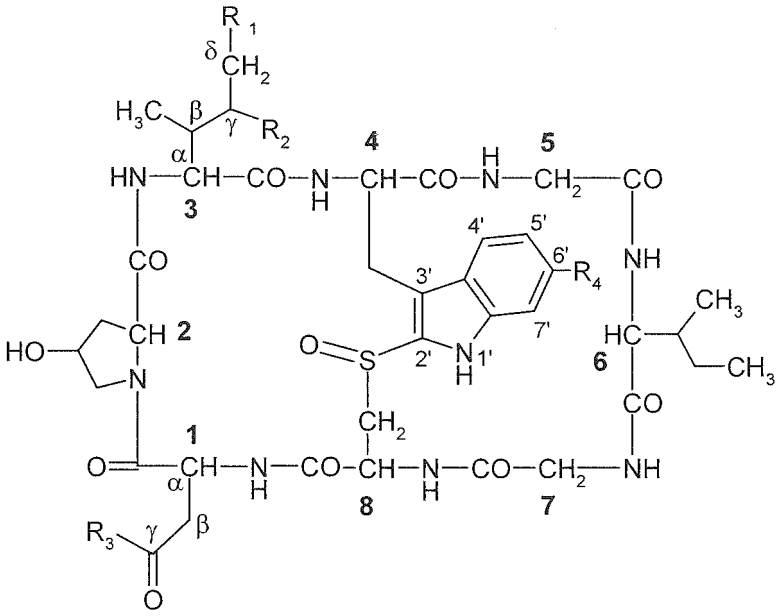
FIGURE 1



	R_1	R_2	R_3	R_4
α-amanitin	OH	OH	NH_2	OH
β-amanitin	OH	OH	OH	OH
γ-amanitin	H	OH	NH_2	OH
ε-amanitin	H	OH	OH	OH
amanin	OH	OH	OH	H
amaninamide	OH	OH	NH_2	H
amanullin	H	H	NH_2	OH
amanullinic acid	H	H	OH	OH
γ-amanin	H	OH	OH	H
γ-amaninamide	H	OH	NH2	H

FIGURE 2

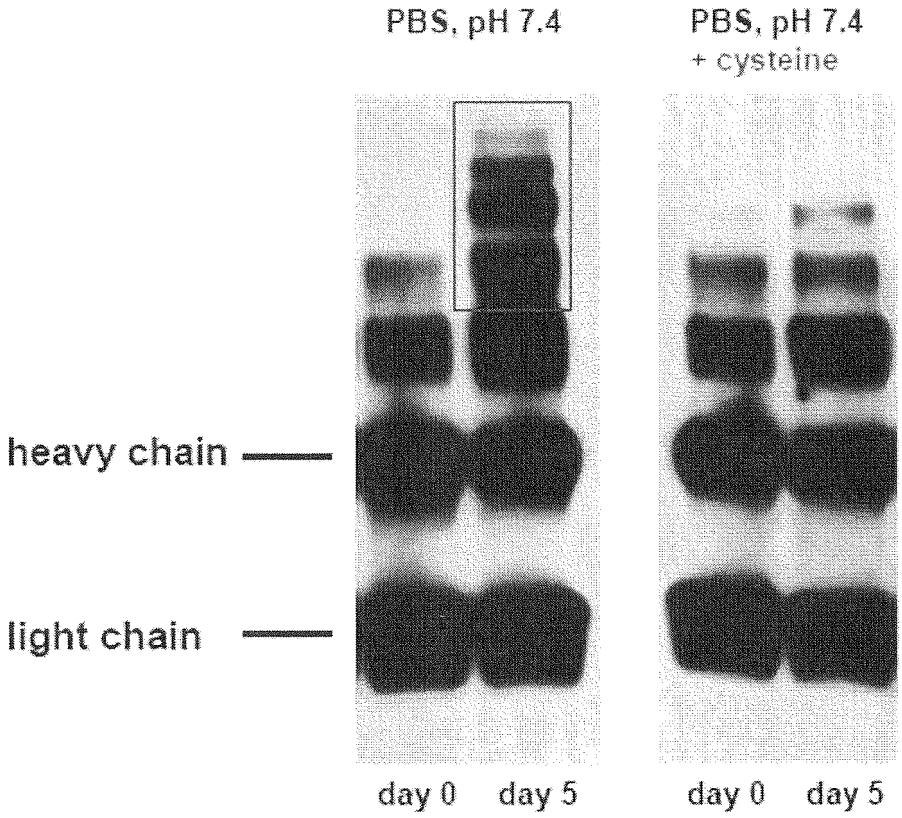

PBS, pH 7.4
PBS, pH 7.4
+ cysteine
heavy chain
light chain
day 0
day 5
day 0
day 5

FIGURE 3

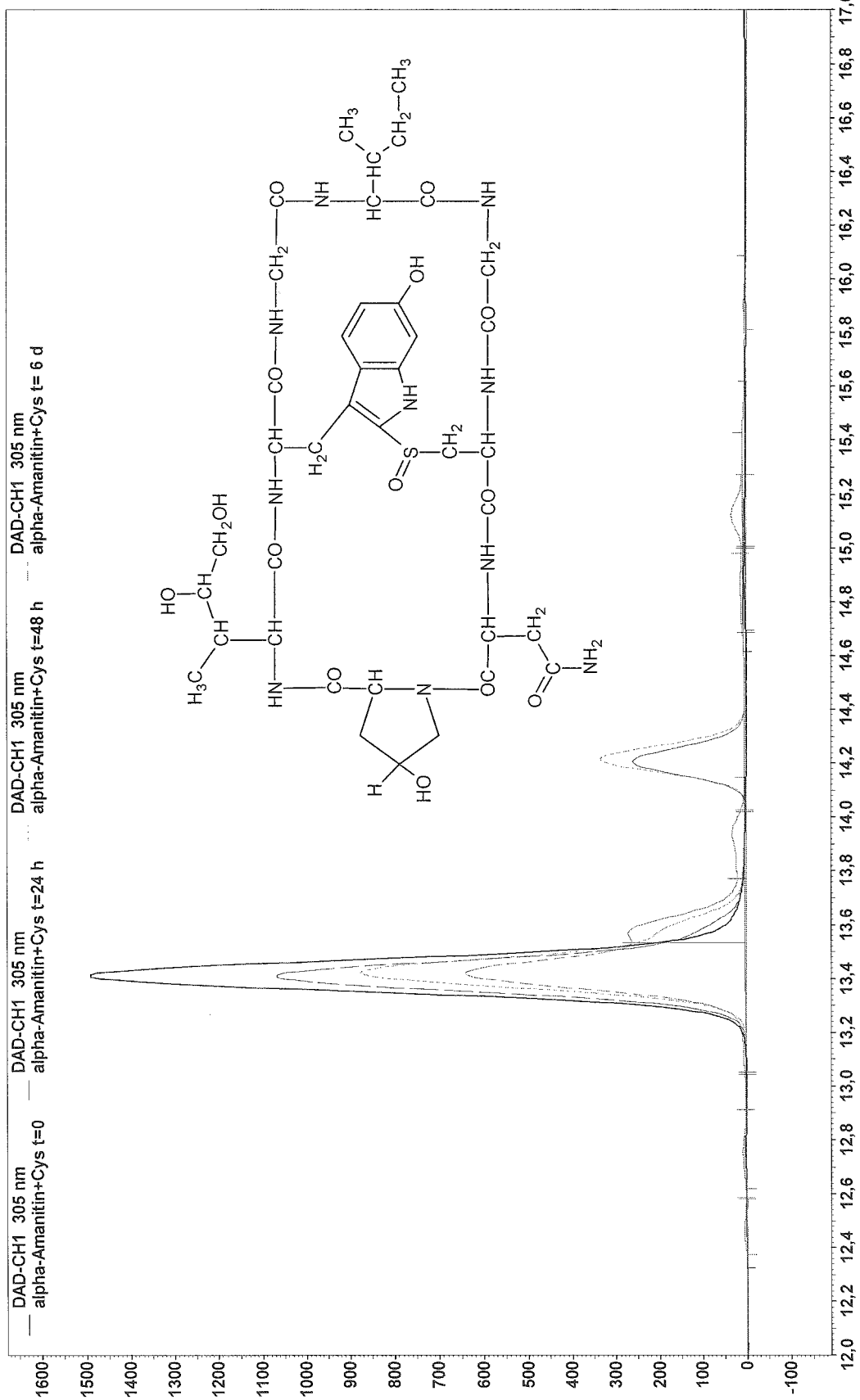

DAD-CH1 305 nm
alpha-Amanitin+Cys t=0
DAD-CH1 305 nm
alpha-Amanitin+Cys t=24 h
DAD-CH1 305 nm
alpha-Amanitin+Cys t=48 h
DAD-CH1 305 nm
alpha-Amanitin+Cys t= 6 d
mAU
Minutes

FIGURE 4

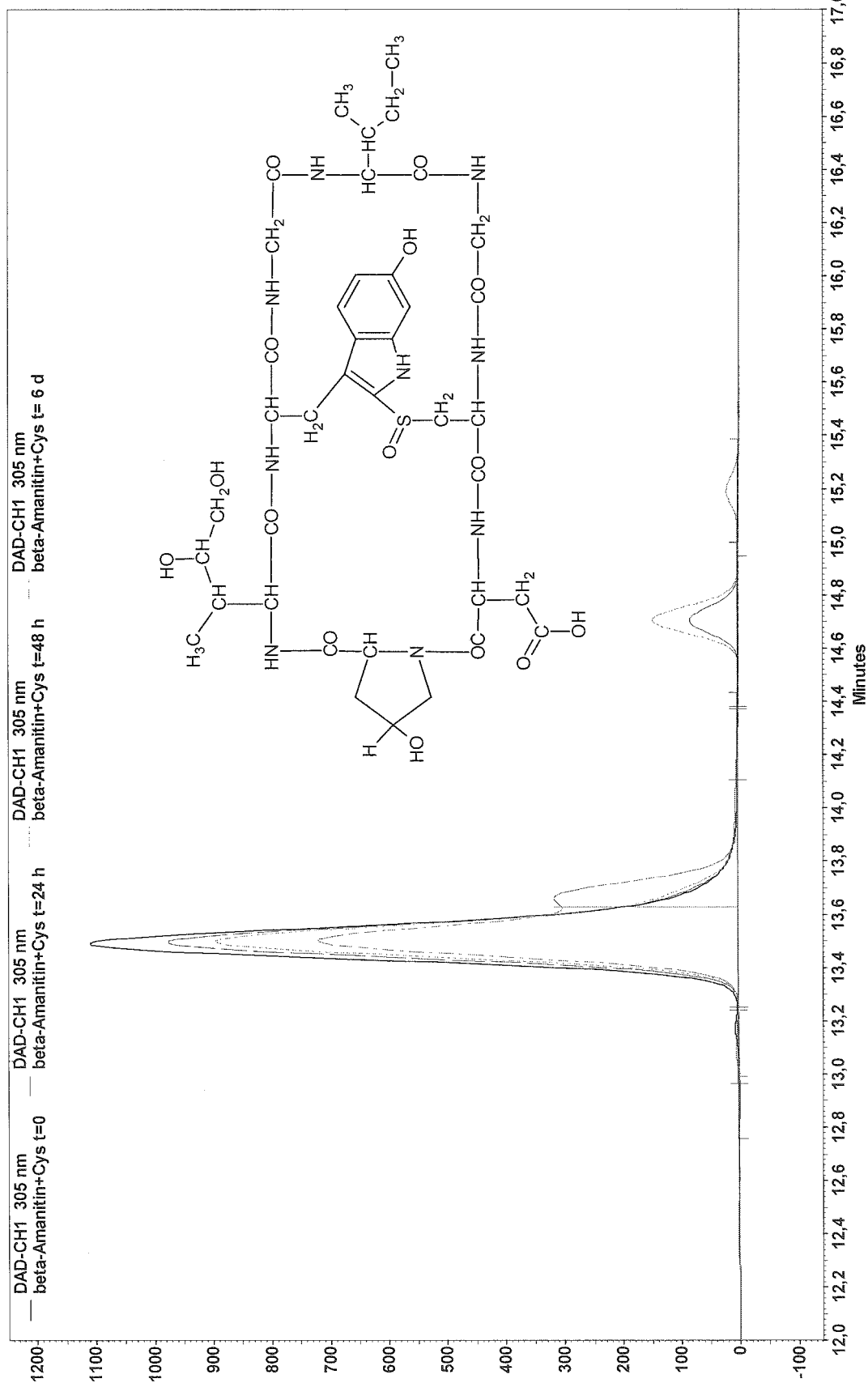

DAD-CH1 305 nm
beta-Amanitin+Cys t=0
DAD-CH1 305 nm
beta-Amanitin+Cys t=24 h
DAD-CH1 305 nm
beta-Amanitin+Cys t=48 h
DAD-CH1 305 nm
beta-Amanitin+Cys t= 6 d
mAU
Minutes

FIGURE 5

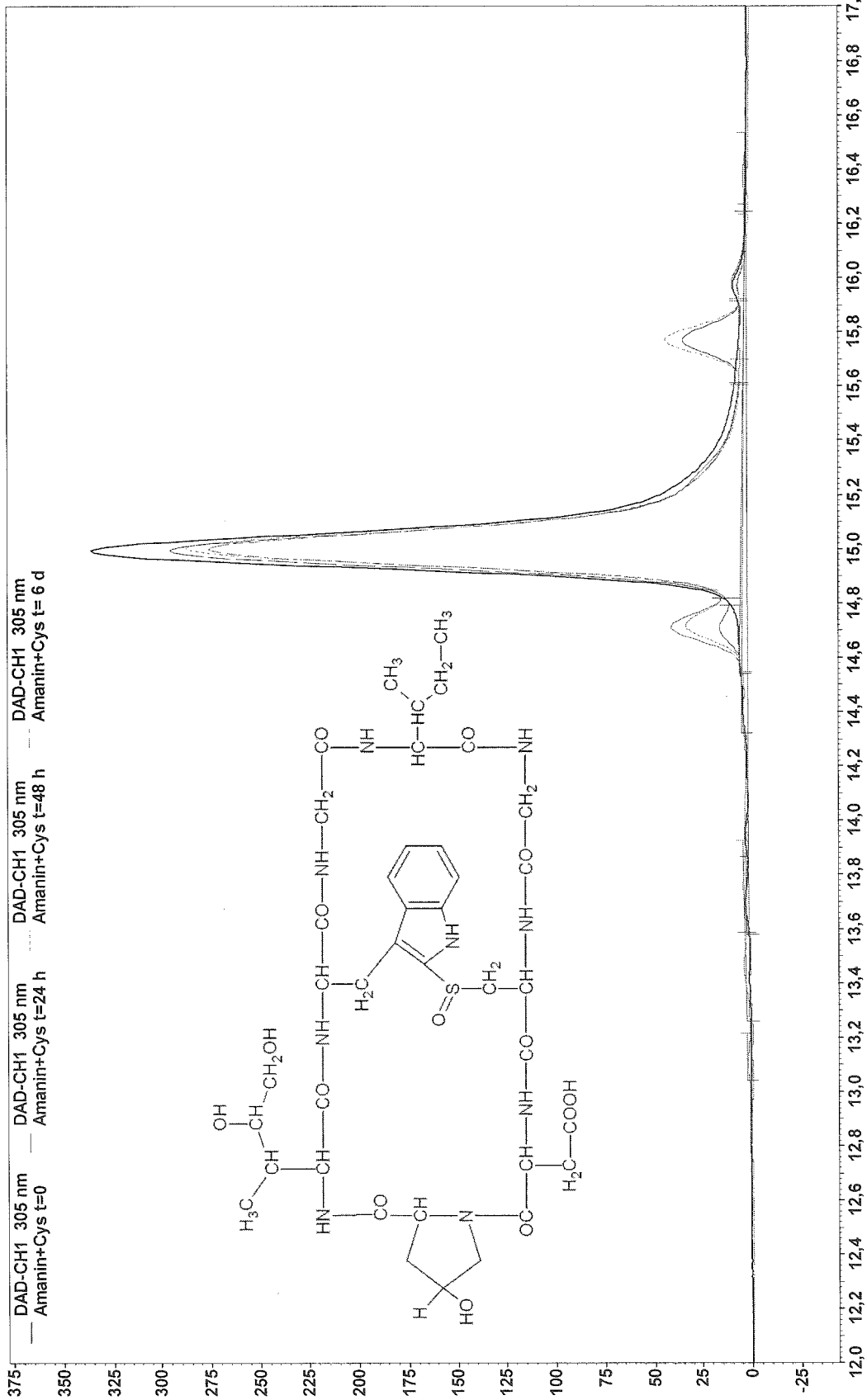

DAD-CH1 305 nm
Amanin+Cys t=0
DAD-CH1 305 nm
Amanin+Cys t=24 h
DAD-CH1 305 nm
Amanin+Cys t=48 h
DAD-CH1 305 nm
Amanin+Cys t= 6 d
mAU
Minutes

FIGURE 6

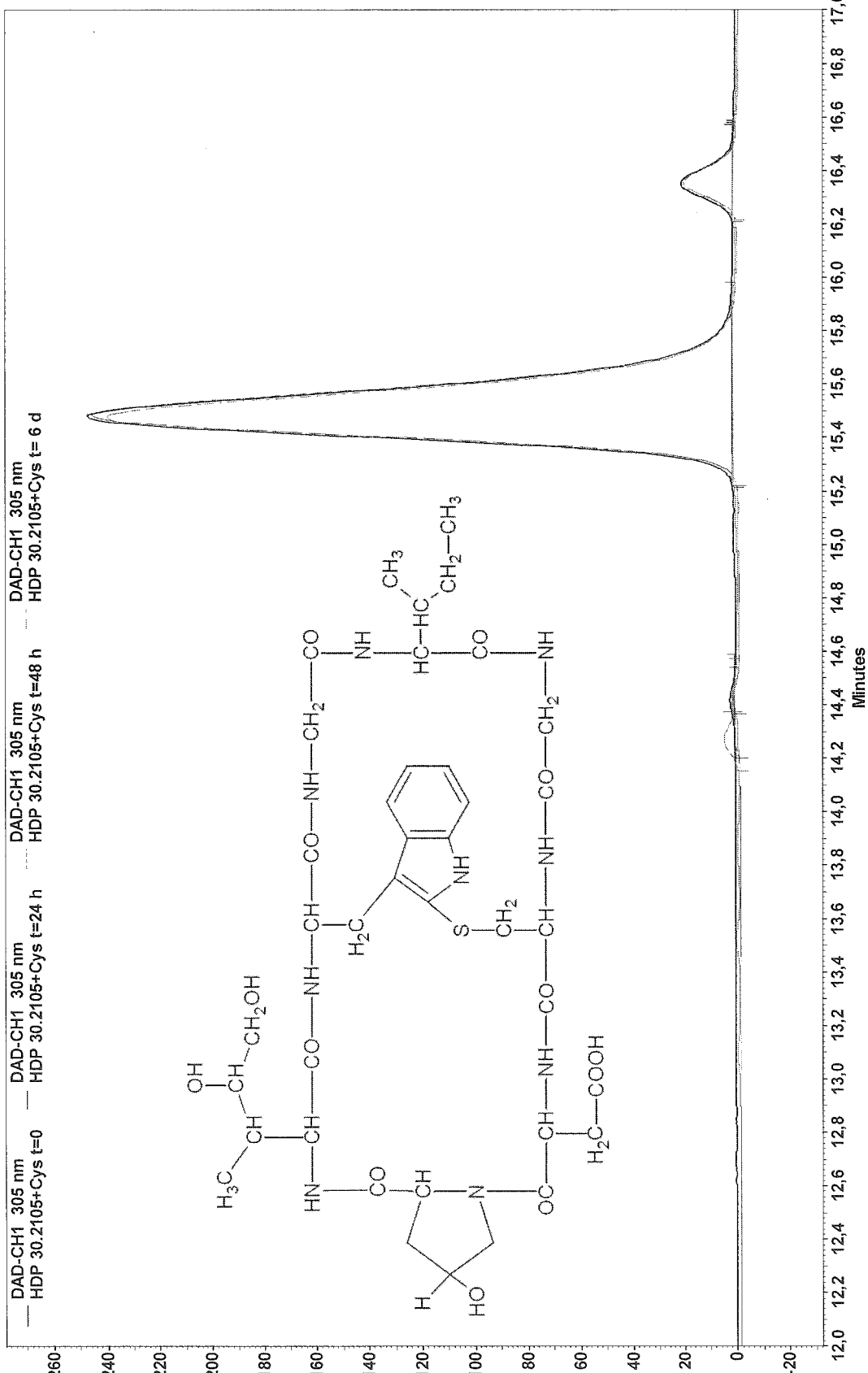

DAD-CH1 305 nm
HDP 30.2105+Cys t=0
DAD-CH1 305 nm
HDP 30.2105+Cys t=24 h
DAD-CH1 305 nm
HDP 30.2105+Cys t=48 h
DAD-CH1 305 nm
HDP 30.2105+Cys t= 6 d
mAU
Minutes

FIGURE 7

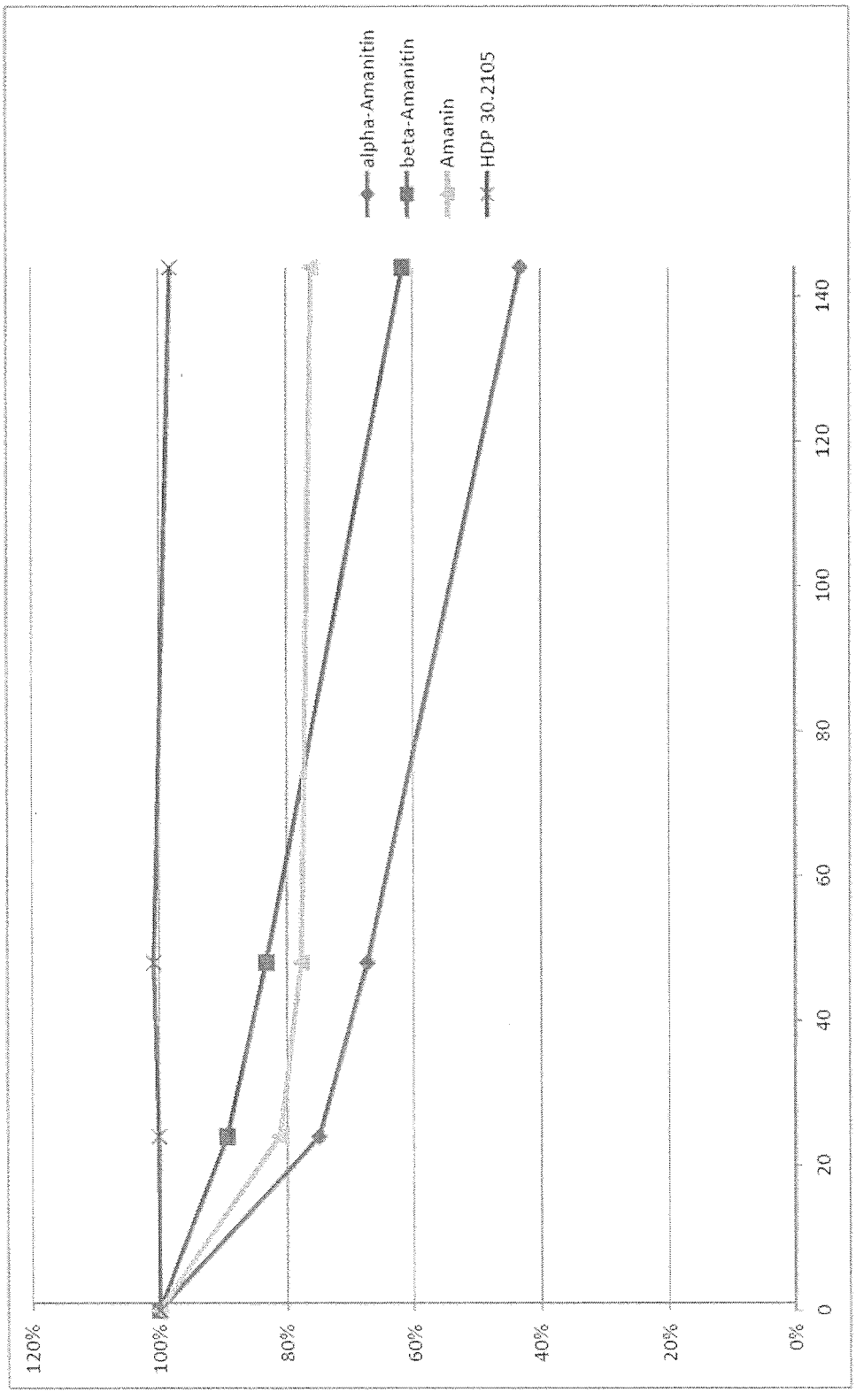

alpha-Amanitin
beta-Amanitin
Amanin
HDP 30.2105
120%
100%
80%
60%
40%
20%
0%
0
20
40
60
80
100
120
140

FIGURE 8

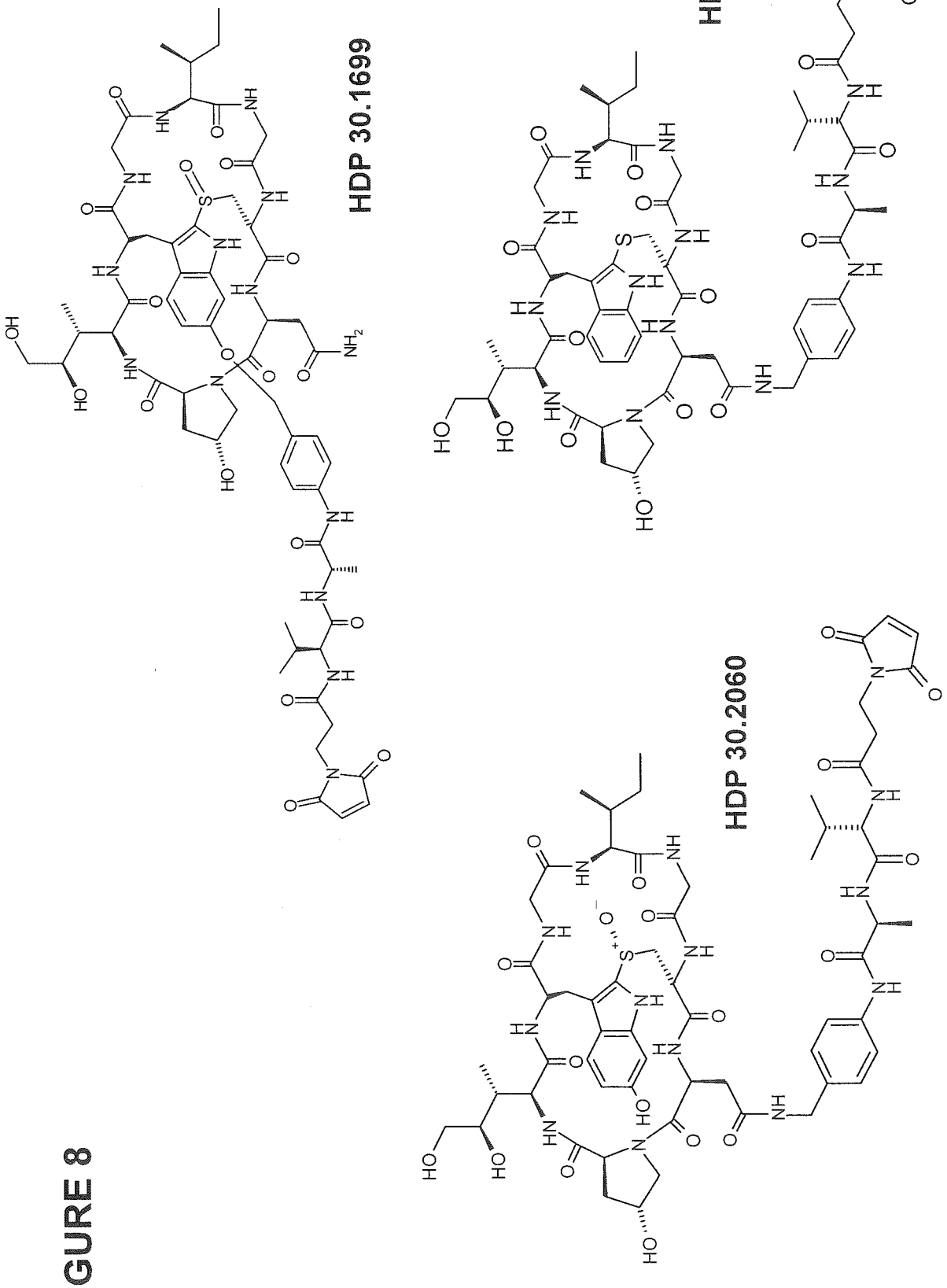
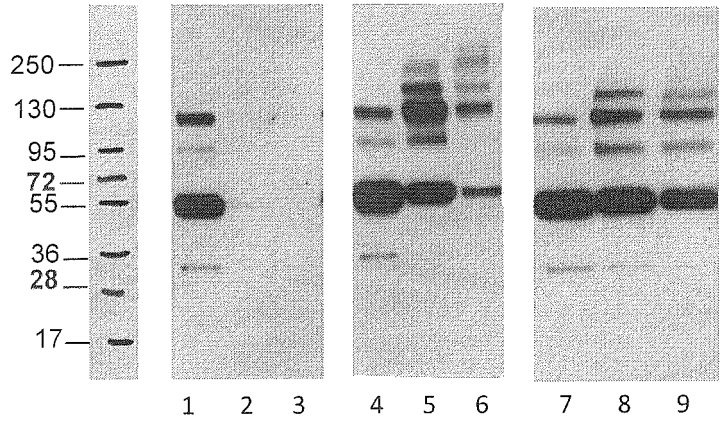
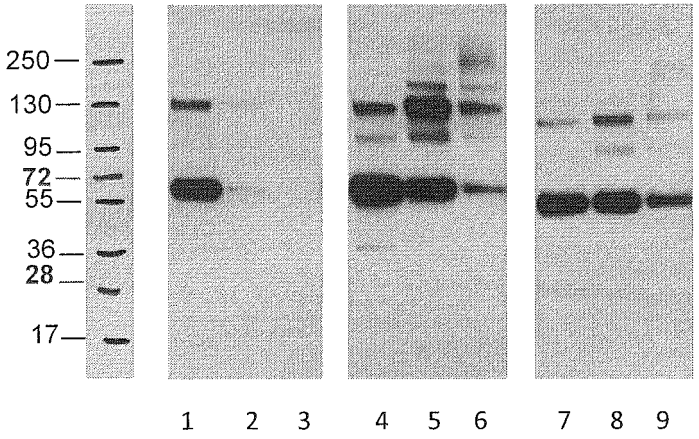


FIGURE 9

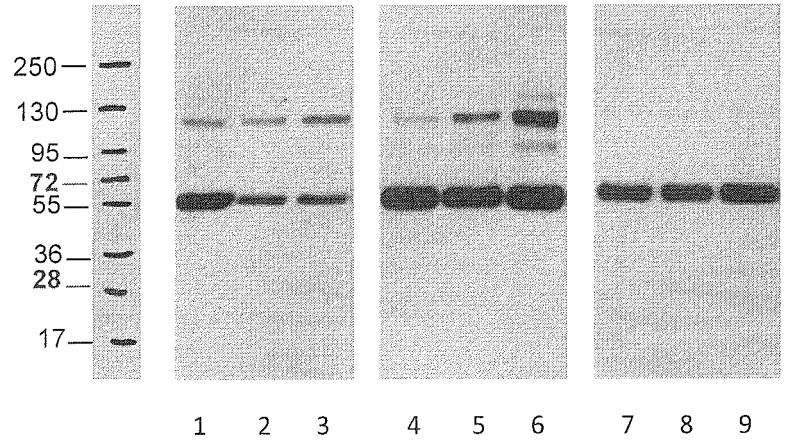
ADCs incubated in Human Plasma



ADCs incubated in Mouse Plasma



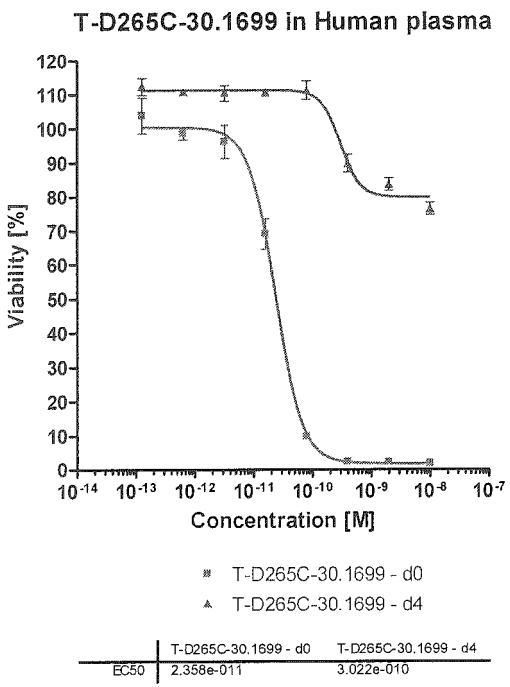
ADCs incubated in PBS

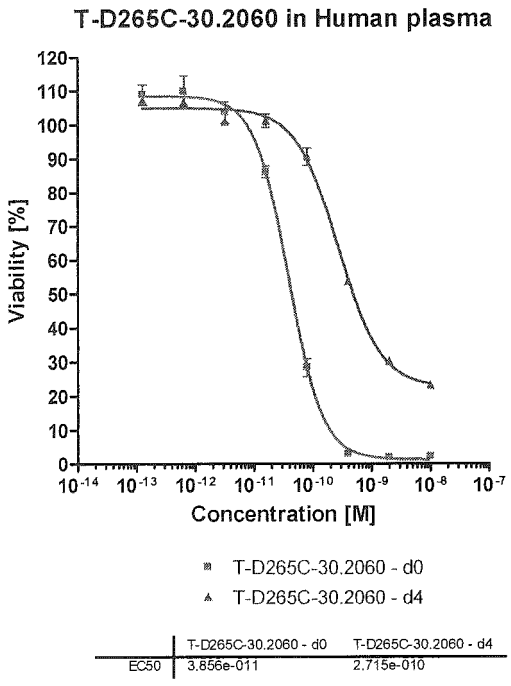


1	T-D265C-30.1699[2.8]-d0
2	T-D265C-30.1699[2.8]-d4
3	T-D265C-30.1699[2.8]–d10
4	T-D265C-30.2060[2.3]-d0
5	T-D265C-30.2060[2.3]-d4
6	T-D265C-30.2060[2.3]-d10
7	T-D265C-30.2115[n.d.]-d0
8	T-D265C-30.2115[n.d.]-d4
9	T-D265C-30.2115[n.d.]-d10

FIGURE 10

Cytotoxicity on SKBR-3 cells after incubation in Human plasma





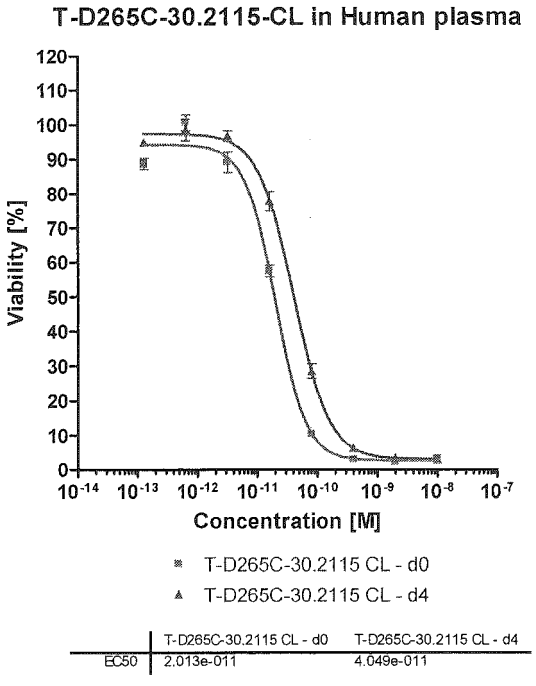
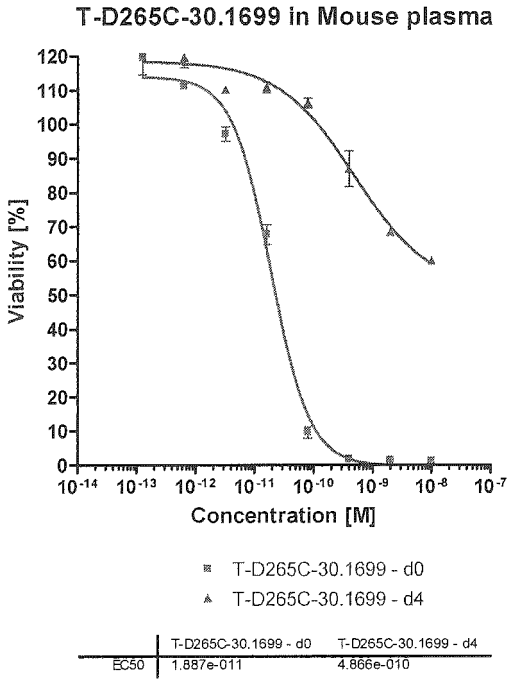
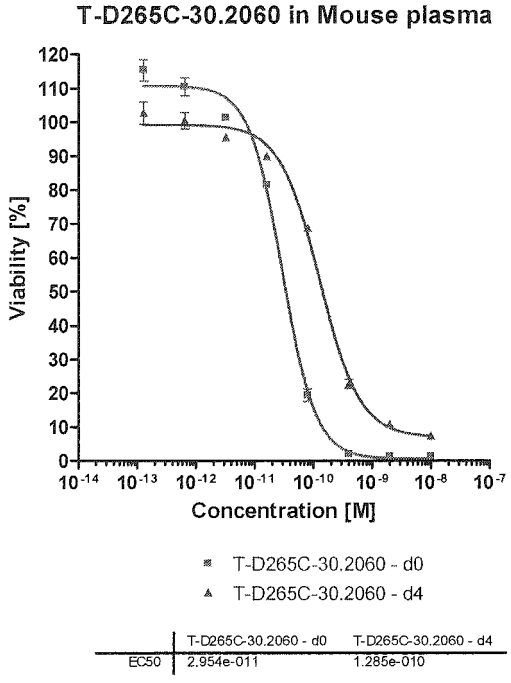


FIGURE 11

Cytotoxicity on SKBR-3 cells after incubation in Mouse plasma





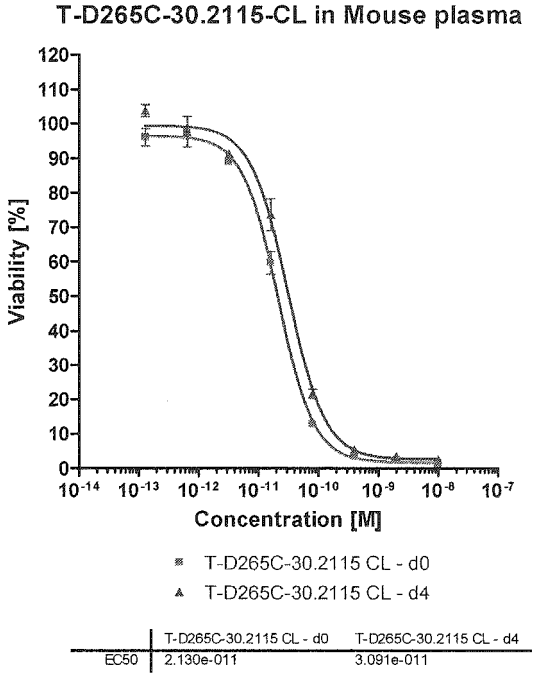
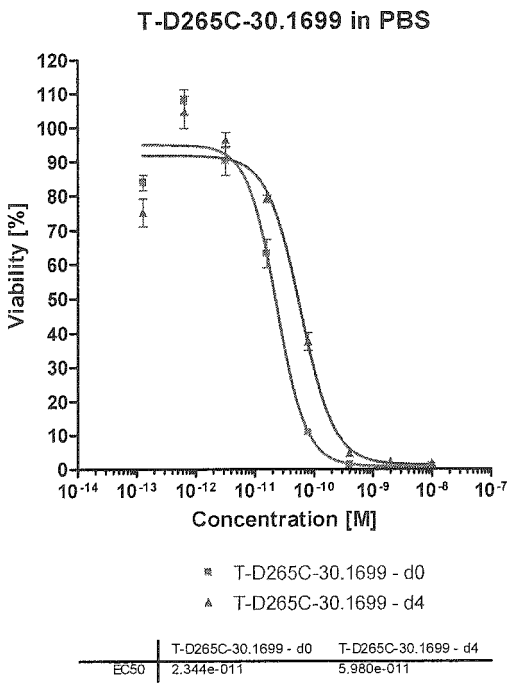
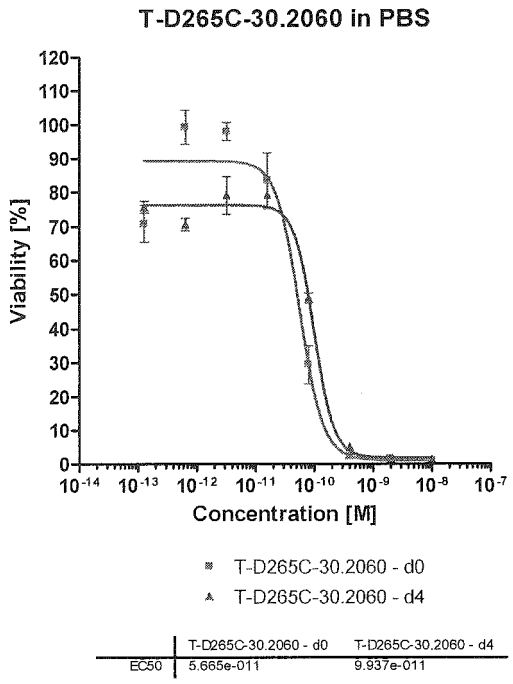


FIGURE 12

Cytotoxicity on SKBR-3 cells after incubation in PBS





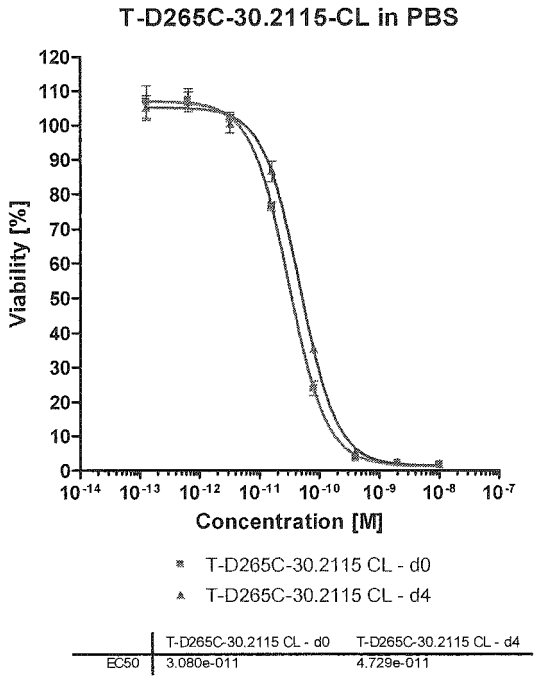


FIGURE 13

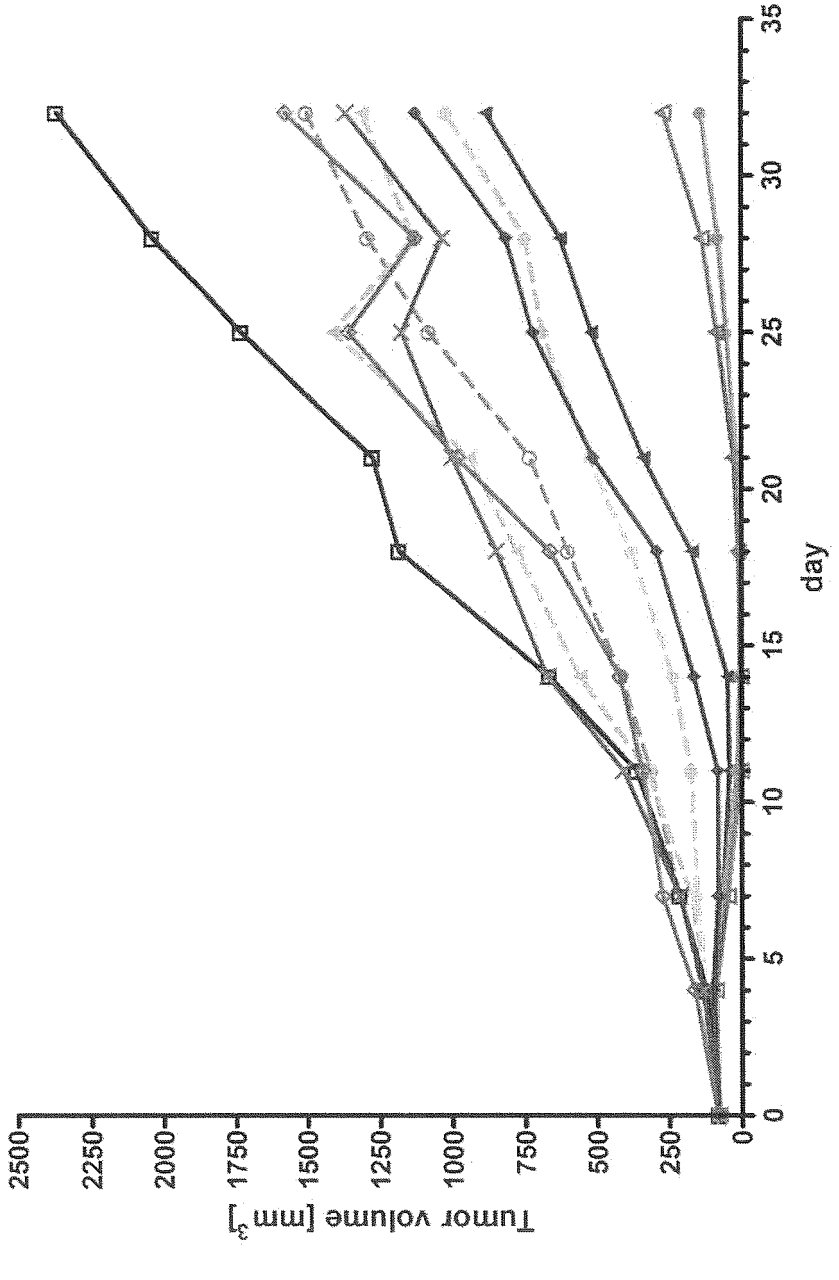
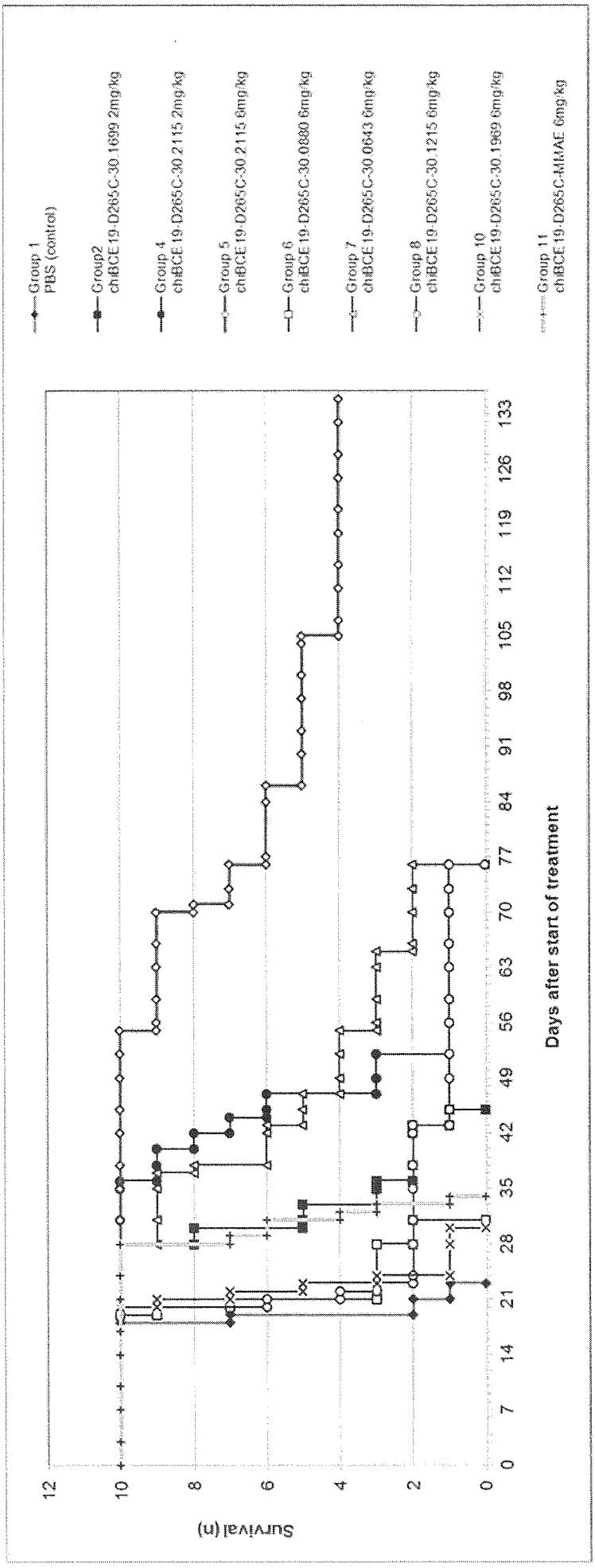

vehicle control (PBS, pH 7.4)
chiBCE19-D265C-30.1699 1mg/kg
chiBCE19-D265C-30.1699 3mg/kg
chiBCE19-D265C-30.2115 2mg/kg
chiBCE19-D265C-30.2115 6mg/kg
chiBCE19-D265C-30.0880 6mg/kg
chiBCE19-D265C-30.0643 6mg/kg
chiBCE19-D265C-30.1215 6mg/kg
chiBCE19-D265C-30.2072 3mg/kg
chiBCE19-D265C-30.1969 6mg/kg
Tumor volume [mm³]
2500
2250
2000
1750
1500
1250
1000
750
500
250
0
0
5
10
15
20
25
30
35
day

FIGURE 14


Survival (n)
Days after start of treatment
Group 1
PBS (control)
Group2
chBCE19-D265C-30.1699.2mg/kg
Group 4
chBCE19-D265C-30.2115.2mg/kg
Group 5
chBCE19-D265C-30.2115.6mg/kg
Group 6
chBCE19-D265C-30.0880.6mg/kg
Group 7
chBCE19-D265C-30.0643.6mg/kg
Group 8
chBCE19-D265C-30.1215.6mg/kg
Group 10
chBCE19-D265C-30.1969.6mg/kg
Group 11
chBCE19-D265C-MMAE.6mg/kg