.3	-4.7	-4.9	-5.8
HSP90	-5.5	-5.0	-6.9	-6.2	-5.8	-7.3	-7.4	-6.4
(DFR)	-4.3	-3.4	-4.9	-5.3	-5.7	-6.9	-7.4	-5.9
(NDT)	-4.1	-3.8	-3.5	-4.0	-4.9	-6.9	-7.2	-4.9
(RAK)	-4.0	-3.1	-4.9	-5.3	-4.0	-6.6	-5.3	-5.1