Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information

Controlling an Anticancer Drug Mediated G-quadruplex Formation and Stabilization by a Molecular Container

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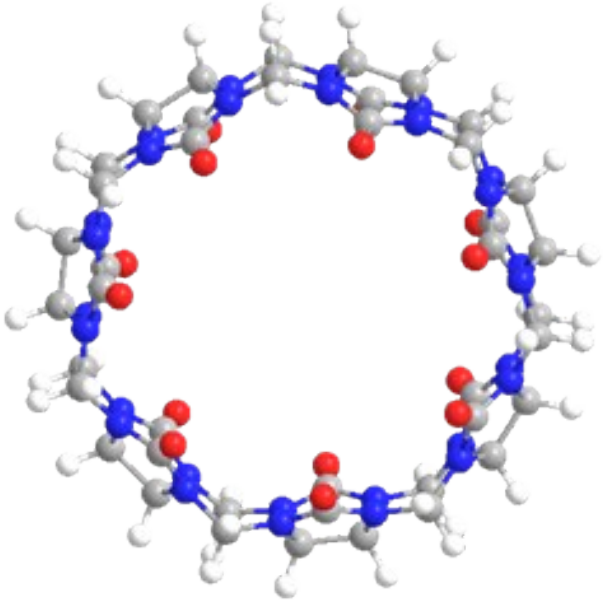

Fig. S1 Molecular structure of cucurbit[7]uril (CB7)

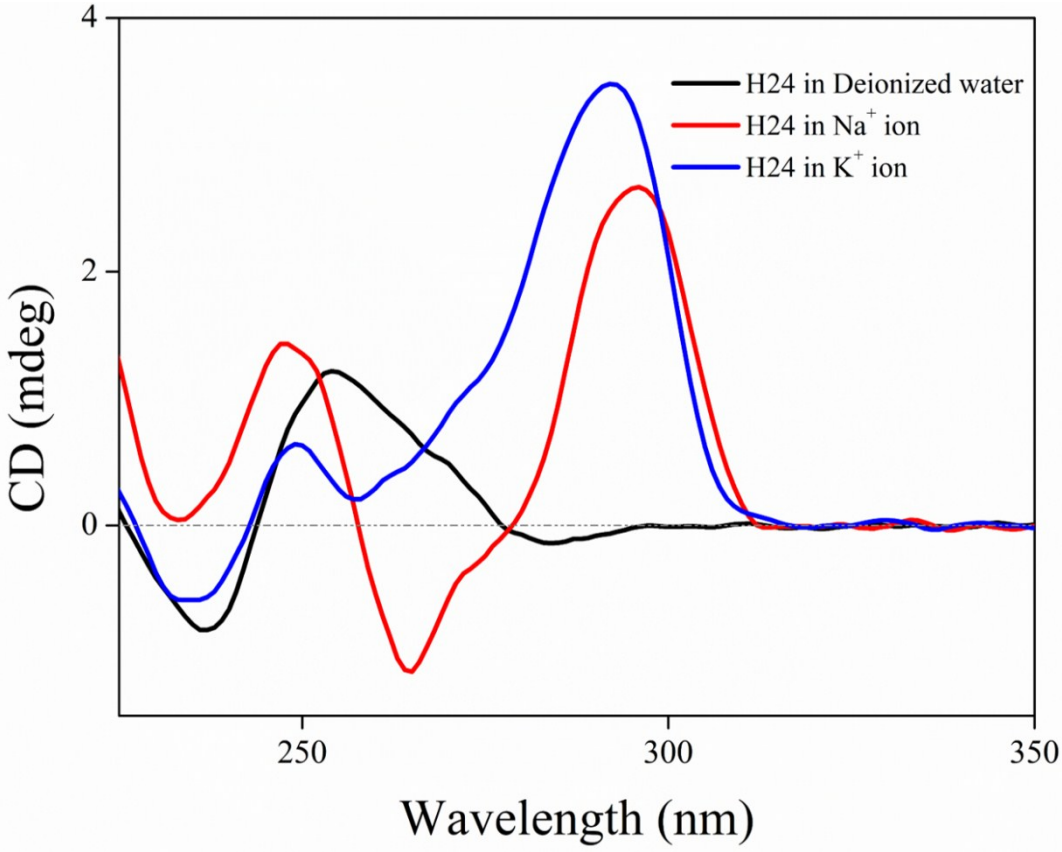

Fig. S2 Circular dichroism spectra of H24 DNA (~ 2 μM) under different conditions. The K^+ ion and Na^+ ion legends indicate the presence of 100 mM KCl and NaCl salt, respectively, in 10 mM tris buffer solution (pH 7.2).

Note S1

For static quenching, the binding constant (K) and the number of binding sites per host (n) can be determined according to the Scatchard equation[1, 2]

$$\log\left(\frac{F_0 - F}{F}\right) = logK + nlog[Q]$$

Where, F_0 and F are the relative fluorescence intensities of TPT in the absence and presence of the H24 DNA, respectively. $[Q]$ is the concentration of H24 DNA in the course of experiment. K and n can be determined from the slope and intercept value of log((F_0-F) /F)) versus log [Q] plot.

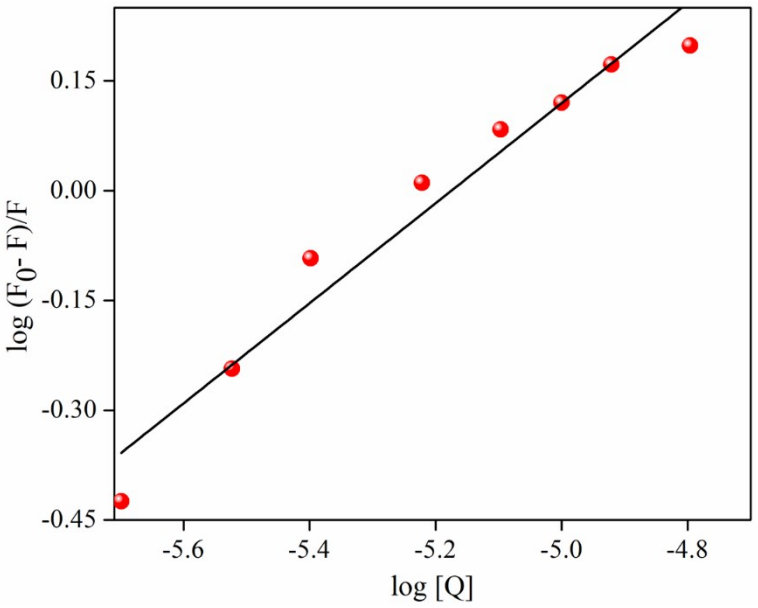

Fig. S3 Scatchard plot of log((F_0-F) /F)) versus log [Q] for the binding constant determination of H24-TPT complex.

Binding constant (K) for the H24-TPT complex is found to be 3451.4 M^{-1} and the number of binding sites of TPT per DNA (n) is 0.68 which is very close to 3 TPT molecules per 2 H24 DNA. This binding stoichiometry (n) is found to be similar to the binding of GQ DNA with other drugs such as, ellipticine[3], proflavine[4] etc. Higher binding constant value of TPT-CB7 complex (K = 5000 M^{-1}) makes the translocation of TPT from GQ DNA to CB7 nano-cavity feasible.

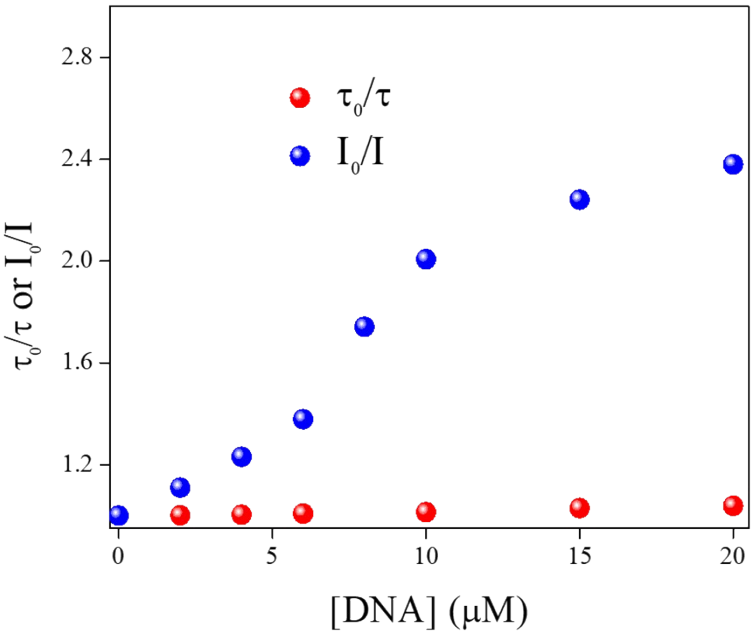

Fig. S4 Static quenching of zwitterionic form of TPT (Z^*) (emission and lifetime collected at 530 nm by exciting at 375 nm) in presence of H24 DNA.

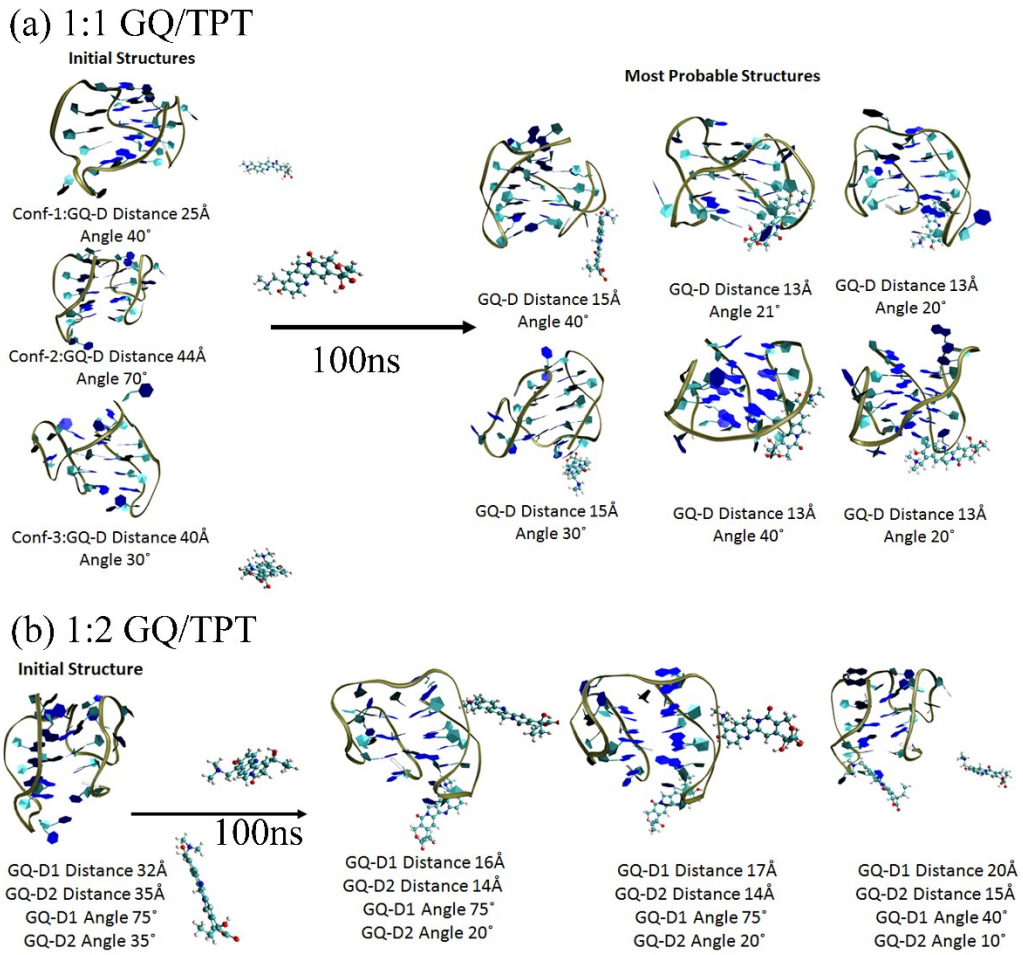

Fig. S5 Initial structure and most probable structures obtained after 100 ns of normal MD simulation (a) 1:1 GQ/TPT (b) 1:2 GQ/TPT. "D" denotes the TPT in (a) and "D1" and "D2" are two TPT molecules in (b).

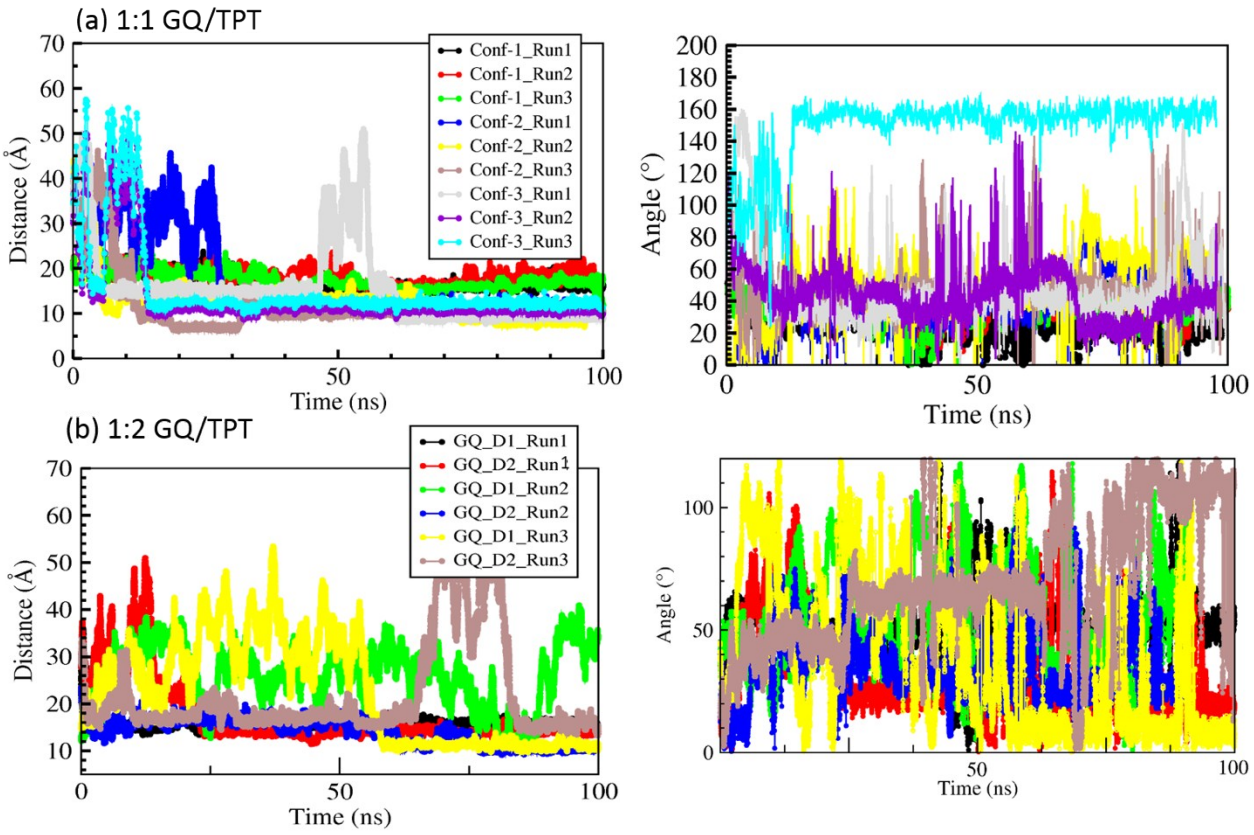

Fig. S6 Variation of distance (between COM's of GQ and TPT) and angle (between GQ axis vector and COM of GQ to COM TPT vector; see simulation method section for detail) with time from an initial random distribution of TPT in (a) 1:1 GQ/TPT complex (b) 1:2 GQ/TPT complex. Left column shows the variation of distances and right column shows the change in angle. Three random configurations (Conf-1, Conf-2, Conf-3) were created for 1:1 complex while one random configuration was created for 1:2 complex. Each random configuration was simulated three times with different velocity distribution (denoted as Run1, Run2 and Run3). Color code is same for distance and angle in 1:1 GQ/TPT complex and 1:2 GQ/TPT complex.

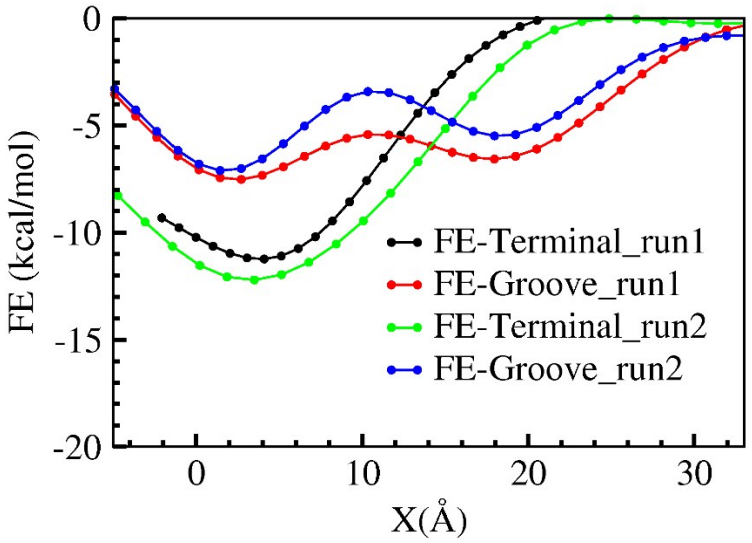

Fig. S7 Free energy of unbinding of TPT from GQ obtained from two metadynamics simulations denoted as run1, run2. Black and green color represent the free energy profiles for the terminal-bound state, while red and blue color represent the free energy profiles for the groove-bound state.

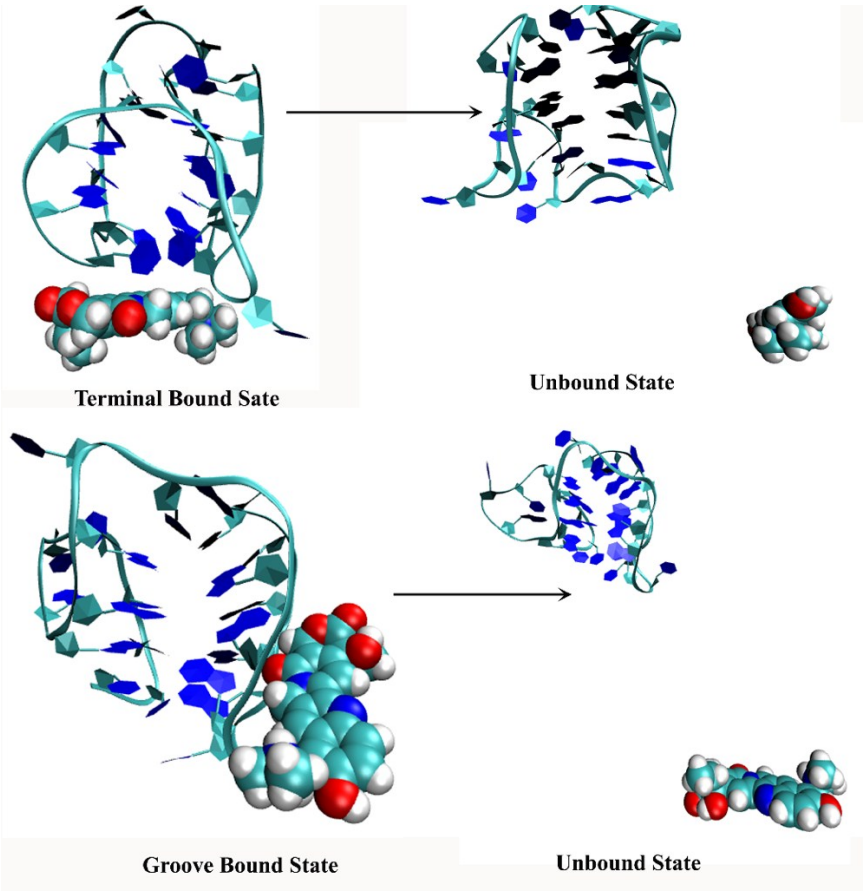

Fig. S8 Bound and unbound states of GQ and TPT obtained from well-tempered metadynamics simulation (obtained from first metadynamic run).

Table S1. Fluorescence transient fittings (collected at 530 nm) of TPT (Z*) in deionized water (pH 6.2), H24 DNA (20 μM) and in presence of both H24 DNA and CB7 (1.5 mM).

Sample	a_1	τ_1 (ns)	a_2	τ_2 (ns)	a_3	τ_3 (ns)	τ_{avg} [#] (ns)	χ^2	λ_{ex} (nm)	λ_{col} (nm)
TPT in water	-	-	-	-	1	5.88	5.88	1.04	375	530
TPT + H24 2 μM	-	-	0.04	2.71	0.96	5.95	5.83	1.08	375	530
TPT + H24 4 μM	-	-	0.06	1.96	0.94	5.94	5.71	1.04	375	530
TPT + H24 20 μM	-	-	0.10	2.69	0.90	6.01	5.66	0.99	375	530
TPT + H24 CB 7 100 μM	-	-	0.17	0.93	0.83	5.84	5.00	1.06	375	530
TPT + H24 CB 7 560 μM	-	-	0.16	1.31	0.84	5.69	4.98	1.07	375	530
TPT + H24 CB 7 1.5 mM	-	-	0.22	1.88	0.78	5.28	4.54	1.09	375	530

[#] $\tau_{avg} = a_1\tau_1 + a_2\tau_2 + a_3\tau_3$;

Table S2. Fluorescence transient fittings (collected at 430 nm) of TPT (C*) in deionized water (pH 6.2), H24 DNA (20 μM) and in presence of both H24 DNA and CB7 (1.5 mM).

Sample	a_1	τ_1 (ns)	a_2	τ_2 (ns)	a_3	τ_3 (ns)	τ_{avg} [#] (ns)	χ^2	λ_{ex} (nm)	λ_{col} (nm)
TPT in water	0.99	0.038	-	-	0.01	0.837	0.042	0.99	375	430
TPT + H24 CB 7 100 μM	0.72	0.049	0.12	0.56	0.16	2.16	0.452	1.01	375	430
TPT + H24 CB 7 560 μM	0.41	0.063	0.11	0.65	0.48	2.18	1.15	1.002	375	430
TPT + H24 CB 7 1.5 mM	0.22	0.18	0.09	0.94	0.68	2.19	1.62	1.09	375	430

[#] $\tau_{avg} = a_1\tau_1 + a_2\tau_2 + a_3\tau_3$;

Table S3. Force-field parameter of TPT molecule.

Sigma and Epsilon of each atom.

Atom Type	Sigma (σ) nm	Epsilon (ε) kJ/mol
HO	0.00000e+00	0.00000e+00
N3	3.25000e-01	7.11280e-01
NC	3.25000e-01	3.25000e-01
CB	3.39967e-01	3.59824e-01
N*	3.25000e-01	7.11280e-01
OS	3.00001e-01	7.11280e-01
CT	3.39967e-01	4.57730e-01
C	3.39967e-01	3.59824e-01
OH	3.06647e-01	8.80314e-01
CA	3.39967e-01	3.59824e-01
O	2.95992e-01	8.78640e-01
H1	2.64953e-01	6.56888e-02
HA	2.64953e-01	6.56888e-02
HC	2.64953e-01	6.56888e-02
H	1.06908e-01	6.56888e-02
HP	2.64953e-01	6.56888e-02

Charges on each atom

Atom Type	**Atom**	**Charge**
NC	N	-0.63905
CB	C	0.62518
CB	C	-0.12025
CA	C	-0.24053
HA	H	0.19936
CA	C	0.06023
CT	C	0.28472
CT	C	0.03754
CT	C	-0.23287
HC	H	0.07057
HC	H	0.07057

HC	H	0.07057
HC	H	0.01456
HC	H	0.01456
OH	O	-0.64834
HO	H	0.42637
C	C	0.70340
O	O	-0.56104
OS	O	-0.43894
CT	C	0.16112
H1	H	0.08559
H1	H	0.08559
CA	C	-0.16967
C	C	0.56964
O	O	-0.61127
N*	N	-0.07541
CT	C	-0.12097
H1	H	0.14311
H1	H	0.14311
CB	C	-0.12129
CA	C	-0.17380
HA	H	0.18987
CA	C	-0.12615
CA	C	0.41327
CA	C	-0.12886
HA	H	0.20014
CA	C	-0.38272
HA	H	0.21738
CA	C	0.36839
OH	O	-0.66510
HO	H	0.49419
CA	C	-0.09885
CT	C	-0.05269
HP	H	0.12940

HP	H	0.12940
N3	N	-0.01498
CT	C	-0.31243
HP	H	0.16667
HP	H	0.16667

References

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