Supporting Information

An orally active peptide vector allows using cannabis to fight pain while avoiding side effects

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1. Supporting Information Tables

Table S1. Design and synthesis of TMs 5 and 6 short analogs

Peptide	Sequence[a,b]	Theoretical mass (Da)	Experimental mass (Da)	HPLC gradient[c] (% ACN)	HPLC retention time (min)
TM5-Tat	ETYLMFWIGVTSVLLLFIVYAYMYILWGRKKRRQRRR	4726.8	4725.8	40-90 %	6.86
1	VYAYMYILWGRKKRRQRRR	2599.2	2598.7	10-50 %	5.99
2	VYAYMYILW	1220.5	1219.4	25-60%	7.75
Tat-TM6	GRKKRRQRRRKTLVLILVVLIICWGPLLAIMVYDVF	4322.5	4322.6	0-95 %	10.75
3	GRKKRRQRRRKTLVLILVV	2375.0	2375.1	10-60 %	5.81
4	KTLVLILVV	996.3	995.7	20-60%	9.50
TM7-Tat	LIKTVFAFCSMLCLLNSTVNPIIYALRGRKKRRQRRR	4420.4	4421.4	30-60 %	5.87

[a] All peptides are *C*-terminal carboxamides; [b] Tat(48-57) sequence GRKKRRQRRR; [c] linear gradient over 15 min, initial and final ACN concentrations noted.

Table S2. HIV-Tat replacement by shorter CPPs

Peptide	Sequence[a,b,c]	Theoretical mass (Da)	Experimental mass (Da)	HPLC gradient[d] (% ACN)	HPLC retention time (min)
1	VYAYMYILWGRKKRRQRRR	2599.2	2598.7	10-50	5.99
5	VYAYMYILWAGILKRW	2045.5	2045.4	25-50	8.83
6	VYAYMYILWSKSKSK	1866.3	1866.1	15-50	8.19
7	VYAYMYILWRLRWR	1988.4	1988.1	25-55	6.57
8	VYAYMYILWRKR	1661.0	1661.5	20-45	6.09
3	GRKKRRQRRRKTLVLILVV	2375.0	2375.1	10-60	5.81
9	AGILKRWKTLVLILVV	1821.4	1820.9	25-55	7.10
10	SKSKSKKTLVLILVV	1642.1	1642.7	15-60	7.43
11	RLRWRKTLVLILVV	1764.3	1764.2	15-70	8.25
12	RKRKTLVLILVV	1436.9	1436.6	20-45	6.01

[a] All peptides are *C*-terminal carboxamides; [b] residues in red correspond to Tat(48-57); [c] residues in blue correspond to various shorter CPPs (see main text); [d] linear gradient over 15 min, initial and final ACN concentrations noted.

Table S3. Applying CPP stereochemistry change

Peptide	Sequence[a,b]	Theoretical mass (Da)	Experimental mass (Da)	HPLC gradient[c] (% ACN)	HPLC retention time (min)
5	VYAYMYILWAGILKRW	2045.5	2045.4	25-50	8.83
6	VYAYMYILWSKSKSK	1866.3	1866.1	15-50	8.19
13	VYAYMYILWaGilkrw	2045.5	2045.3	30-60	4.89
14	VYAYMYILWsksksk	1866.3	1867.5	15-50	8.01
9	AGILKRWKTLVLILVV	1821,4	1820.9	25-55	7.10
10	SKSKSKKTLVLILVV	1642.1	1642.1	15-60	7.43
15	aGilkrwKTLVLILVV	1821.4	1821.2	25-50	5.90
16	sksksKTLVLILVV	1642.1	1642.8	15-60	7.17

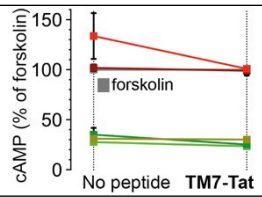
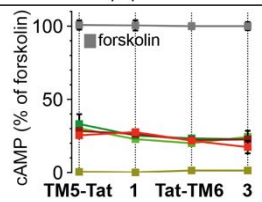
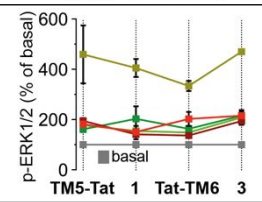
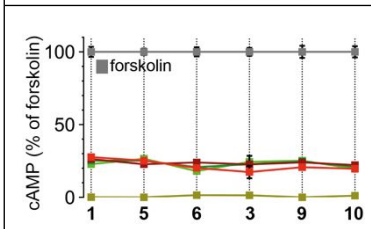
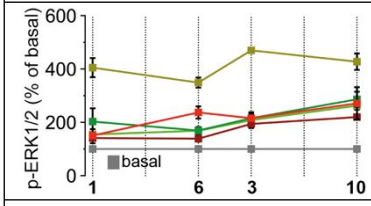
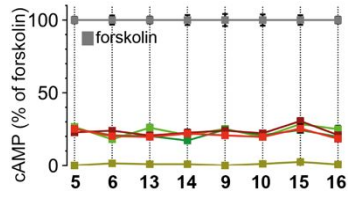
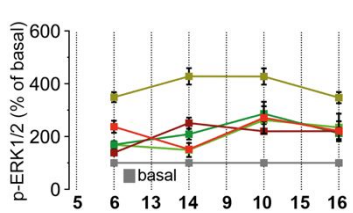
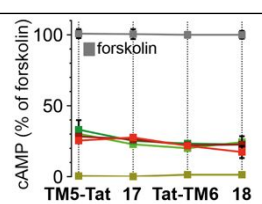
[a] All peptides are *C*-terminal carboxamides; [b] residues in blue correspond to the *in vitro* optimally performing L- amino acid CPPs (see Figure S2); in magenta to the D-CPP counterparts; [c] linear gradient over 15 min, initial and final ACN concentrations noted.

Table S4. Applying configurational switch and sequence reversal for last-stage lead optimization

Peptide	Sequence[a,b,c]	Theoretical mass (Da)	Experimental mass (Da)	HPLC gradient[d] (% ACN)	HPLC retention time (min)
13	VYAYMYILWaGilkrw	2045.5	2045.3	30-60	4.89
17	wliymyayvaGilkrw	2045.5	2045.3	30-55	6.93
15	aGilkrwKTLVLILVV	1821.4	1821.2	25-50	5.90
18	aGilkrwvvlilvltk	1821.4	1821.2	30-60	6.14

[a] All peptides are *C*-terminal carboxamides; [b] residues in magenta correspond to the *in vitro* optimally performing CPP/BBB shuttle (see Figure S2-S3); [c] upper and lowercase denote L- and D-residues, respectively; [d] linear gradient over 15 min, initial and final ACN concentrations noted.

Table S5. Statistical analyses used in signaling experiments

	Factor	p-value	Conclusions
	ligand peptide interaction	<0.0001 0.049 0.218	$5HT_{2A}$Rago < FK (p<0.0001) CB_1Rago < FK (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < $5HT_{2A}$Rago (p=0.981) $5HT_{2A}$Rago+CB_1Rago < CB_1Rago (p>0.999) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (p<0.0001) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (p<0.0001)
	ligand peptide interaction	<0.0001 0.004 0.297	$5HT_{2A}$Rago < FK (p<0.0001) CB_1Rago < FK (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < $5HT_{2A}$Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < CB_1Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (p=0.99) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (p=0.49) **TM5-Tat** vs. **1** (p=0.200) **Tat-TM6** vs. **3** (p>0.999)
	ligand peptide interaction	<0.0001 0.018 0.605	$5HT_{2A}$Rago > basal (p=0.007) CB_1Rago > basal (p=0.001) $5HT_{2A}$Rago+CB_1Rago > $5HT_{2A}$Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Rago > CB_1Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (p=0.999) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (p=0.922) **TM5-Tat** vs. **1** (p=0.661) **Tat-TM6** vs. **3** (p=0.02)
	ligand peptide interaction	<0.0001 0.04 0.412	$5HT_{2A}$Rago < FK (p<0.0001) CB_1Rago < FK (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < $5HT_{2A}$Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < CB_1Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (p=0.975) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (p=0.821) **1** vs. **5** (p=0.999) **1** vs. **6** (p=0.141) **3** vs. **9** (p=0.958) **3** vs. **10** (p=0.981)
	ligand peptide interaction	<0.0001 <0.0001 0.061	$5HT_{2A}$Rago > basal (p<0.0001) CB_1Rago > basal (p<0.0001) $5HT_{2A}$Rago+CB_1Rago > $5HT_{2A}$Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Rago > CB_1Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (p=0.658) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (p>0.999) **1** vs. **6** (p=0.999) **3** vs. **10** (p=0.192)
	ligand peptide interaction	<0.0001 0.0001 0.095	$5HT_{2A}$Rago < FK (p<0.0001) CB_1Rago < FK (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < $5HT_{2A}$Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < CB_1Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (p=0.999) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (p=0.999) **5** vs. **13** (p=0.497) **6** vs. **14** (p>0.999) **9** vs. **15** (p=0.131) **10** vs. **16** (p>0.999)
	ligand peptide interaction	<0.0001 0.002 0.007	$5HT_{2A}$Rago > basal (**6**:p=0.19;**14**:p=0.37;**10**:p=0.0001;**16**:p=0.002) CB_1Rago > basal (**6**:p=0.18;**14**:p=0.02;**10**:p<0.0001;**16**:p=0.01) $5HT_{2A}$Rago+CB_1Rago > $5HT_{2A}$Rago (**6**,**14**,**10**:p<0.001;**16**:p=0.01) $5HT_{2A}$Rago+CB_1Rago > CB_1Rago (**6**,**14**,**10**:p<0.001;**16**:p=0.002) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (**6**,**10**,**16**:p>0.8;**14**:p=0.053) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (**6**,**14**, **16**,**10**:p>0.58) **6** vs. **14** ($5HT_{2A}$Rago:p=0.94; CB_1Rago:p=0.67; $5HT_{2A}$Rago+CB_1Rago:p=0.12; $5HT_{2A}$Rago+CB_1Ranta:p=0.01; CB_1Rago+$5HT_{2A}$Ranta:p=0.08) **10** vs. **16** ($5HT_{2A}$Rago:p=0.85; CB_1Rago:p=0.15; $5HT_{2A}$Rago+CB_1Rago:p=0.11; $5HT_{2A}$Rago+CB_1Ranta:p>0.999; CB_1Rago+$5HT_{2A}$Ranta:p=0.47)
	ligand peptide interaction	<0.0001 0.0001 0.057	$5HT_{2A}$Rago < FK (p<0.0001) CB_1Rago < FK (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < $5HT_{2A}$Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Rago < CB_1Rago (p<0.0001) $5HT_{2A}$Rago+CB_1Ranta vs. $5HT_{2A}$Rago (p=0.828) CB_1Rago+$5HT_{2A}$Ranta vs. CB_1Rago (p=0.594) **TM5-Tat** vs. **17** (p<0.0001) **Tat-TM6** vs. **18** (p=0.432)

Two-way ANOVA followed by Tukey's multiple comparison tests was used to analyze the data depicted in the left column.

2. Supporting Information Figures

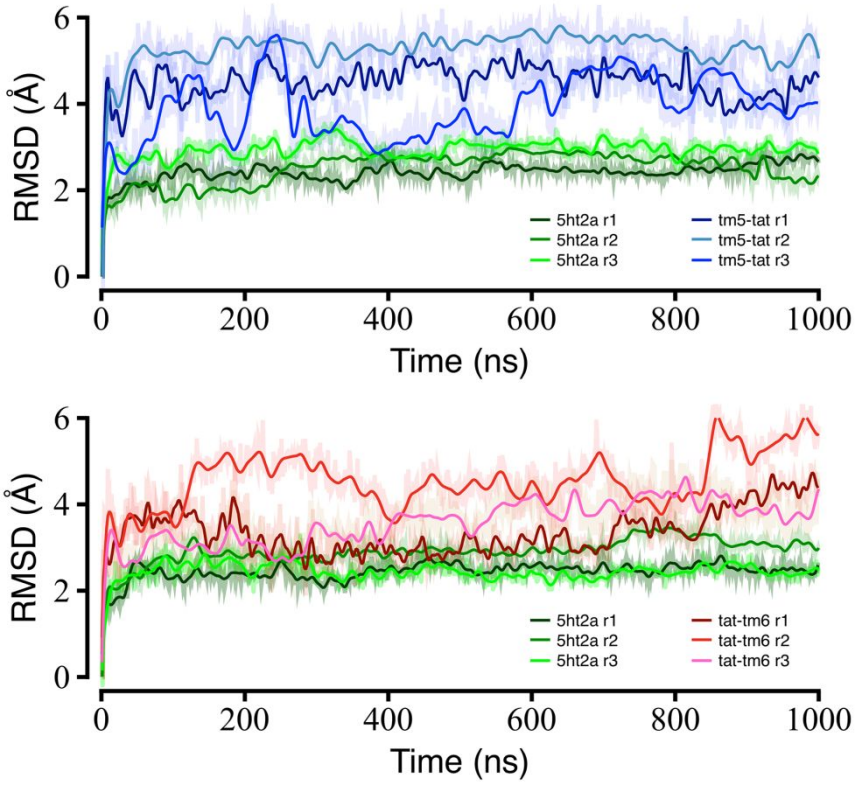


Figure S1. The stabilities of the peptide-receptor complexes, during the three replicas (r1, r2, r3) of unbiased MD simulations, are analyzed via root mean-square deviations (RMSD) of the $5HT_{2A}R$ backbone atoms (in green), **TM5-Tat** (in blue) and **Tat-TM6** (in red) peptides, derived from CB_1R. As expected, rmsd values of the peptides are larger than those of the $5HT_{2A}R$ backbone atoms, largely due to the flexibility of the Tat sequence in the water environment.

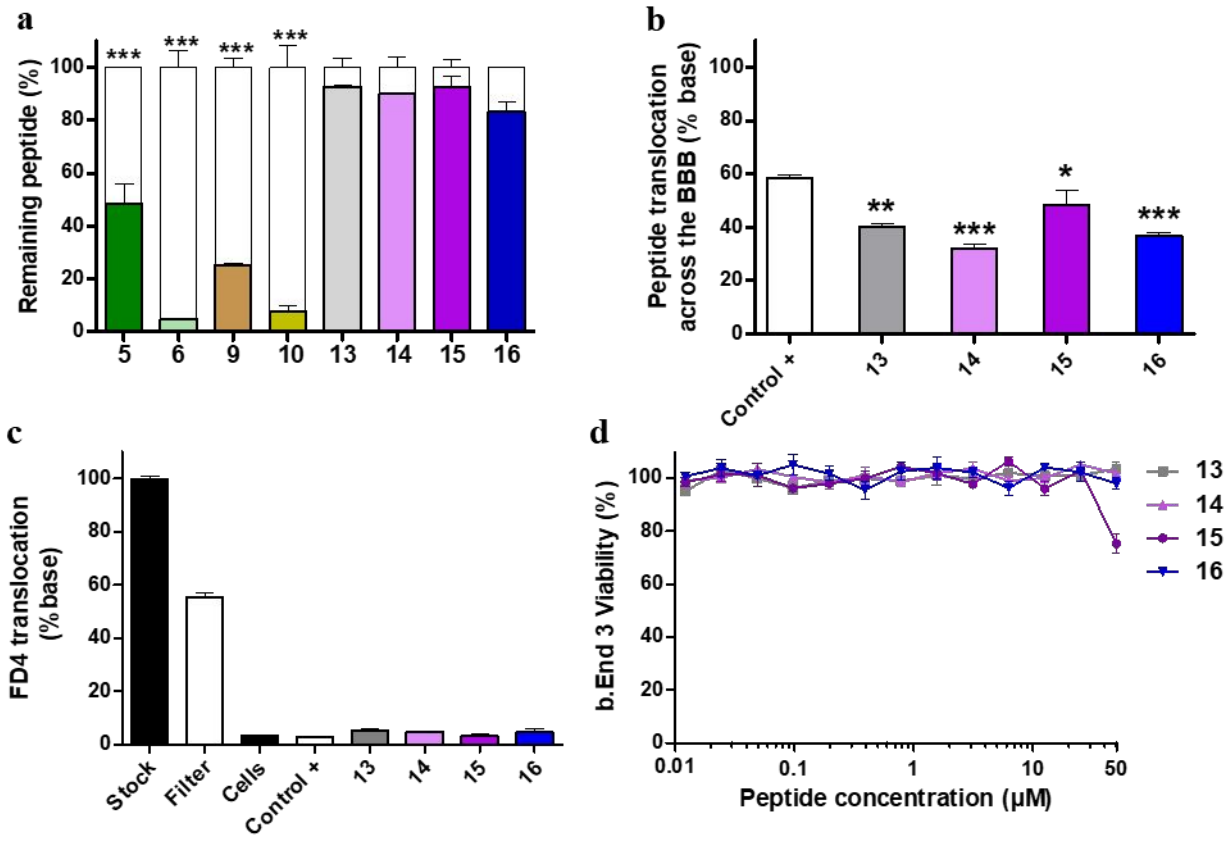


Figure S2. a, Effect of CPP stereochemistry on trypsin digestion. Unaltered peptide (color-filled bar) remaining after 24 h trypsin incubation. Main peak integrated areas at 0 h denote 100% undigested peptide (empty bars). The data are presented as mean ± SEM of n=2. One-way ANOVA followed by a Dunnett post hoc test showed a significant poor survival for **5**, **6**, **9**, **10** after 24 h vs 0 h ($^{***}p < 0.001$). **b, *In vitro* translocation of peptides 13-16.** Translocation (%) across the transwell BBB model quantified as fluorescence in the basolateral chamber after 24 h. A peptide with trans-BBB property was used as positive control. Values are mean ± SEM of n= 3–6. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs positive control (One-way ANOVA followed by a Dunnett post hoc tests). **c, BBB integrity to peptides 13-16.** Measured as permeability of fluorescent FD4 dextran upon peptide exposure. Values are mean ± SEM of n= 3–6. Statistical significance analysis was evaluated with a one-way ANOVA followed by Tukey's multiple comparison test and no statistical significance difference was observed between samples. **d, *In vitro* cytotoxicity of 13-16 towards bEnd.3 cells.** Viability (%) upon peptide incubation (0.01 – 50 µM) determined by CellTiter-Blue® Assay. Values are mean ± SEM of n= 3–6.

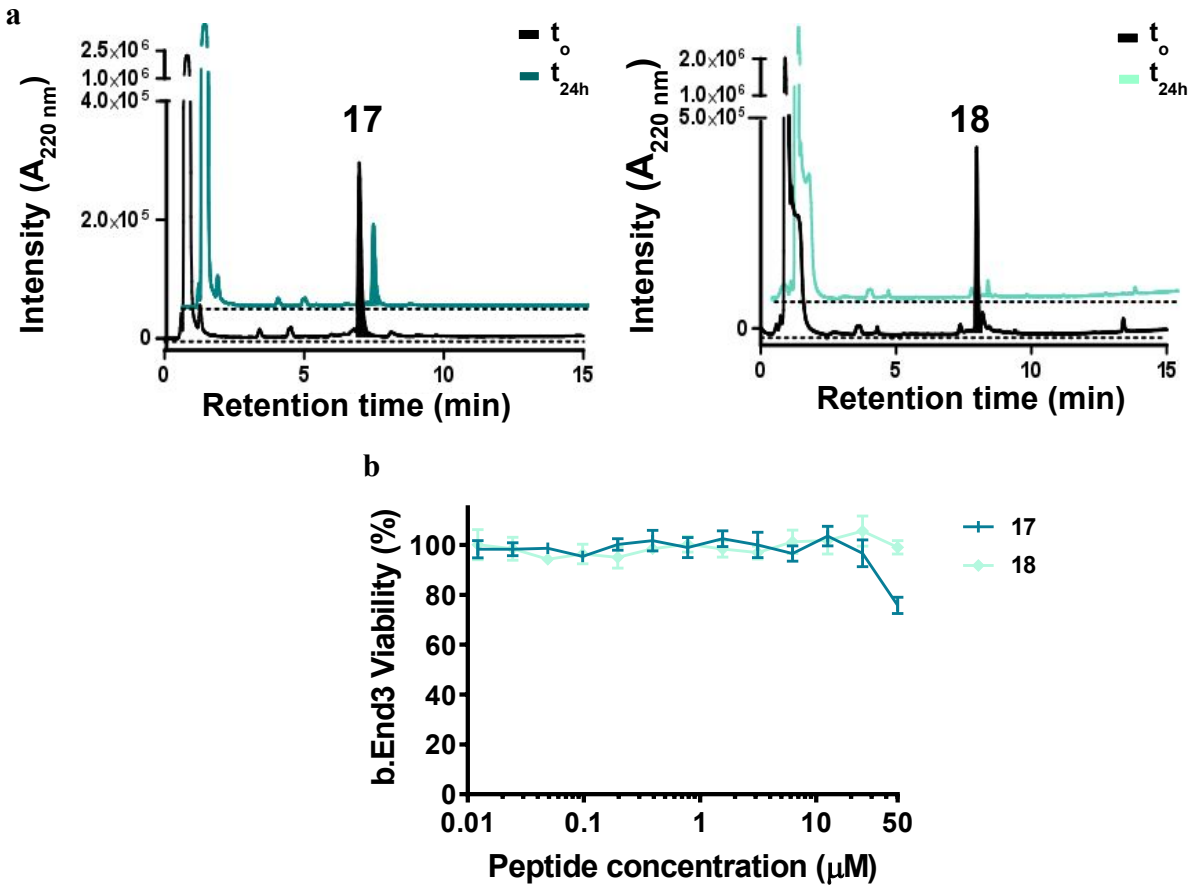
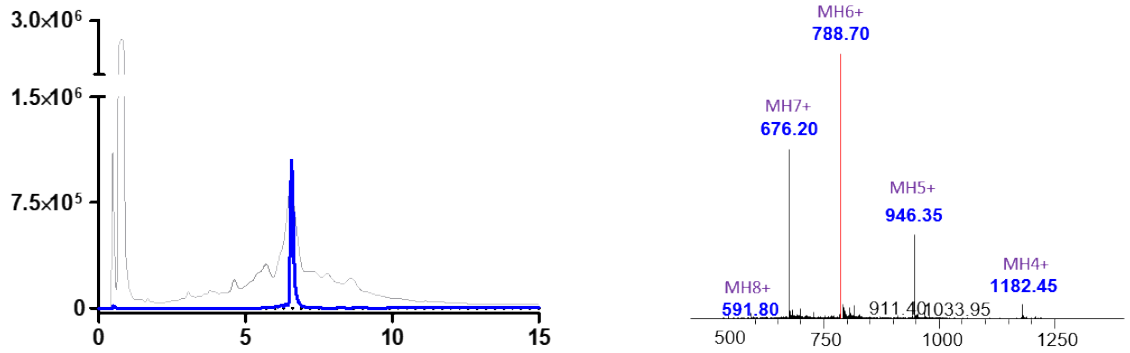


Figure S3. a, HPLC analysis of serum-incubated peptides 17 and 18. No significant new peaks referring to digested fragments were identified after 24 h. Peptide peak area decrease at 24h could be presumably attributed to binding to serum proteins. **b, *In vitro* cytotoxicity of 17 and 18 towards bEnd.3 cells.** Viability (%) upon peptide incubation (0.01 – 50 μM) determined by CellTiter-Blue® Assay. Values are mean ± SEM of n= 3–6.

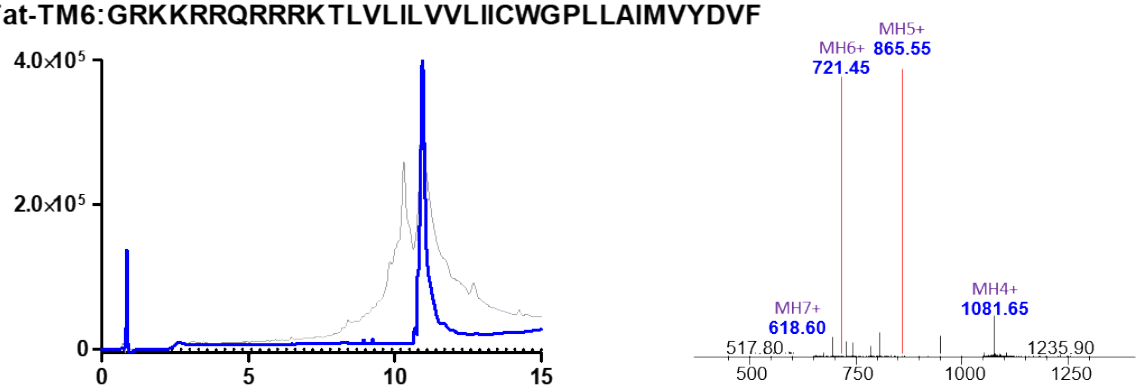
3. Analytical data

HPLC-MS analysis. Left: Overlaid HPLC traces of crude (grey) and purified peptide products (blue). Right: ESI-MS spectra of pure peptides.

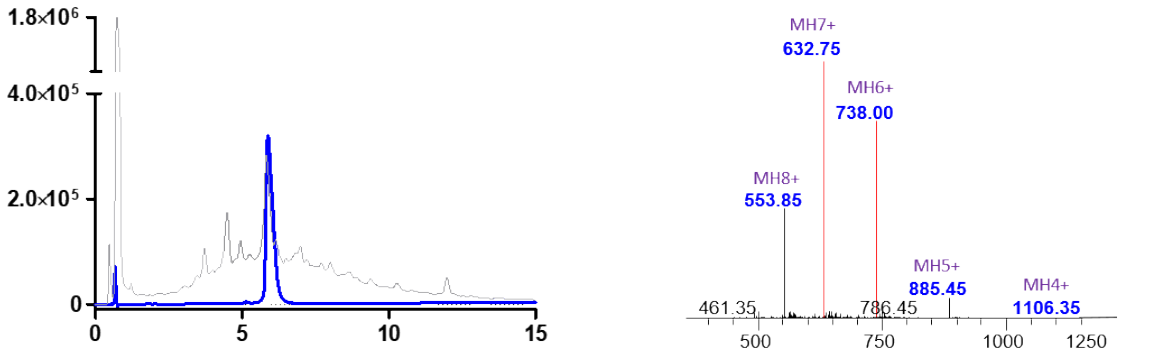
TM5-Tat: ETYLMFWIGVTSVLLLFIVYAYMYILWGRKKRRQRRR



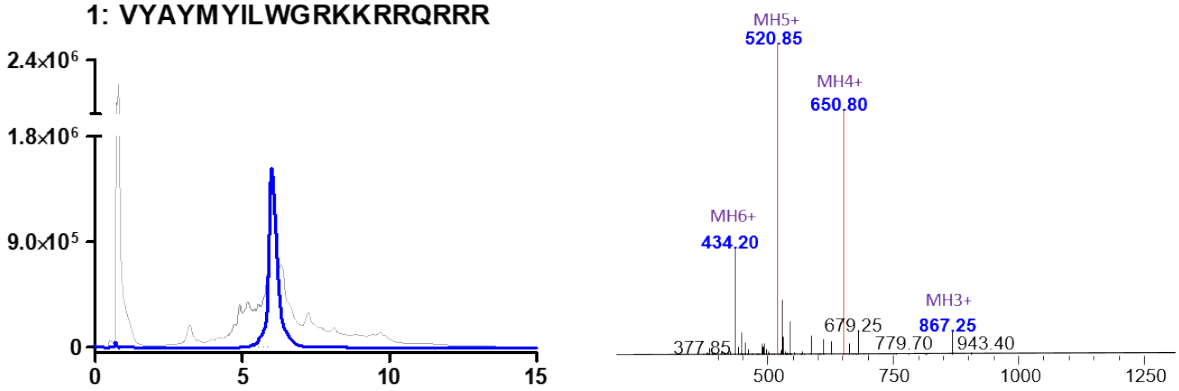
Tat-TM6: GRKKRRQRRRKTLVLILVVLIICWGPLLAIMVYDVF



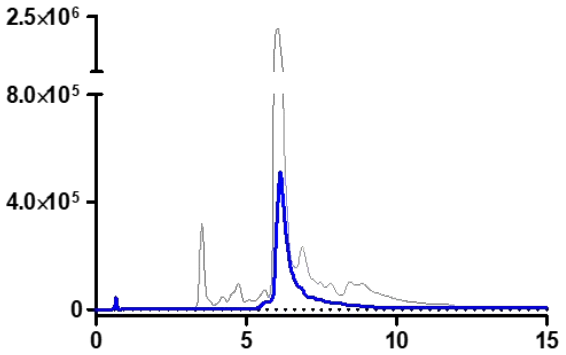
TM7-Tat: LIKTVFAFCSMLCLLNSTVNPIIYALRGRKKRRQRRR

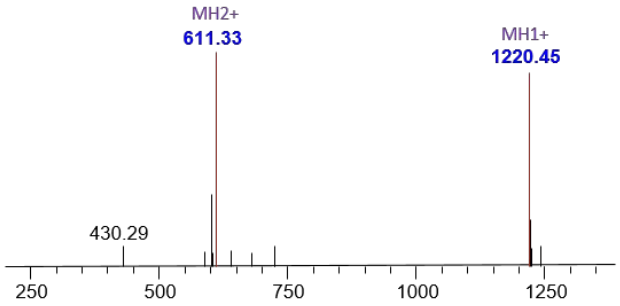


1: VYAYMYILWGRKKRRQRRR

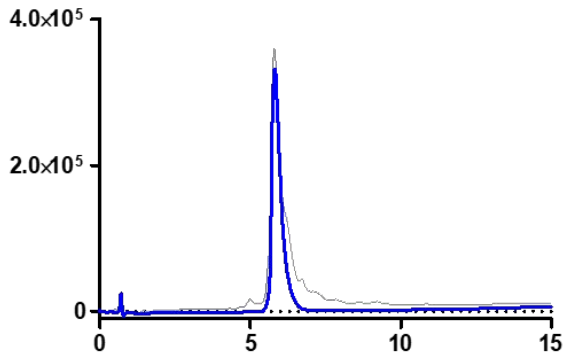


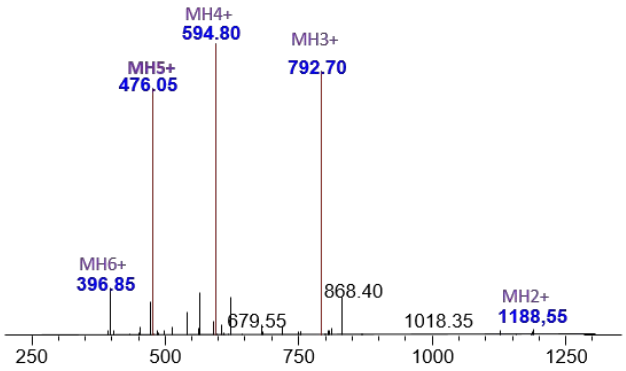
2: VYAYMYILW



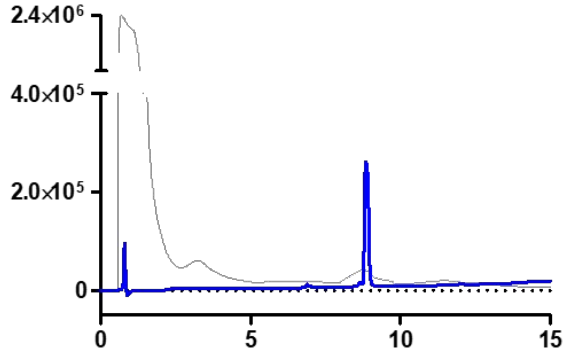


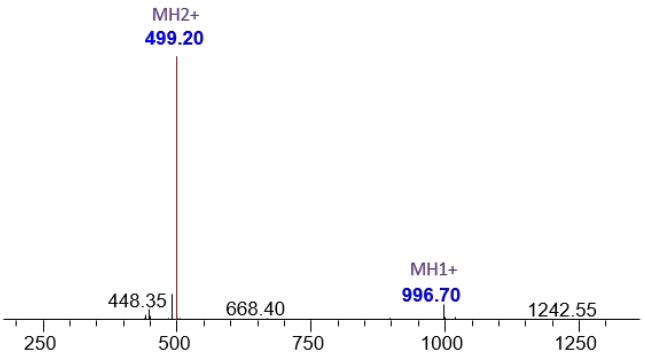
3: GRKKRRQRRRKTLVLILVV



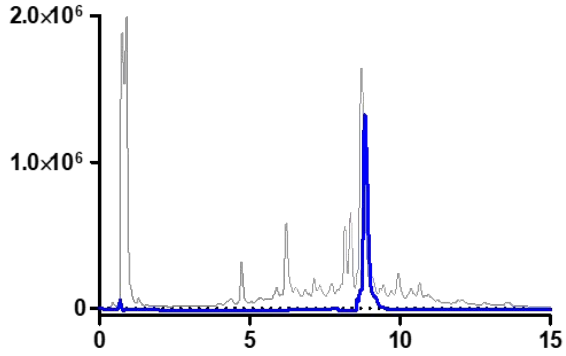


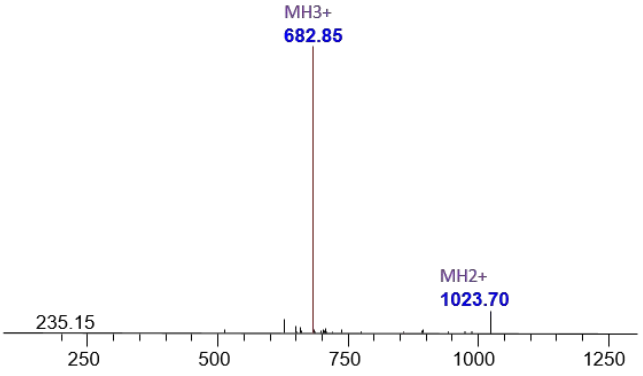
4: KTLVLILVV



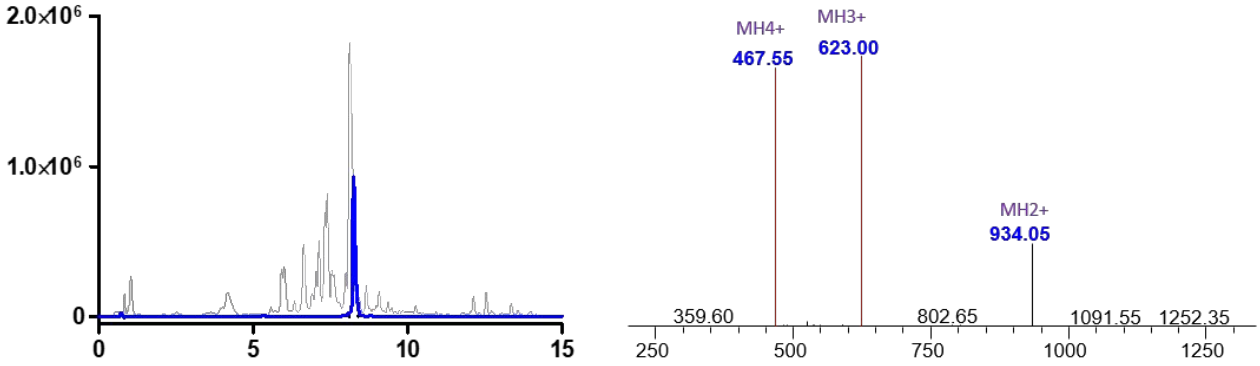


5: VYAYMYILWAGILKRW

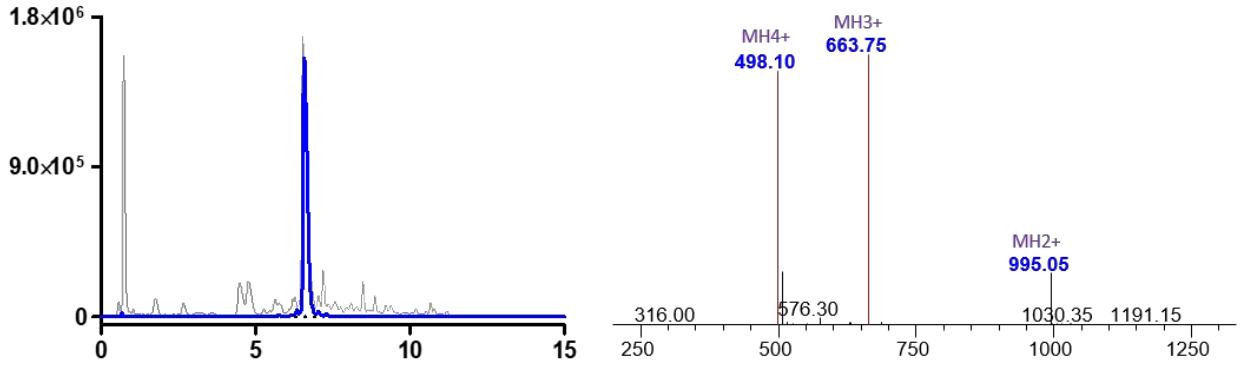




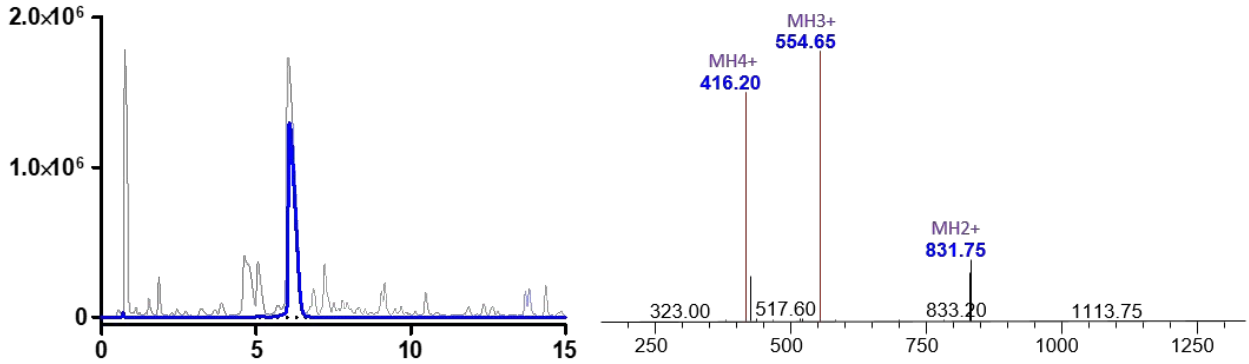
6: VYAYMYILWSKSKSK



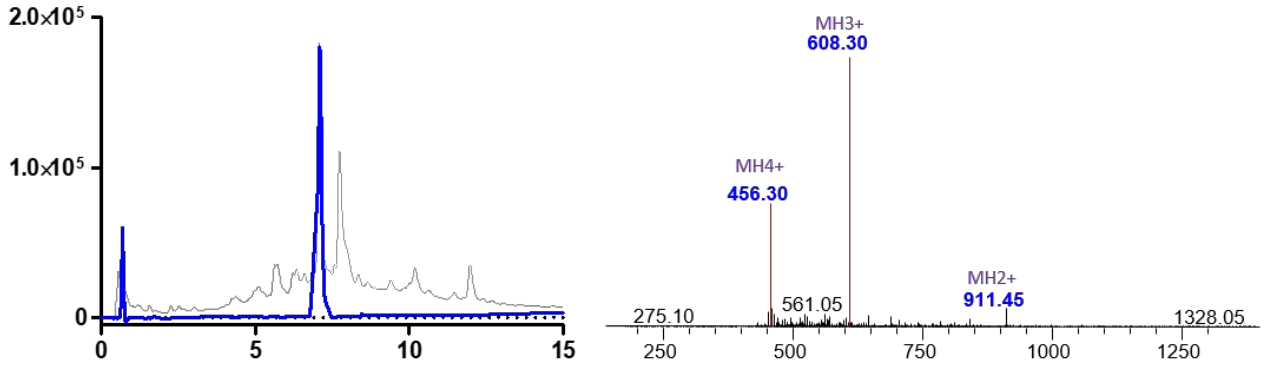
7: VYAYMYILWRLRWR



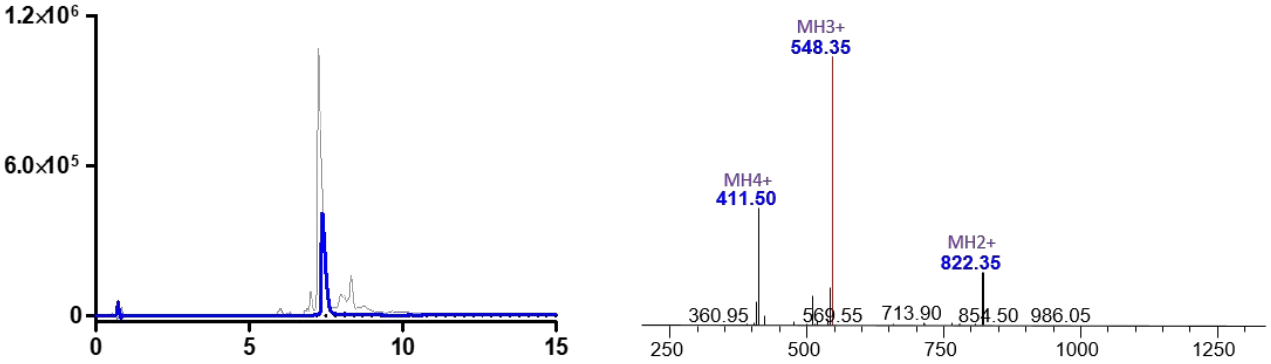
8: VYAYMYILWRKR



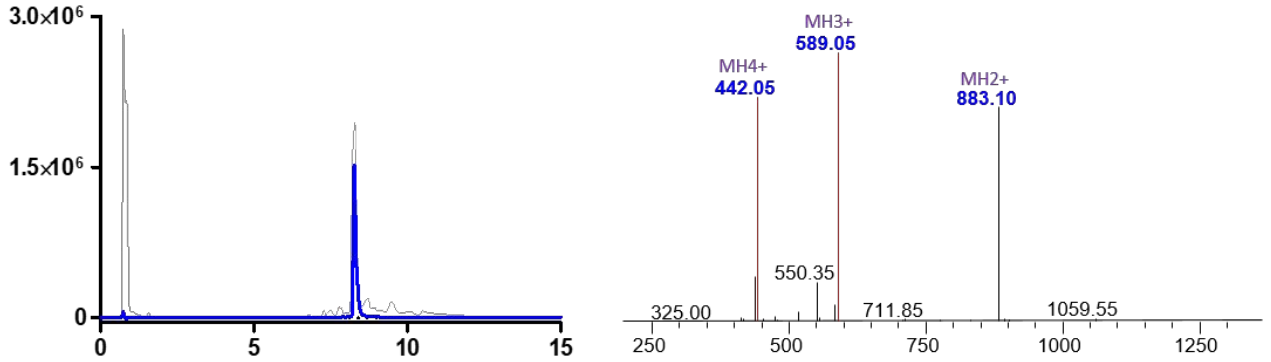
9: AGILKRWKTLVLILVV



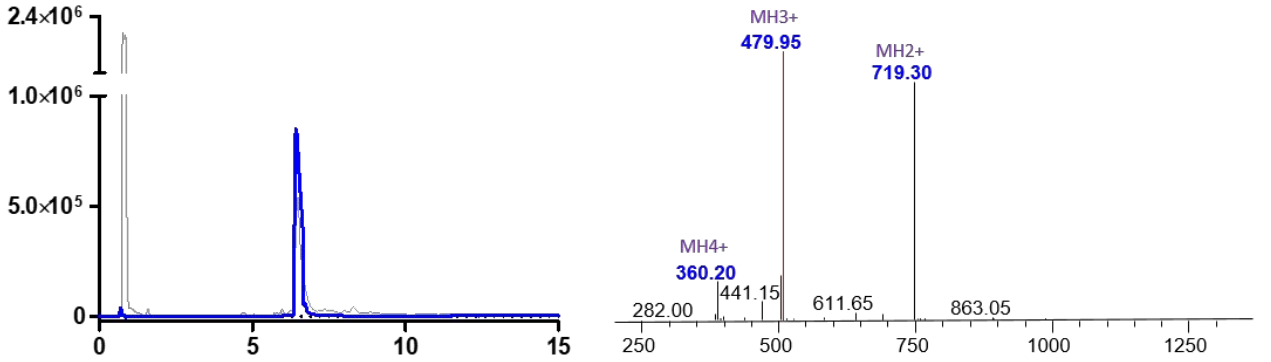
10: SKSKSKKTLVLILVV



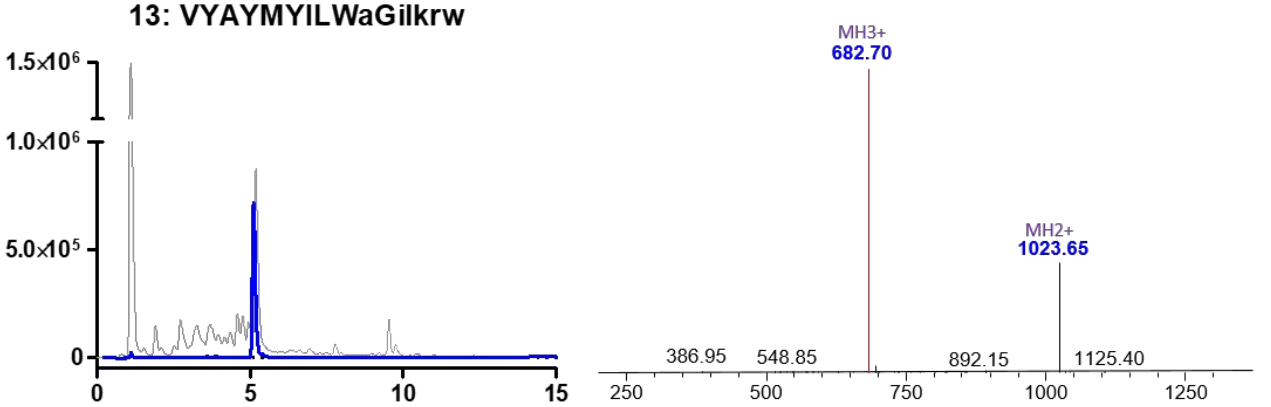
11: RLRWRKTLVLILVV

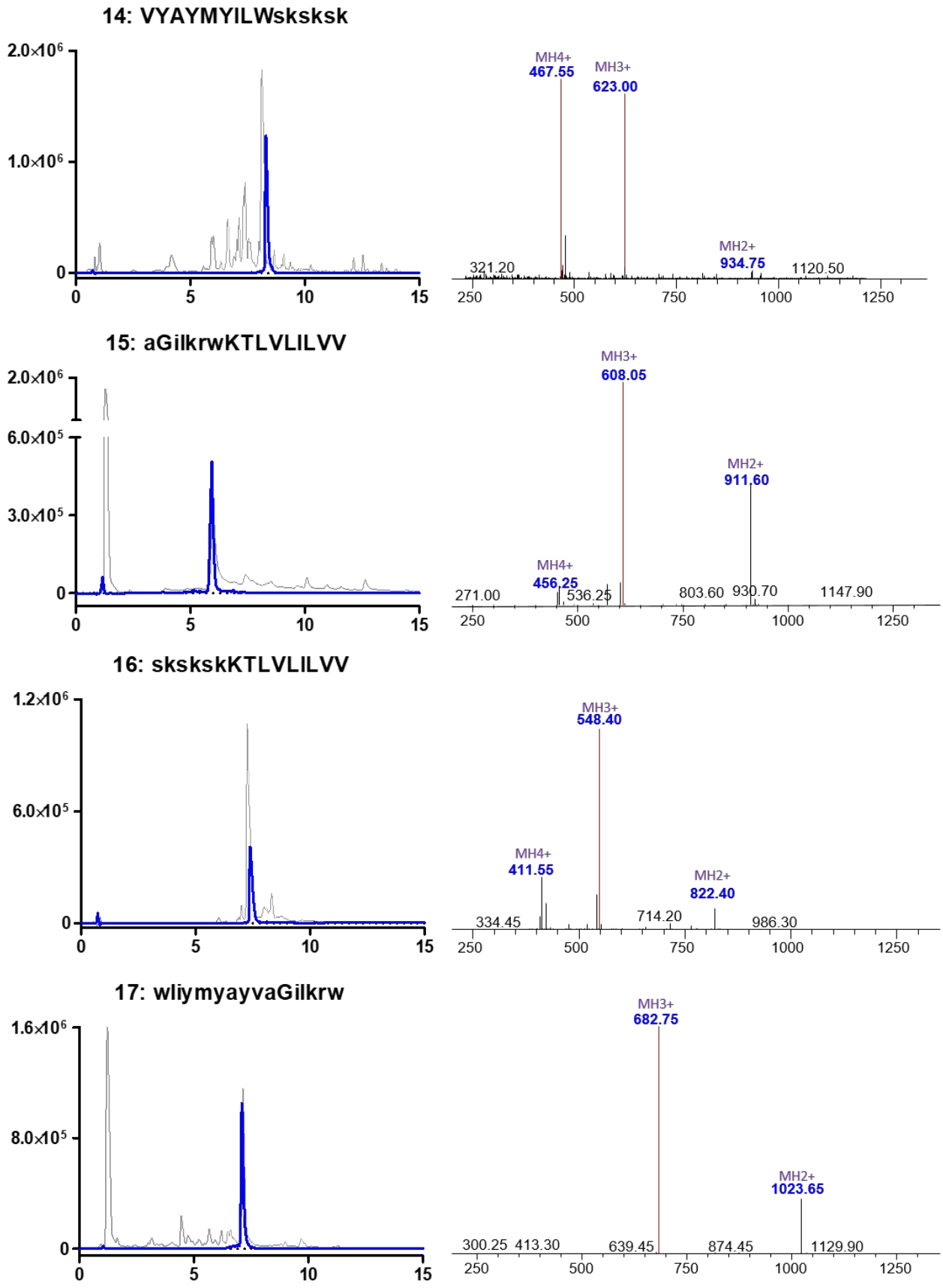


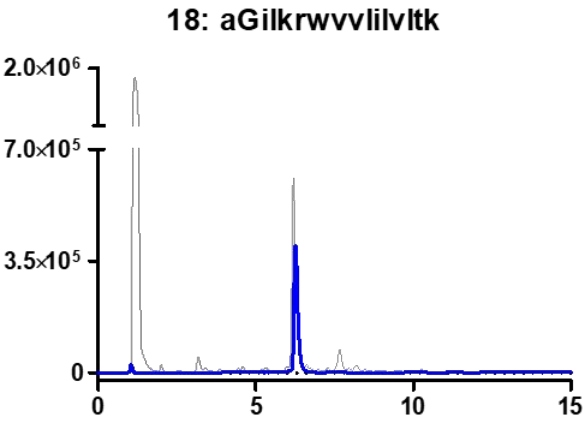
12: RKRKTLVLILVV

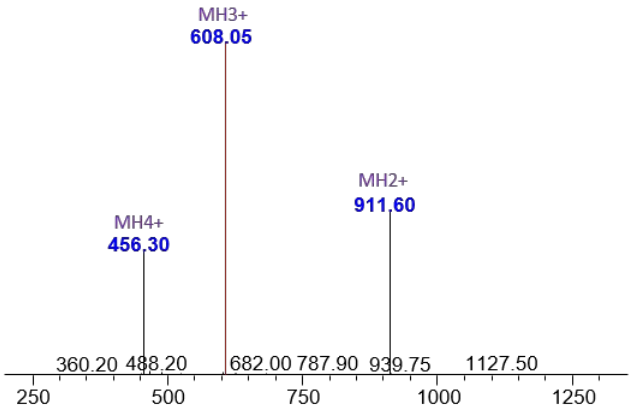


13: VYAYMYILWaGilkrw




14: VYAYMYILWskskskk
2.0×10⁶
1.0×10⁶
0
0
5
10
15
MH4+
467.55
MH3+
623.00
MH2+
934.75
321.20
1120.50
250
500
750
1000
1250
15: aGilkrwKTLVLILVV
2.0×10⁶
6.0×10⁵
3.0×10⁵
0
MH3+
608.05
MH2+
911.60
MH4+
456.25
271.00
536.25
803.60
930.70
1147.90
16: skskskKTLVLILVV
1.2×10⁶
6.0×10⁵
0
MH3+
548.40
MH4+
411.55
MH2+
822.40
334.45
714.20
986.30
17: wliymyayvaGilkrw
1.6×10⁶
8.0×10⁵
0
MH3+
682.75
MH2+
1023.65
300.25
413.30
639.45
874.45
1129.90


18: aGilkrwvvlilvltk
2.0×10⁶
7.0×10⁵
3.5×10⁵
0
0
5
10
15


MH3+
608.05
MH2+
911.60
MH4+
456.30
360.20
488.20
682.00
787.90
939.75
1127.50
250
500
750
1000
1250

4. Molecular Formula Strings

SMILES notations. Molecular formula strings of Tables 1-4 compounds.

COMPOUND	SMILES NOTATIONS	MOLECULAR FORMULA
TM5-Tat	N[C@@H](CCC(O)=O)C(N[C@@H](C(C)O)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](CC(C)C)C(N[C@@H](CCSC)C(N[C@@H](CC2=CC=CC=C2)C(N[C@@H](CC3=CNC4=C3C=CC=C4)C(N[C@@H](C(CC)C)C(NC([H])C(N[C@@H](C(C)C)C(N[C@@H](C(C)O)C(N[C@@H](CO)C(N[C@@H]([C@H](C)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC5=CC=CC=C5)C(N[C@@H](C(CC)C)C(N[C@@H](C(C)C)C(N[C@@H](CC6=CC=C(O)C=C6)C(N[C@@H](C)C(N[C@@H](CC7=CC=C(O)C=C7)C(N[C@@H](CCSC)C(N[C@@H](CC8=CC=C(O)C=C8)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC9=CNC%10=C9C=CC=C%10)C(NC([H])C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCC(N)=O)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{225}H_{351}N_{61}O_{47}S_2$
Tat-TM6	NC([H])C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCC(N)=O)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@H](C)C)C(N[C@@H](C(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](C(CC)C)C(N[C@H](CS)C(N[C@@H](CC1=CNC2=C1C=CC=C2)C(NC([H])C(N3[C@H](C(N[C@@H](CC(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C)C(N[C@@H](C(CC)C)C(N[C@@H](CCSC)C(N[C@@H](C(C)C)C(N[C@@H](CC4=CC=C(O)C=C4)C(N[C@@H](CC(O)=O)C(N[C@@H](C(C)C)C(N[C@@H](CC5=CC=CC=C5)C(O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)CCC3)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{201}H_{345}N_{59}O_{42}S_2$

TM7-Tat	N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H]([C@H](C)C)C(N[C@H](CC1=CC=CC=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=CC=C2)C(N[C@@H](CS)C(N[C@@H](CO)C(N[C@@H](CCSC)C(N[C@@H](CC(C)C)C(N[C@H](CS)C(N[C@H](CC(C)C)C(N[C@H](CC(C)C)C(N[C@H](CC(N)=O)C(N[C@H](CO)C(N[C@@H](C(C)O)C(N[C@H](C(C)C)C(N[C@H](CC(N)=O)C(N3[C@H]([C@@](N[C@@H](C(CC)C)C(N[C@@H](C(CC)C)C(N[C@H](CC4=CC=C(O)C=C4)C(N[C@H](C)C(N[C@H](CC(C)C)C(N[C@H](CCCNC(N)=N)C(NC([H])C(N[C@H](CCCNC(N)=N)C(N[C@H](CCCCN)C(N[C@H](CCCCN)C(N[C@H](CCCNC(N)=N)C(N[C@H](CCCNC(N)=N)C(N[C@H](CCC(N)=O)C(N[C@H](CCCNC(N)=N)C(N[C@H](CCCNC(N)=N)C(N[C@H](CCCNC(N)=N)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)CCC3)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{196}H_{339}N_{65}O_{45}S_3$
1	N[C@@H](C(C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(NC([H])C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCC(N)=O)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{118}H_{192}N_{42}O_{23}S$
2	N[C@@H]([C@@H](C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{63}H_{85}N_{11}O_{12}S$
3	NC([H])C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCC(N)=O)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](C(C)C)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{104}H_{200}N_{42}O_{21}$
4	O=C(N[C@@H](CC(C)C)C(N[C@@H](C(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](C(C)C)C(N)=O)=O)=O)=O)=O)=O)=O)[C@@H](NC([C@H](CCCCN)N)=O)C(C)O	$C_{49}H_{93}N_{11}O_{10}$

5	N[C@@H](C(C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(N[C@@H](C)C(NC([H])C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CC6=CNC7=C6C=CC=C7)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{103}H_{149}N_{23}O_{19}S$
6	N[C@@H](C(C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(N[C@@H](CO)C(N[C@@H](CCCCN)C(N[C@@H](CO)C(N[C@@H](CCCCN)C(N[C@@H](CO)C(N[C@@H](CCCCN)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{90}H_{136}N_{20}O_{21}S$
7	N[C@@H]([C@@H](C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CC(C)C)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CC6=CNC7=C6C=CC=C7)C(N[C@@H](CCCNC(N)=N)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{98}H_{142}N_{26}O_{17}S$
8	N[C@@H](C(C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{81}H_{121}N_{21}O_{15}S$
9	N[C@@H](C)C(NC([H])C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CC1=CNC2=C1C=CC=C2)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H](C(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H]([C@@H](C)C)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{89}H_{157}N_{23}O_{17}$

10	N[C@@H](CO)C(N[C@@H](CCCCN)C(N[C@@H](CO)C(N[C@@H](CCCCN)C(N[C@@H](CO)C(N[C@@H](CCCCN)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](C(C)C)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{76}H_{144}N_{20}O_{19}$
11	N[C@@H](CCCNC(N)=N)C(N[C@@H](CC(C)C)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CC1=CNC2=C1C=CC=C2)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H](C(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(C)C)C(N[C@@H]([C@H](C)C)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{84}H_{150}N_{26}O_{15}$
12	N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](CCCNC(N)=N)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](C(C)C)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{67}H_{129}N_{21}O_{13}$
13	N[C@@H](C(C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(N[C@H](C)C(NC([H])C(N[C@H](C(CC)C)C(N[C@H](CC(C)C)C(N[C@H](CCCCN)C(N[C@H](CCCNC(N)=N)C(N[C@H](CC6=CNC7=C6C=CC=C7)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{103}H_{149}N_{23}O_{19}S$
14	N[C@@H](C(C)C)C(N[C@@H](CC1=CC=C(O)C=C1)C(N[C@@H](C)C(N[C@@H](CC2=CC=C(O)C=C2)C(N[C@@H](CCSC)C(N[C@@H](CC3=CC=C(O)C=C3)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H](CC4=CNC5=C4C=CC=C5)C(N[C@H](CO)C(N[C@H](CCCCN)C(N[C@H](CO)C(N[C@H](CCCCN)C(N[C@H](CO)C(N[C@H](CCCCN)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{90}H_{136}N_{20}O_{21}S$

15	N[C@H](C)C(NC([H])C(N[C@H](C(CC)C)C(N[C@H](CC(C)C)C(N[C@H](CCCCN)C(N[C@H](CCCNC(N)=N)C(N[C@H](CC1=CNC2=C1C=CC=C2)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H](C(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H]([C@@H](C)C)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{89}H_{157}N_{23}O_{17}$
16	N[C@H](CO)C(N[C@H](CCCCN)C(N[C@H](CO)C(N[C@H](CCCCN)C(N[C@H](CO)C(N[C@H](CCCCN)C(N[C@@H](CCCCN)C(N[C@@H](C(C)O)C(N[C@@H](CC(C)C)C(N[C@@H](C(C)C)C(N[C@@H](CC(C)C)C(N[C@@H](C(CC)C)C(N[C@@H](CC(C)C)C(N[C@@H]([C@@H](C)C)C(N[C@@H](C(C)C)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{76}H_{144}N_{20}O_{19}$
17	N[C@H](CC1=CNC2=C1C=CC=C2)C(N[C@H](CC(C)C)C(N[C@H](C(CC)C)C(N[C@H](CC3=CC=C(O)C=C3)C(N[C@H](CCSC)C(N[C@H](CC4=CC=C(O)C=C4)C(N[C@H](C)C(N[C@H](CC5=CC=C(O)C=C5)C(N[C@H]([C@@H](C)C)C(N[C@H](C)C(NC([H])C(N[C@H](C(CC)C)C(N[C@H](CC(C)C)C(N[C@H](CCCCN)C(N[C@H](CCCNC(N)=N)C(N[C@H](CC6=CNC7=C6C=CC=C7)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{103}H_{149}N_{23}O_{19}S$
18	N[C@H](C)C(NC([H])C(N[C@H](C(CC)C)C(N[C@H](CC(C)C)C(N[C@H](CCCCN)C(N[C@H](CCCNC(N)=N)C(N[C@H](CC1=CNC2=C1C=CC=C2)C(N[C@H](C(C)C)C(N[C@H](C(CC)C)C(N[C@H](CC(C)C)C(N[C@H](C(C)C)C(N[C@H](CC(C)C)C(N[C@H](C(C)O)C(N[C@H](CCCCN)C(N)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O)=O	$C_{89}H_{157}N_{23}O_{17}$