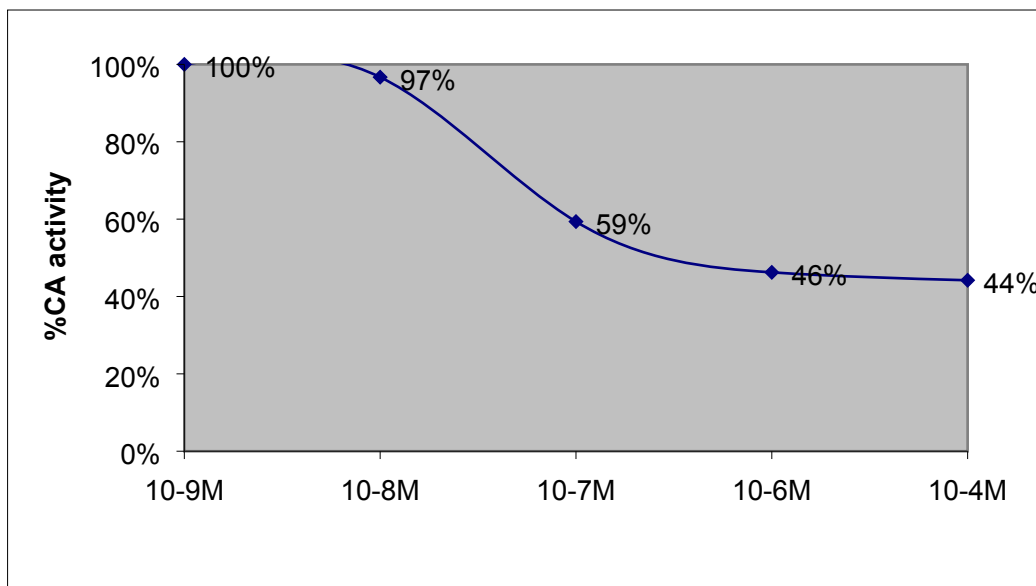


Supporting Information

The anticonvulsant sulfamide JNJ-26990990 and its S,S-dioxide analog strongly inhibit carbonic anhydrases: solution and X-ray crystallographic studies

Anna Di Fiore,^a Giuseppina De Simone,^{*a} Vincenzo Alterio,^a Vincenzo Riccio,^a Jean-Yves Winum,^b Fabrizio Carta^c and Claudiu T. Supuran^{*c}

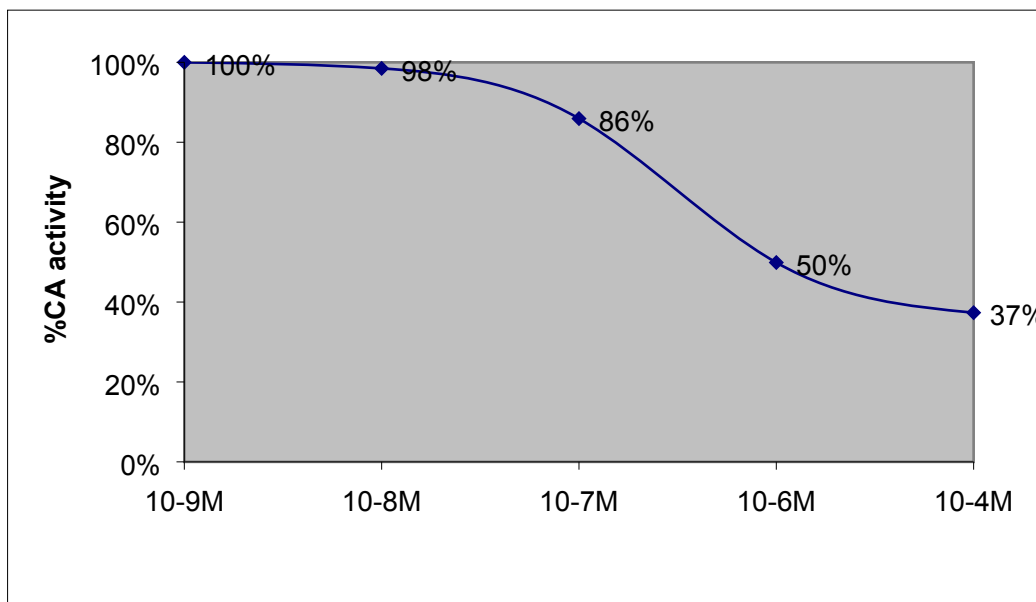
Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAI 9.3 nM			100%	0%	0,0E+00
1	10-9M	1,516	100%	0%	1,0E-09
1	10-8M	1,466	97%	3%	1,0E-08
1	10-7M	0,9	59%	41%	1,0E-07
1	10-6M	0,701	46%	54%	1,0E-06
1	10-4M	0,67	44%	56%	1,0E-04



IC₅₀ = 742 nM

By applying Cheng-Prusoff a K_I of 451±30 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAII 7.5 nM	0		100%	0%	0,0E+00
1	10-9M	1,354	100%	0%	1,0E-09
1	10-8M	1,265	94%	6%	1,0E-08
1	10-7M	0,987	73%	27%	1,0E-07
1	10-6M	0,653	48%	52%	1,0E-06
1	10-4M	0,432	32%	68%	1,0E-04

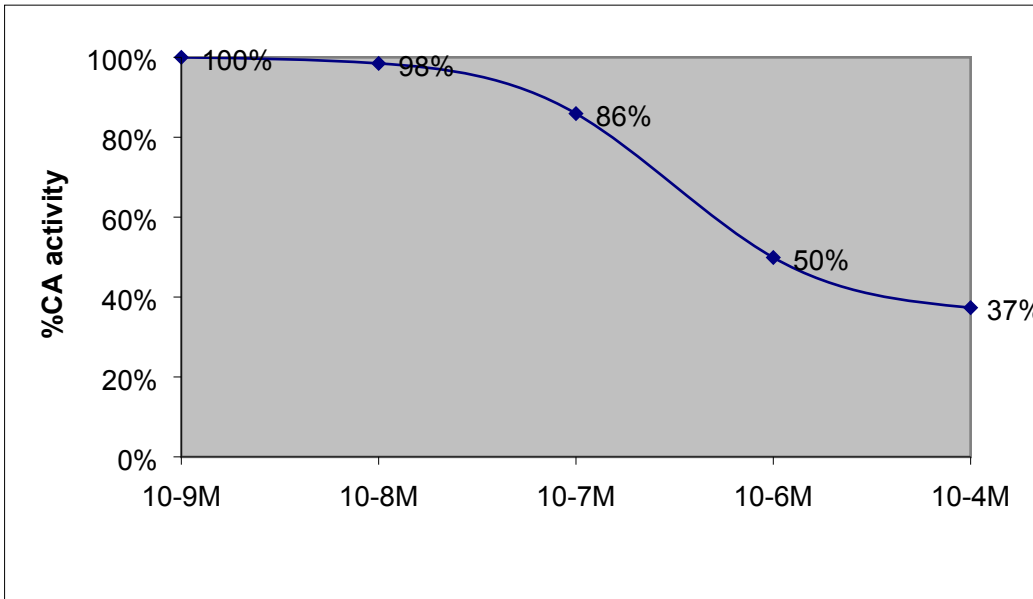


IC₅₀ 7,6932E-08

IC₅₀ = 76.9 nM

By applying Cheng-Prusoff a K_I of 34.8±1.7 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAVII 10.6 nM	0		100%	0%	0,0E+00
1	10-9M	1,456	100%	0%	1,0E-09
1	10-8M	1,366	94%	6%	1,0E-08
1	10-7M	1,032	71%	29%	1,0E-07
1	10-6M	0,613	42%	58%	1,0E-06
1	10-4M	0,519	36%	64%	1,0E-04

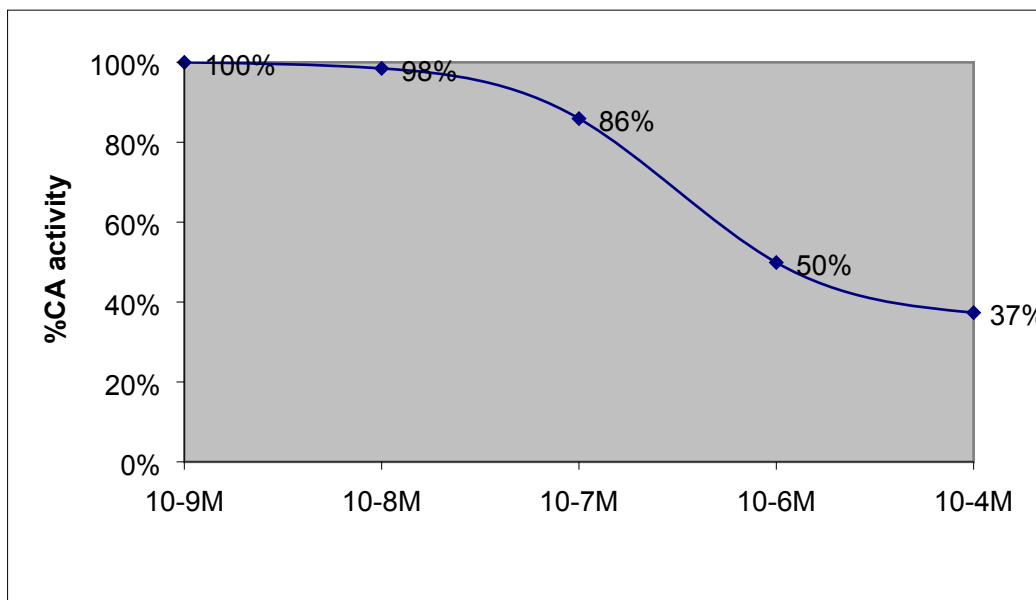


IC₅₀ 8,0889E-08

IC₅₀ = 80.9 nM

By applying Cheng-Prusoff a K_I of 49.2±3 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAIX 8.4 nM	0		100%	0%	0,0E+00
1	10-9M	1,589	100%	0%	1,0E-09
1	10-8M	1,204	76%	24%	1,0E-08
1	10-7M	0,593	37%	63%	1,0E-07
1	10-6M	0,323	20%	80%	1,0E-06
1	10-4M	0,232	15%	85%	1,0E-04

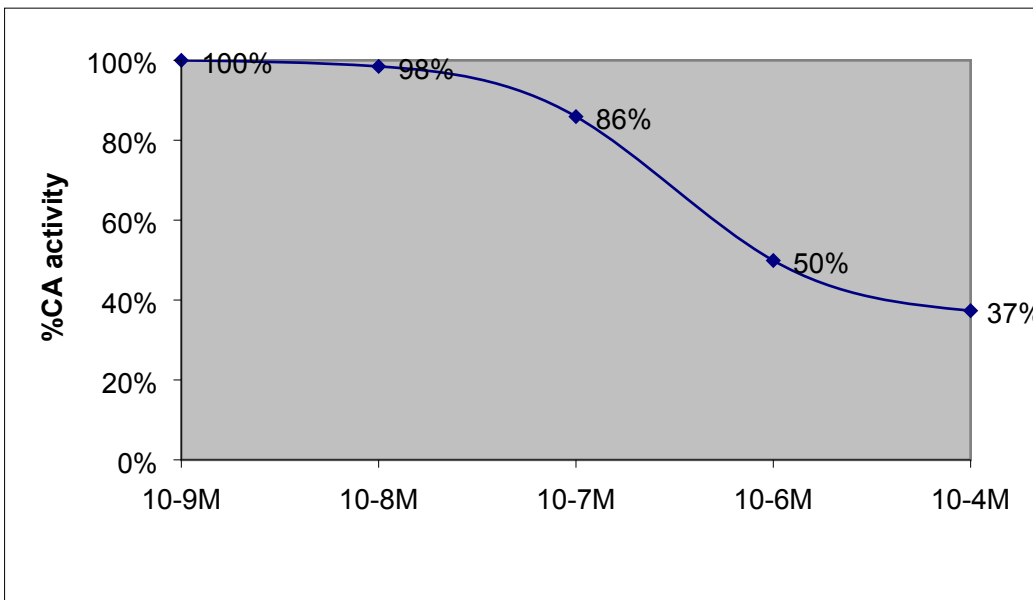


IC₅₀ **2,0636E-08**

IC₅₀ = 20.6 nM

By applying Cheng-Prusoff a K_I of 12.1±1 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAXII 12.6 nM	0		100%	0%	0,0E+00
1	10-9M	1,613	100%	0%	1,0E-09
1	10-8M	1,117	69%	31%	1,0E-08
1	10-7M	0,613	38%	62%	1,0E-07
1	10-6M	0,345	21%	79%	1,0E-06
1	10-4M	0,321	20%	80%	1,0E-04

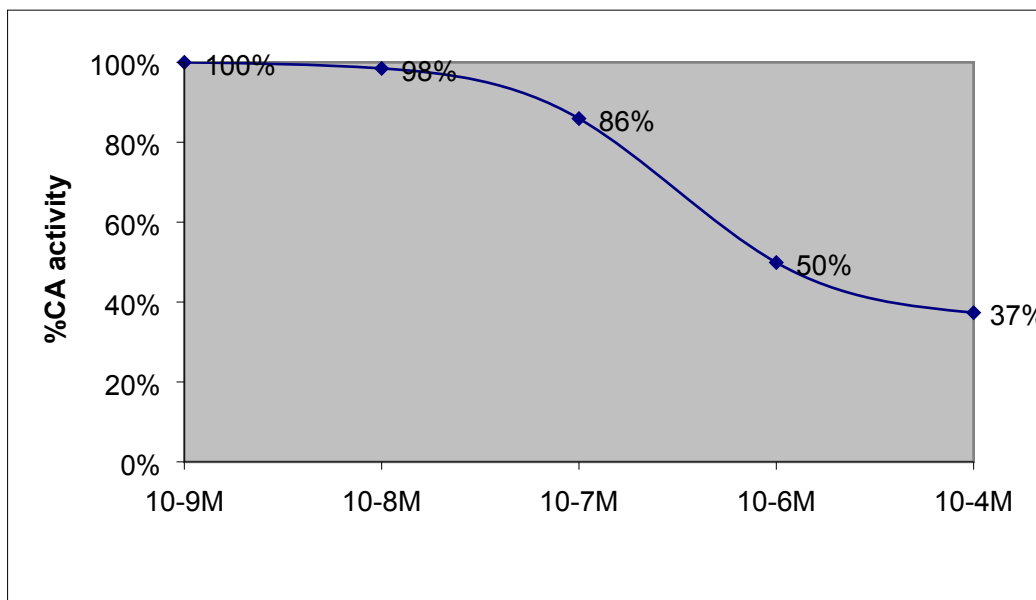


IC50 **1,626E-08**

IC₅₀ = 16.3 nM

By applying Cheng-Prusoff a K_I of 8.3±0.4 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAXIV 15.4 nM	0		100%	0%	0,0E+00
1	10-9M	1,513	100%	0%	1,0E-09
1	10-8M	1,324	88%	12%	1,0E-08
1	10-7M	1,025	68%	32%	1,0E-07
1	10-6M	0,733	48%	52%	1,0E-06
1	10-4M	0,632	42%	58%	1,0E-04

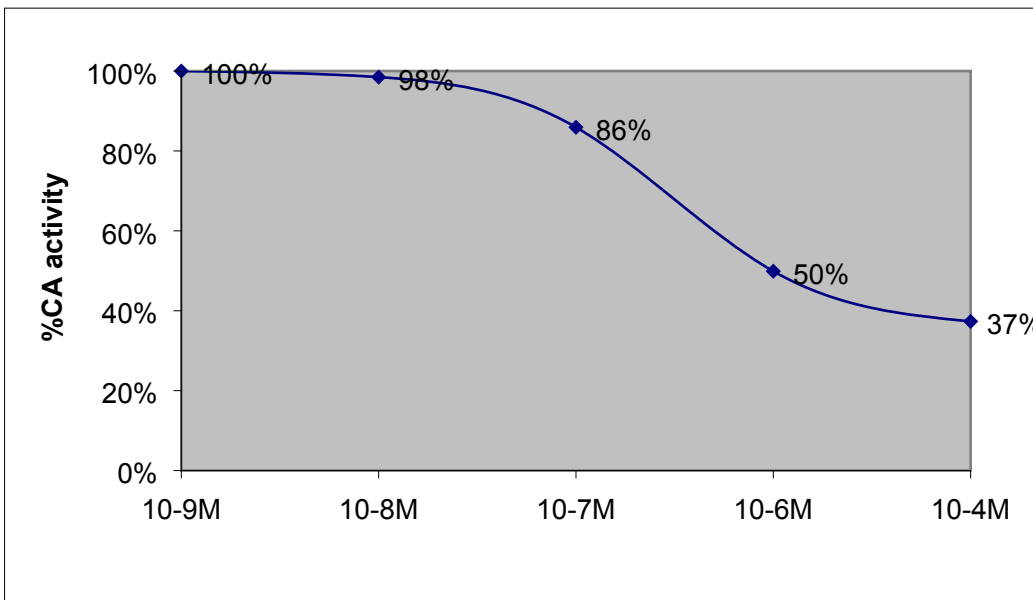


IC50 **4,0026E-08**

IC₅₀ = 40.0 nM

By applying Cheng-Prusoff a K_I of 23.5±1.1 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAI 9.3 nM	0		100%	0%	0,0E+00
4	10-9M	1,449	100%	0%	1,0E-09
4	10-8M	1,427	98%	2%	1,0E-08
4	10-7M	1,245	86%	14%	1,0E-07
4	10-6M	0,723	50%	50%	1,0E-06
4	10-4M	0,541	37%	63%	1,0E-04

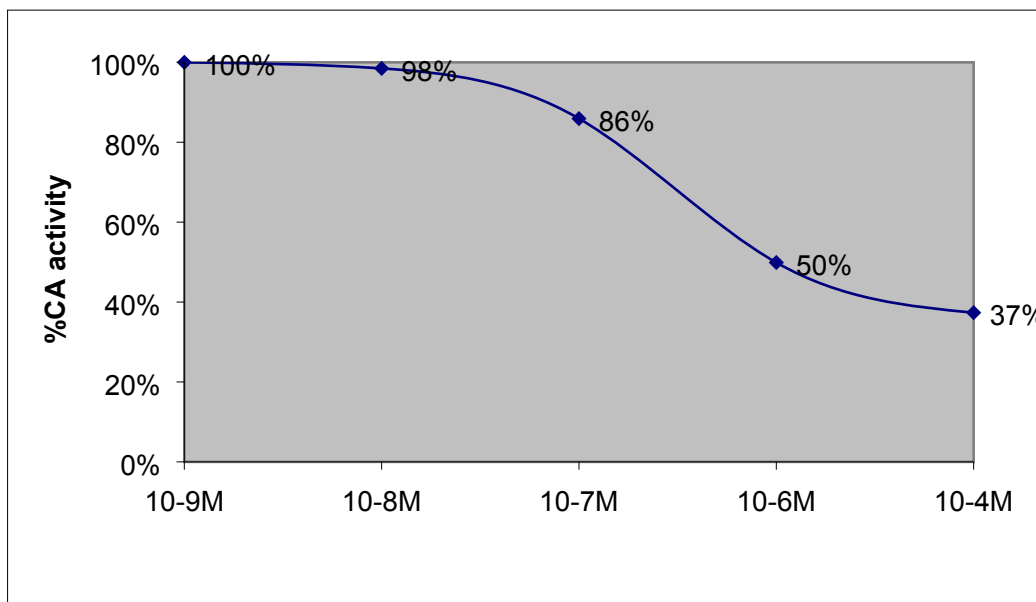


IC₅₀ 5,2932E-07

IC₅₀ = 529.3 nM

By applying Cheng-Prusoff a K_I of 362±21 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAII 7.5 nM	0		100%	0%	0,0E+00
4	10-9M	1,356	100%	0%	1,0E-09
4	10-8M	1,036	76%	24%	1,0E-08
4	10-7M	0,621	46%	54%	1,0E-07
4	10-6M	0,4295	32%	68%	1,0E-06
4	10-4M	0,319	24%	76%	1,0E-04

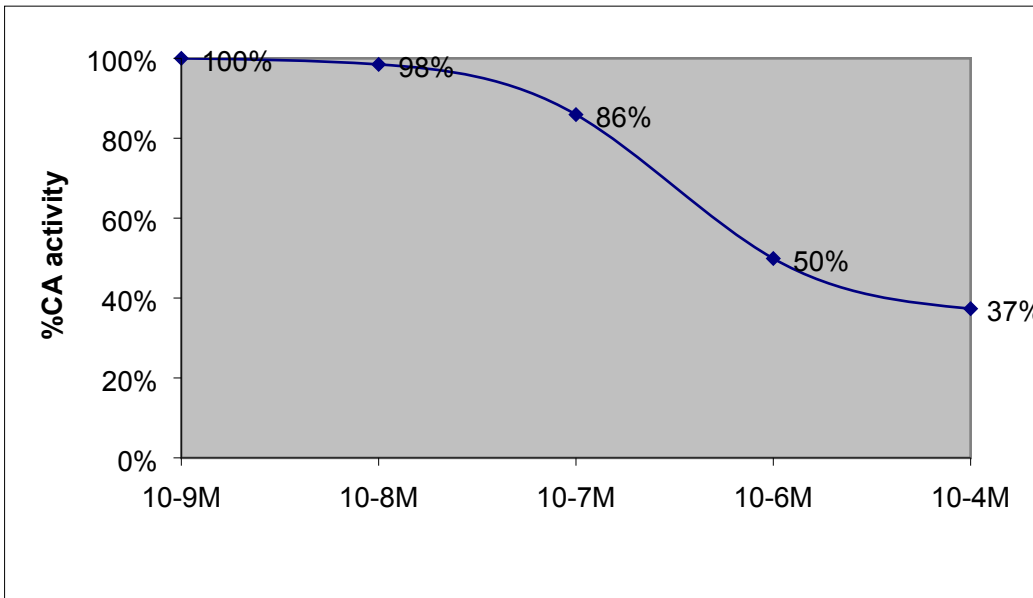


IC₅₀ 3,1188E-08

IC₅₀ = 31.2 nM

By applying Cheng-Prusoff a K_I of 18.5±0.8 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAVII 10.6 nM	0		100%	0%	0,0E+00
4	10-9M	1,356	100%	0%	1,0E-09
4	10-8M	1,236	91%	9%	1,0E-08
4	10-7M	0,924	68%	32%	1,0E-07
4	10-6M	0,4295	32%	68%	1,0E-06
4	10-4M	0,319	24%	76%	1,0E-04

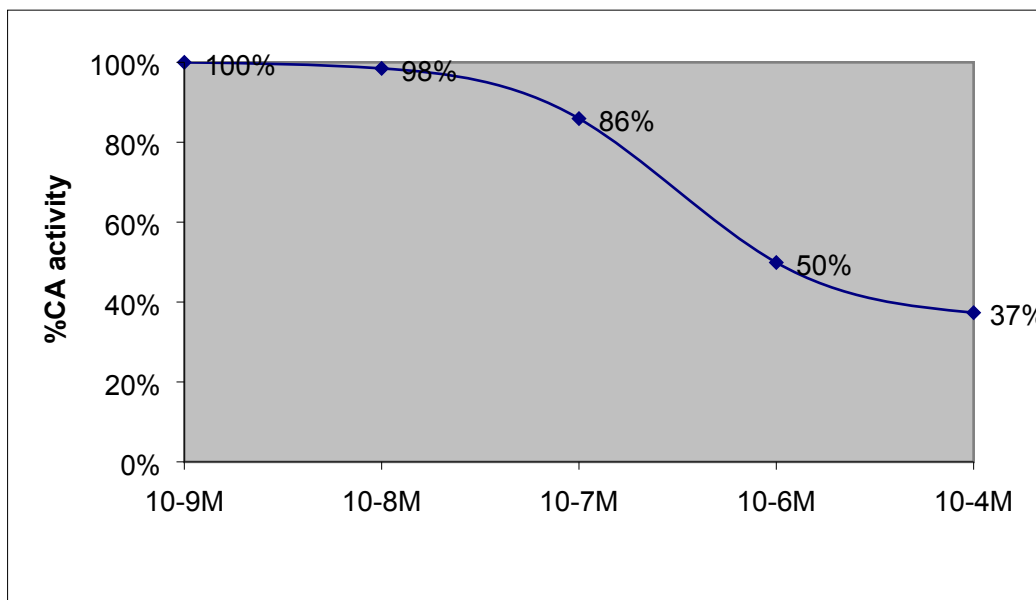


IC₅₀ 5,65E-08

IC₅₀ = 56.5 nM

By applying Cheng-Prusoff a K_I of 26.1±1.4 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAIX 8.4 nM	0		100%	0%	0,0E+00
4	10-9M	1,647	100%	0%	1,0E-09
4	10-8M	1,213	74%	26%	1,0E-08
4	10-7M	0,718	44%	56%	1,0E-07
4	10-6M	0,441	27%	73%	1,0E-06
4	10-4M	0,421	26%	74%	1,0E-04

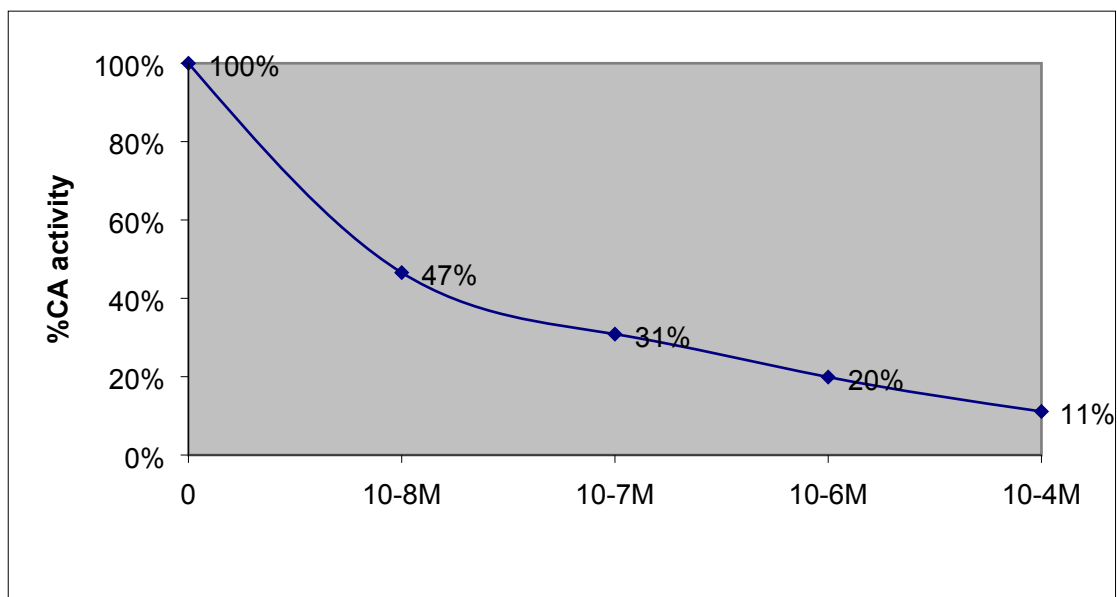


IC50 **1,8975E-08**

IC₅₀ = 18.9 nM

By applying Cheng-Prusoff a K_I of 10.2±0.9 was obtained.

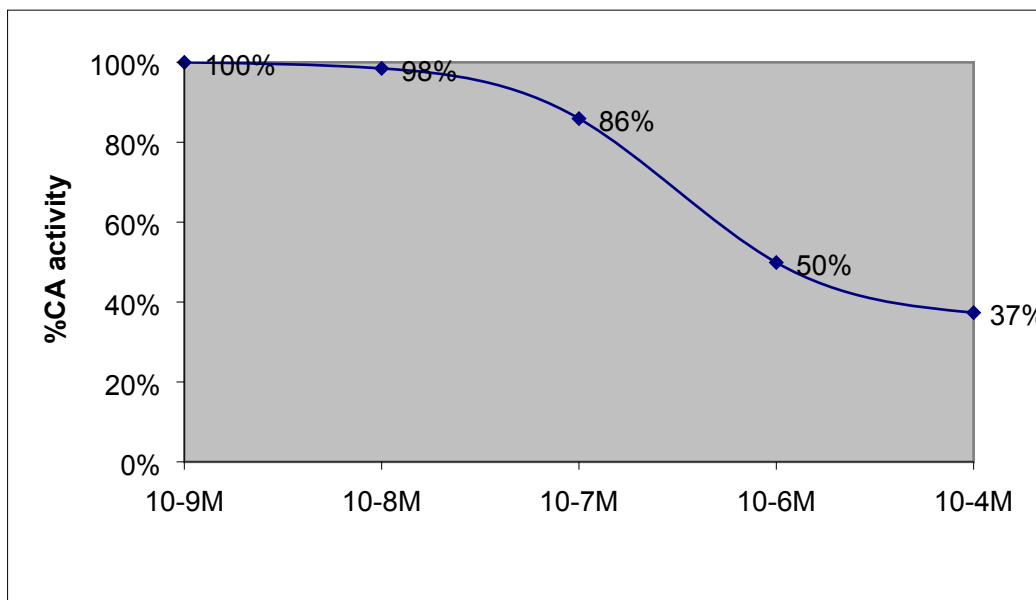
Compound/ hCA XII 12.6nM	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition
4	10-9M	3,713	100%	0%
4	10-8M	1,729	47%	53%
4	10-7M	1,146	31%	69%
4	10-6M	0,739	20%	80%
4	10-4M	0,413	11%	89%



IC₅₀ 9.3574E-09

By applying Cheng-Prusoff a K_I of 7.5±0.6 was obtained.

Compound	Inhibitor concentration	Slope	%Free Enzyme	%Inhibition	
hCAXIV 15.4 nM	0		100%	0%	0,0E+00
4	10-9M	1,535	100%	0%	1,0E-09
4	10-8M	1,232	80%	20%	1,0E-08
4	10-7M	0,639	42%	58%	1,0E-07
4	10-6M	0,503	33%	67%	1,0E-06
4	10-4M	0,411	27%	73%	1,0E-04



IC₅₀ 2,533E-08

IC₅₀ = 25.3 nM

By applying Cheng-Prusoff a K_I of 14.6±0.9 was obtained.