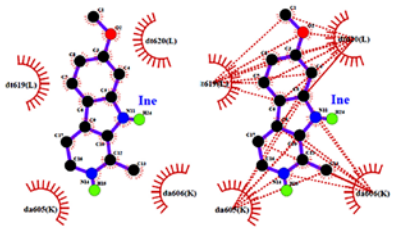
Figure S1. (A) AutoDock Vina and GROMACS (10 ps) predicted the interactions between harmine and the DNA molecule (PDB 1G3X). (B) AutoDock Vina predicted Pose 1 (pose with the lowest binding energy) of harmine which was docked inside of the DNA molecule. There are no H-bonds only hydrophobic interactions between harmine and DNA nucleotides. (C) Hydrophobic interactions and H-bond formed between the original ligand 9-acridine-peptide (acridine-tetra arginine; 9ac) and DNA nucleotides. RMSD, root-mean-square distance between the docking pose and the binding configuration in the crystallographic model; Ine, harmine.

A

Search box centre coordinates		Harmine pose (ZINC number 18847046)	Predicted by AutoDock Vina				DNA residues			
Box center	Box size		Binding energy affinity (kcal/mol)	H-bond	Hydrophobic contributions	RMSD (Å)	Predicted by AutoDock Vina		Predicted by GROMACS (10ps)	
							H-bond	Hydrophobic interactions	H-bond	Hydrophobic interactions
x = 58.447 y = 49.029 z = 60.636	x = 20 y = 20 z = 20	1	-7.6	0.00000	11.78219	0.000	---	da605, da606, dt619, dt620	da606, dt619, dt620	da605, da606, dt619, dt620
		2	-7.3	0.39324	3.62713	1.871	---	da605, da606, dt619, dt620	---	---
		3	-7.2	0.71863	5.06671	3.027	---	da605, da606, dt619, dt620	---	---
		4	-7.1	0.92490	5.78882	1.728	---	da605, da606, dt619, dt620	---	---

B



C

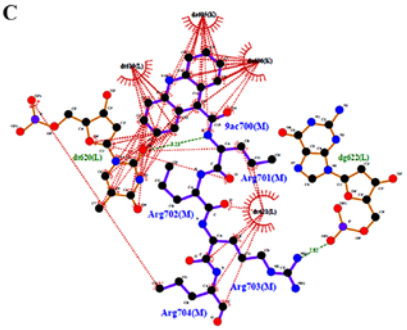


Figure S2. MD simulations with GROMACS predicted the intercalation of harmine inside the hydrophobic cavity of DNA: (A) Number of H-bonds formed between ligand and nucleotides. (B) Harmine and dt620 progression of H-bond distances. (C) Progression of H-bond angles (average angle 49.4175°). (D) Energies of complex (ΔE) calculated using MM-PBSA method. (E) van der Waals Energy (blue line) represented the major contribution to the total Molecular Mechanics Energy calculated in vacuum (red line). (F) Complex Solvation Free Energy (ΔGsolv) related to SASA calculated with MM-PBSA. INE, harmine.