Fig.1

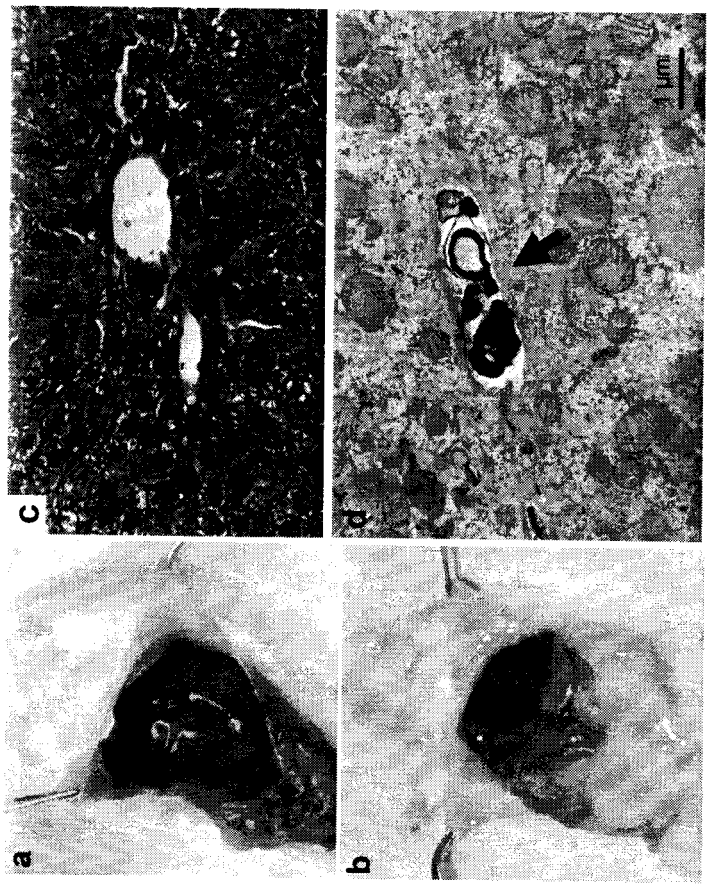


Fig.2

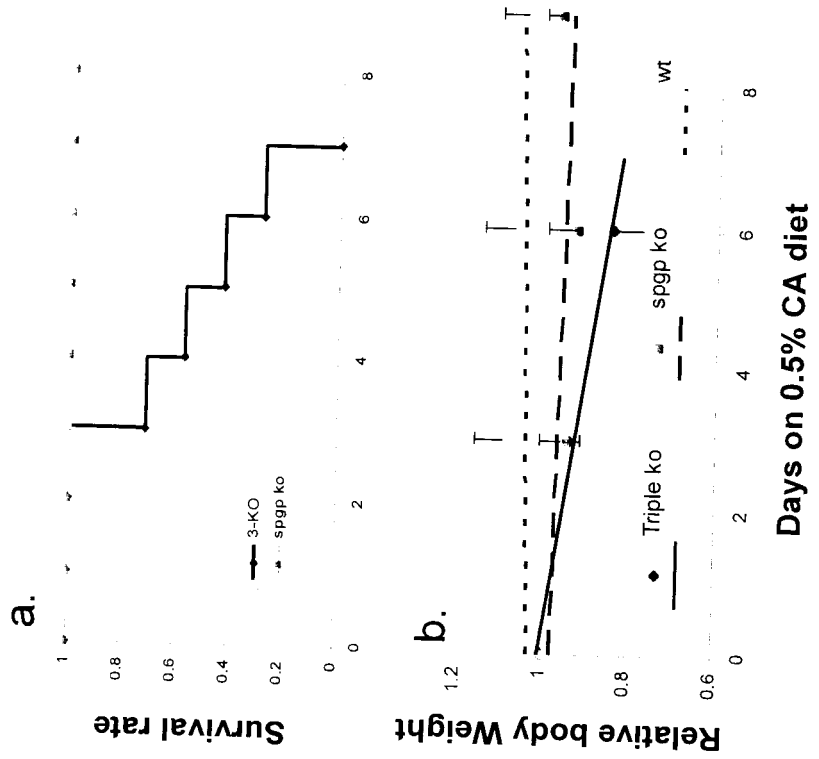

a.
Survival rate
1
0.8
0.6
0.4
0.2
0
0
2
4
6
8
3-KO
spgp ko
b.
Relative body Weight
1.2
1
0.8
0.6
0
2
4
6
8
Days on 0.5% CA diet
Triple ko
spgp ko
wt

Fig. 3

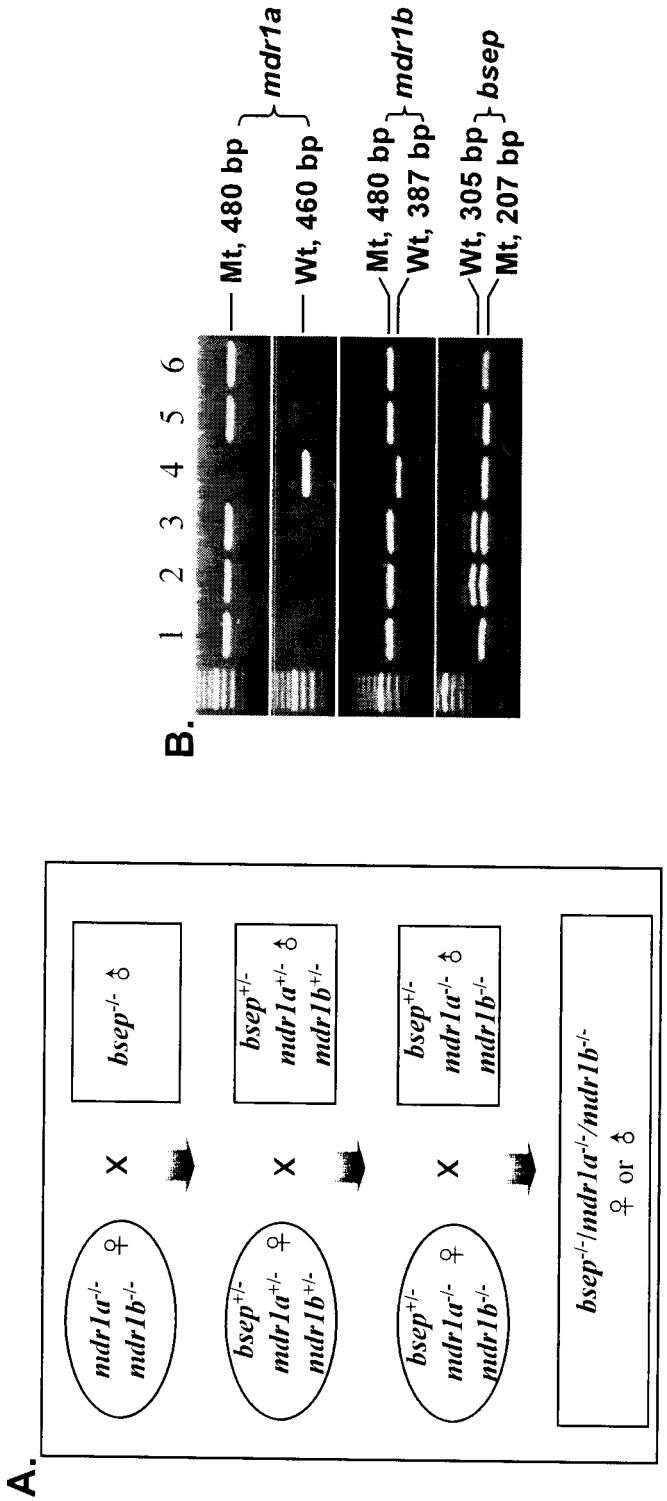

A.
mdr1a-/- mdr1b-/- ♀
bsep-/- ♂
bsep+/- mdr1a+/- mdr1b+/- ♀
bsep+/- mdr1a+/- mdr1b+/- ♂
bsep+/- mdr1a-/- mdr1b-/- ♀
bsep+/- mdr1a-/- mdr1b-/- ♂
bsep-/-/mdr1a-/-/mdr1b-/-
♀ or ♂
B.
1 2 3 4 5 6
Mt, 480 bp
Wt, 460 bp
mdr1a
Mt, 480 bp
Wt, 387 bp
mdr1b
Wt, 305 bp
Mt, 207 bp
bsep

Fig.4

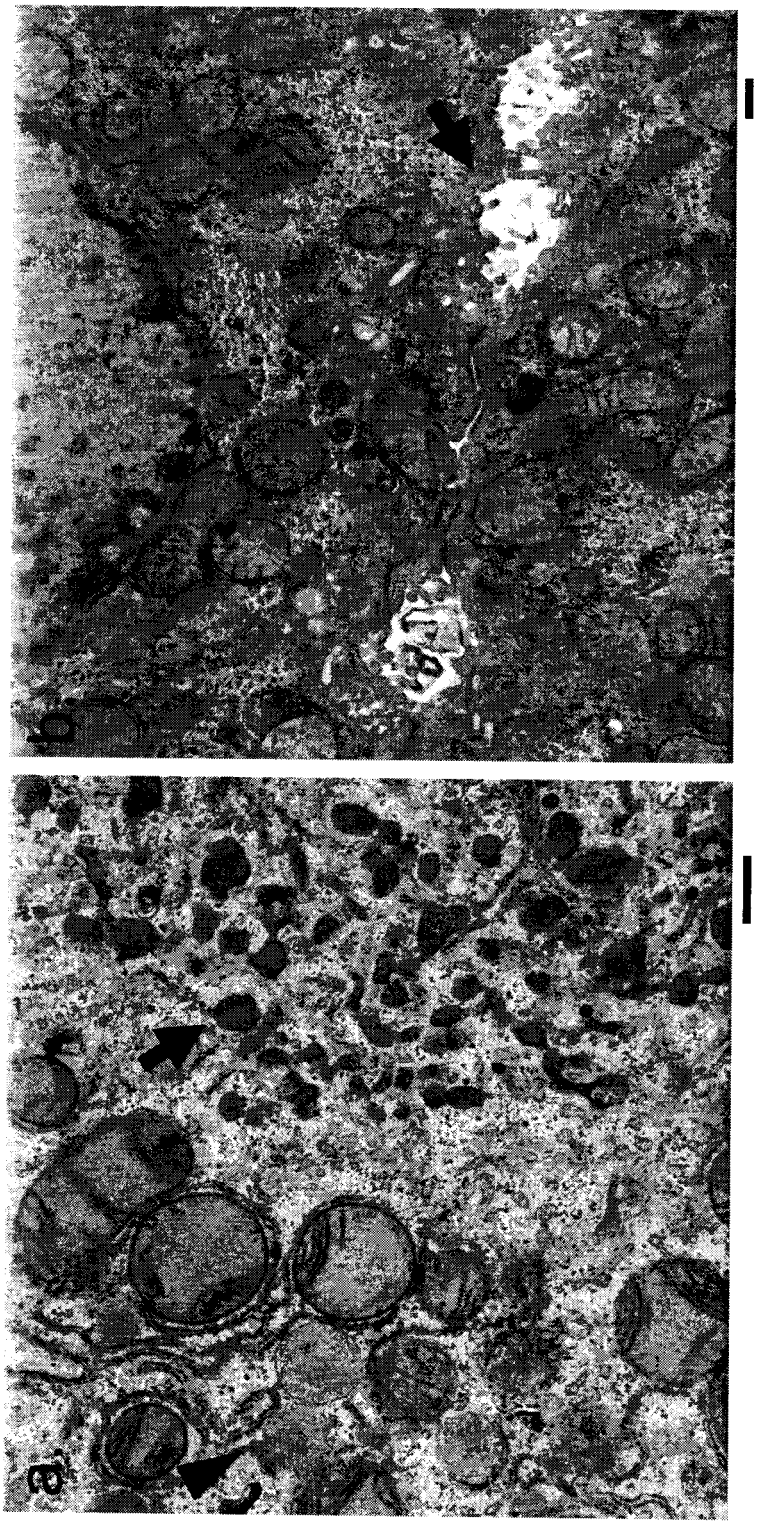
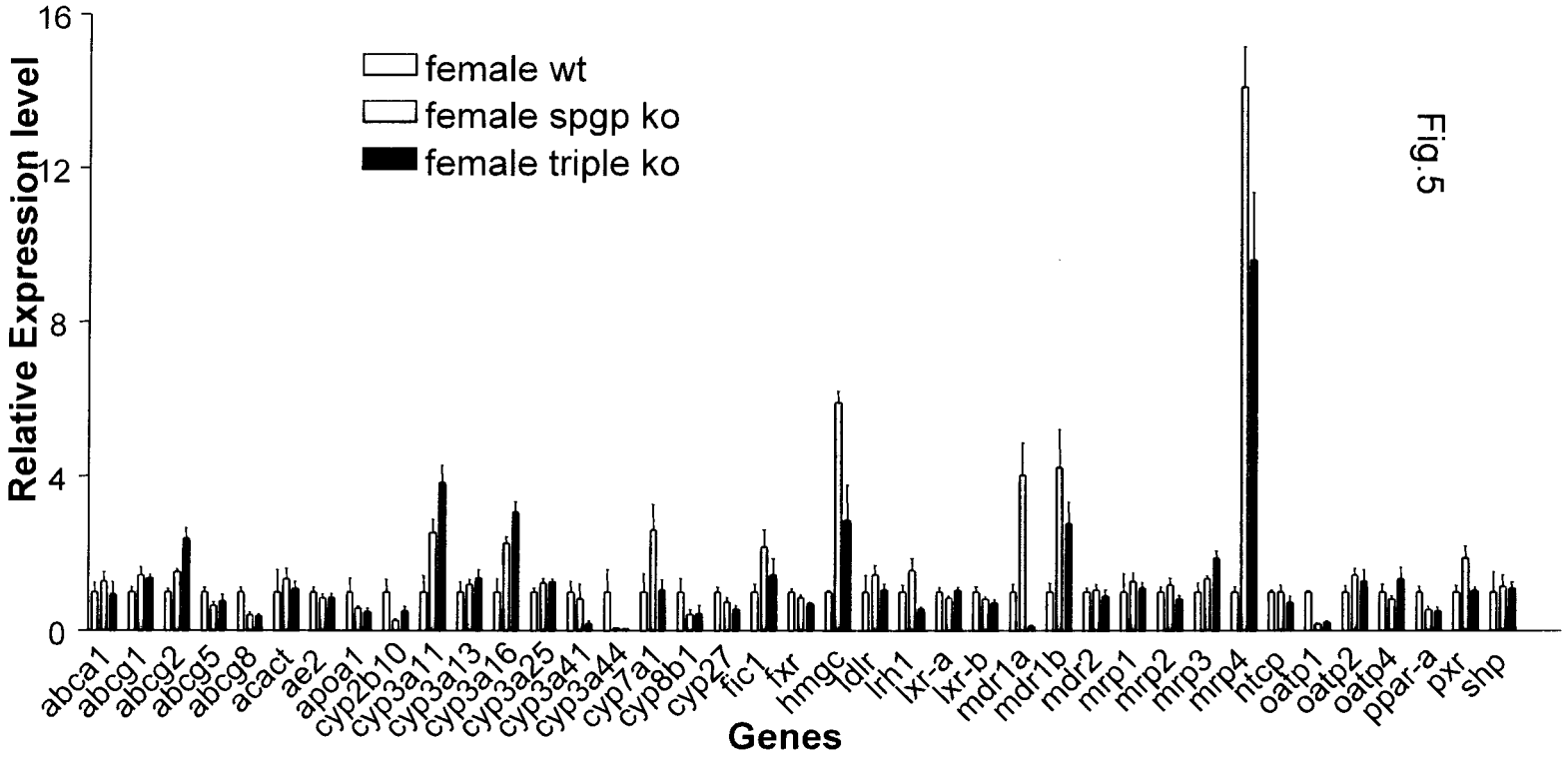


Fig.5

a.



b. Abcb1b transcript with exon 4 deletion

```
  1 atggagtttgaagagaaccttaagggaagagcagacaagaacttctcgaagatgggcaaaaagagtaaaaaggagaagaaagaaaagaaa
    M  E  F  E  E  N  L  K  G  R  A  D  K  N  F  S  K  M  G  K  K  S  K  K  E  K  K  E  K  K
 91 cctgctgttggcgtatttgggatggtggacccaacagtactctga (SEQ. ID NO:4)
    P  A  V  G  V  F  G  M  V  D  P  T  V  L  *   (SEQ. ID NO:5)
```

c. Abcb1b transcript with exons 4, 5, 6 deletion

```
  1  atggagtttgaagagaaccttaagggaagagcagacaagaacttctcgaagatgggcaaaaagagtaaaaaggagaagaaagaaaagaaa
     M  E  F  E  E  N  L  K  G  R  A  D  K  N  F  S  K  M  G  K  K  S  K  K  E  K  K  E  K  K
 91  cctgctgttggcgtatttgggatggaattggtgacaaaattgggatgttttttcagtccataa (SEQ. ID NO:6)
     P  A  V  G  V  F  G  M  E  L  V  T  K  L  G  C  F  F  S  P  *   (SEQ. ID NO:7)
```

Fig.6

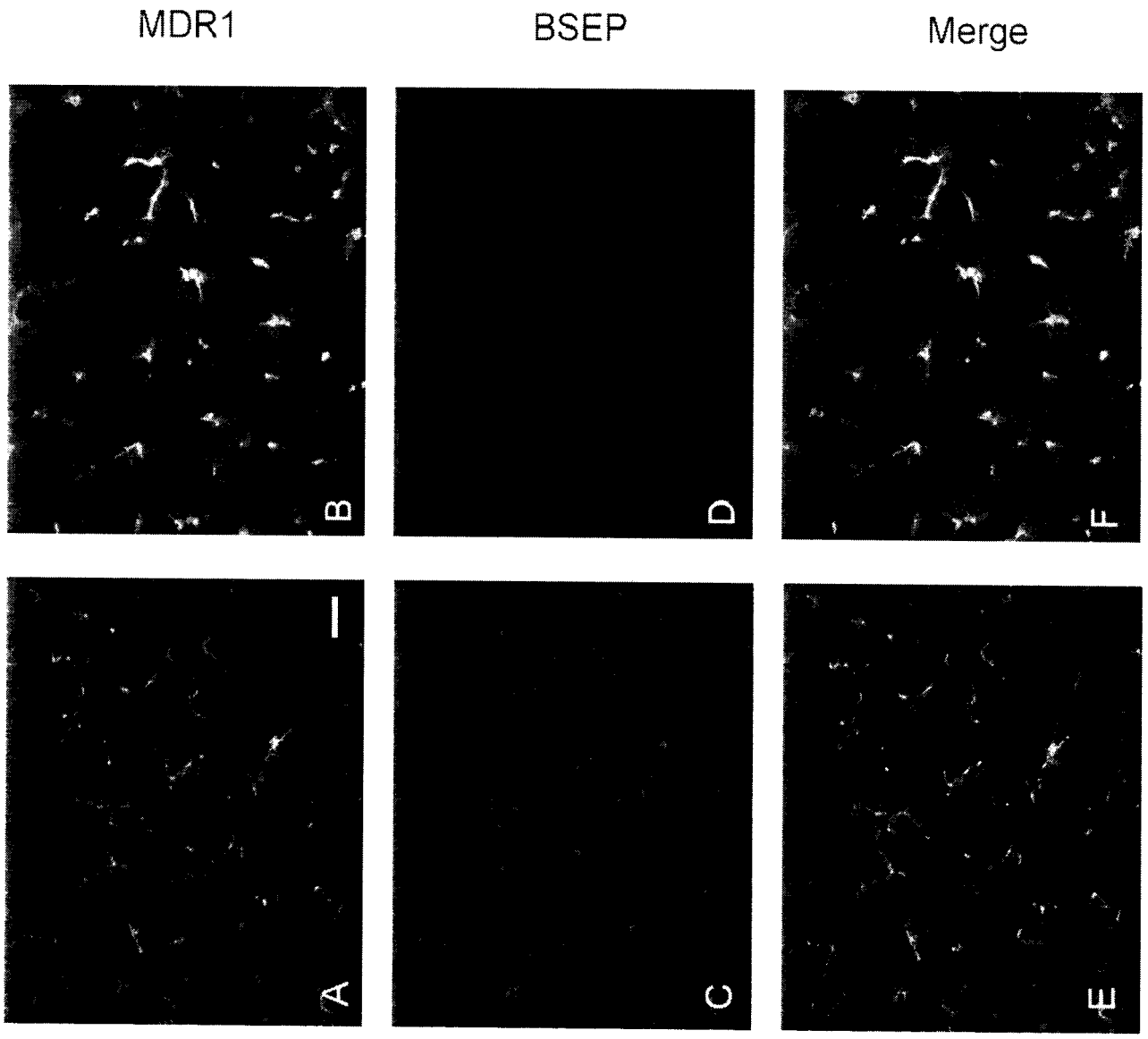


Fig. 7

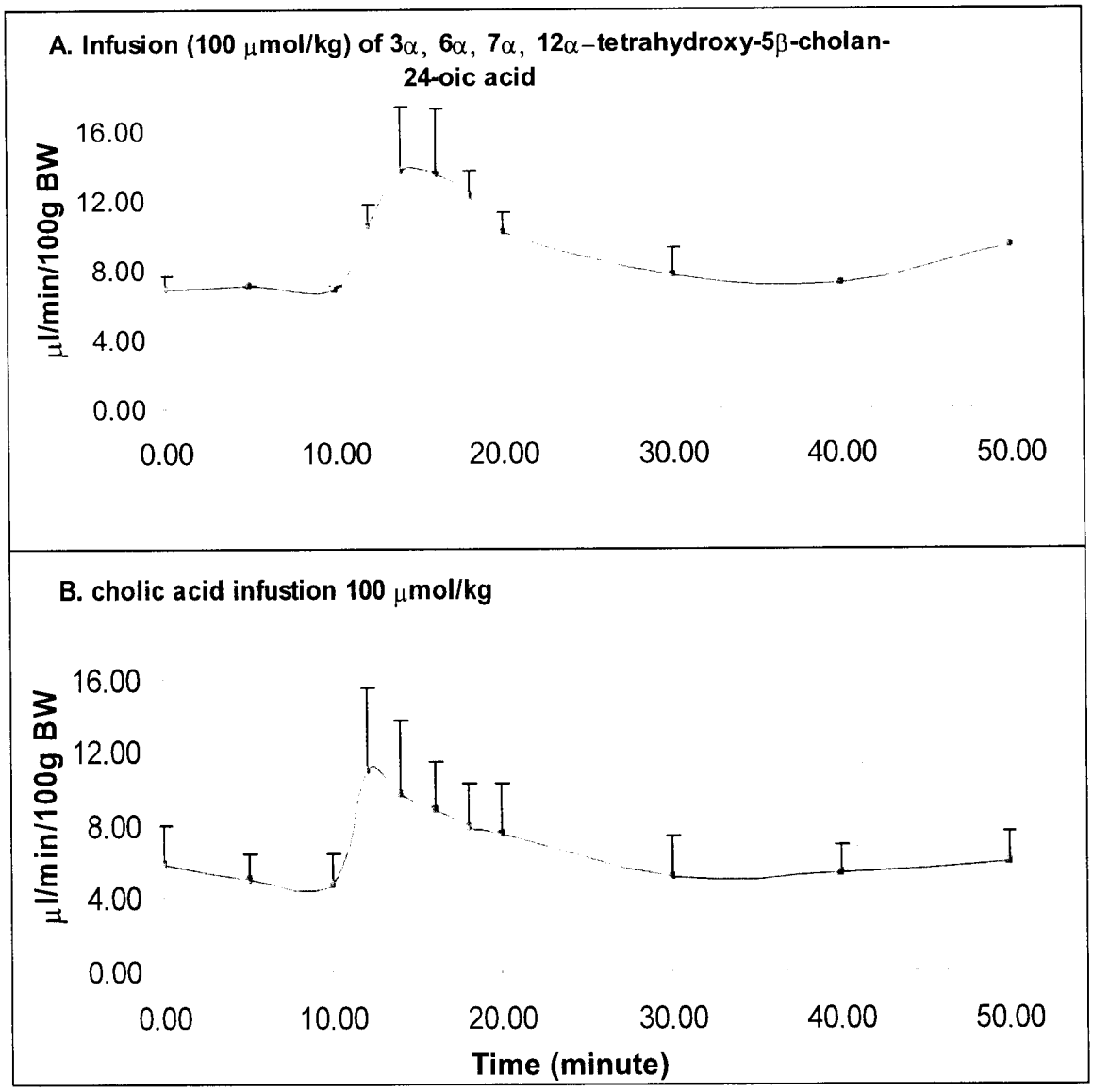

A. Infusion (100 μmol/kg) of 3α, 6α, 7α, 12α–tetrahydroxy-5β-cholan-24-oic acid
μl/min/100g BW
16.00
12.00
8.00
4.00
0.00
0.00
10.00
20.00
30.00
40.00
50.00
B. cholic acid infustion 100 μmol/kg
μl/min/100g BW
16.00
12.00
8.00
4.00
0.00
0.00
10.00
20.00
30.00
40.00
50.00
Time (minute)

Fig. 8

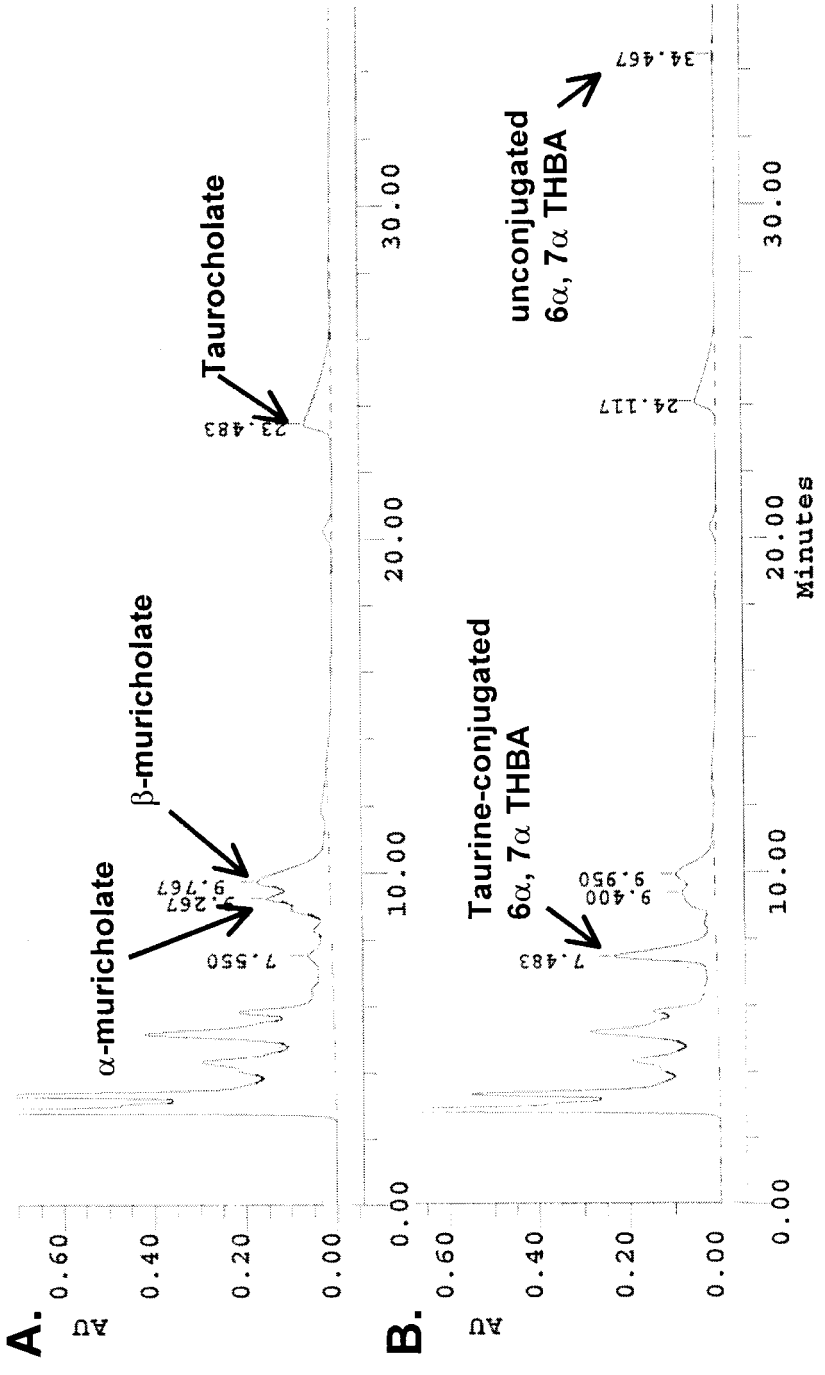
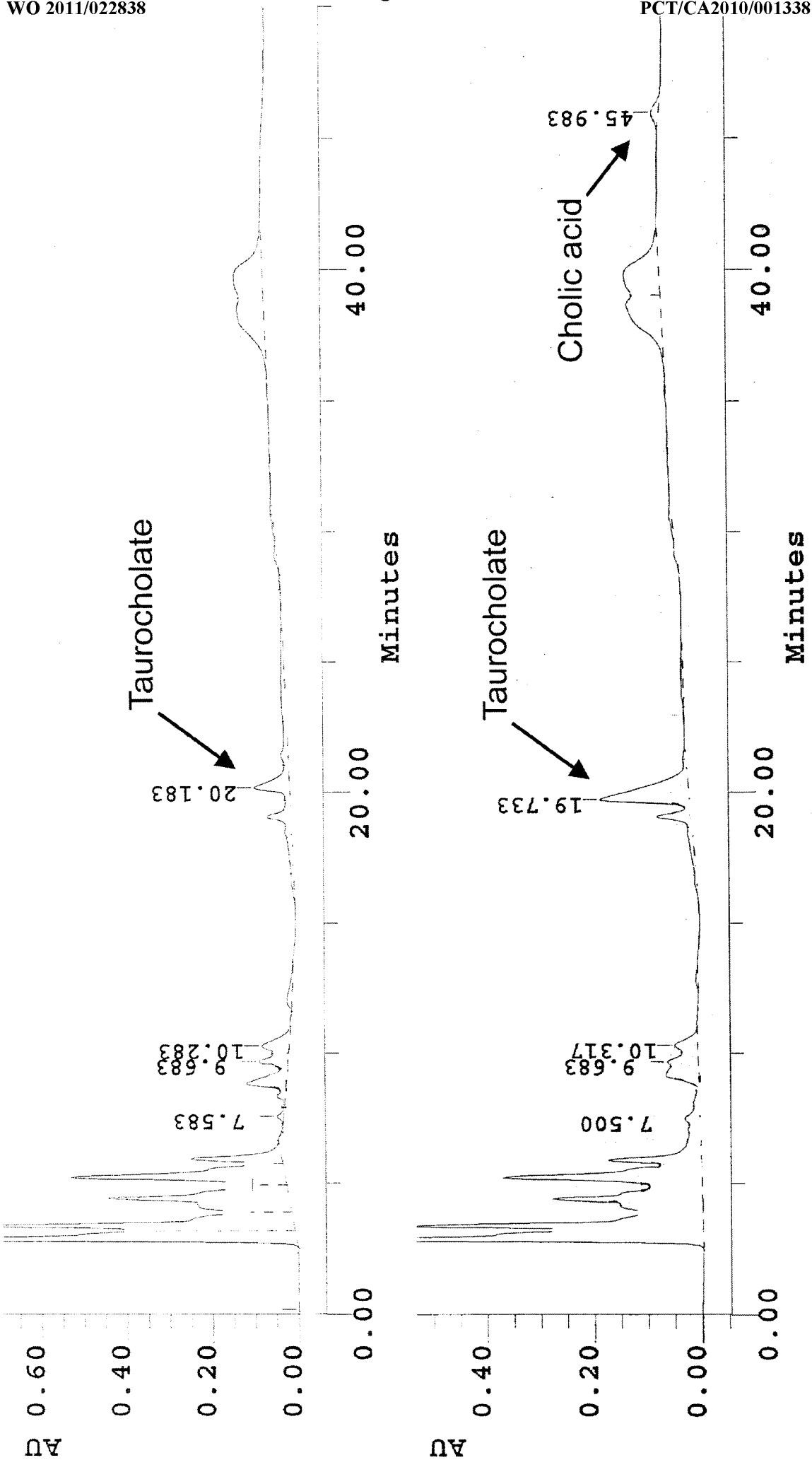

A.
AU
0.60
0.40
0.20
0.00
α-murichocolate
β-murichocolate
Taurocholate
7.550
9.267
9.767
23.483
10.00
20.00
30.00
B.
AU
0.60
0.40
0.20
0.00
Taurine-conjugated 6α, 7α THBA
unconjugated 6α, 7α THBA
7.483
9.400
9.950
24.117
34.467
10.00
20.00
30.00
Minutes

Fig. 8C


Taurocholate
20.183
7.583
9.683
10.283
Minutes
AU
0.00
20.00
40.00
0.00
0.20
0.40
0.60
Taurocholate
19.733
7.500
9.683
10.317
Cholic acid
45.983
Minutes
AU
0.00
20.00
40.00
0.00
0.20
0.40

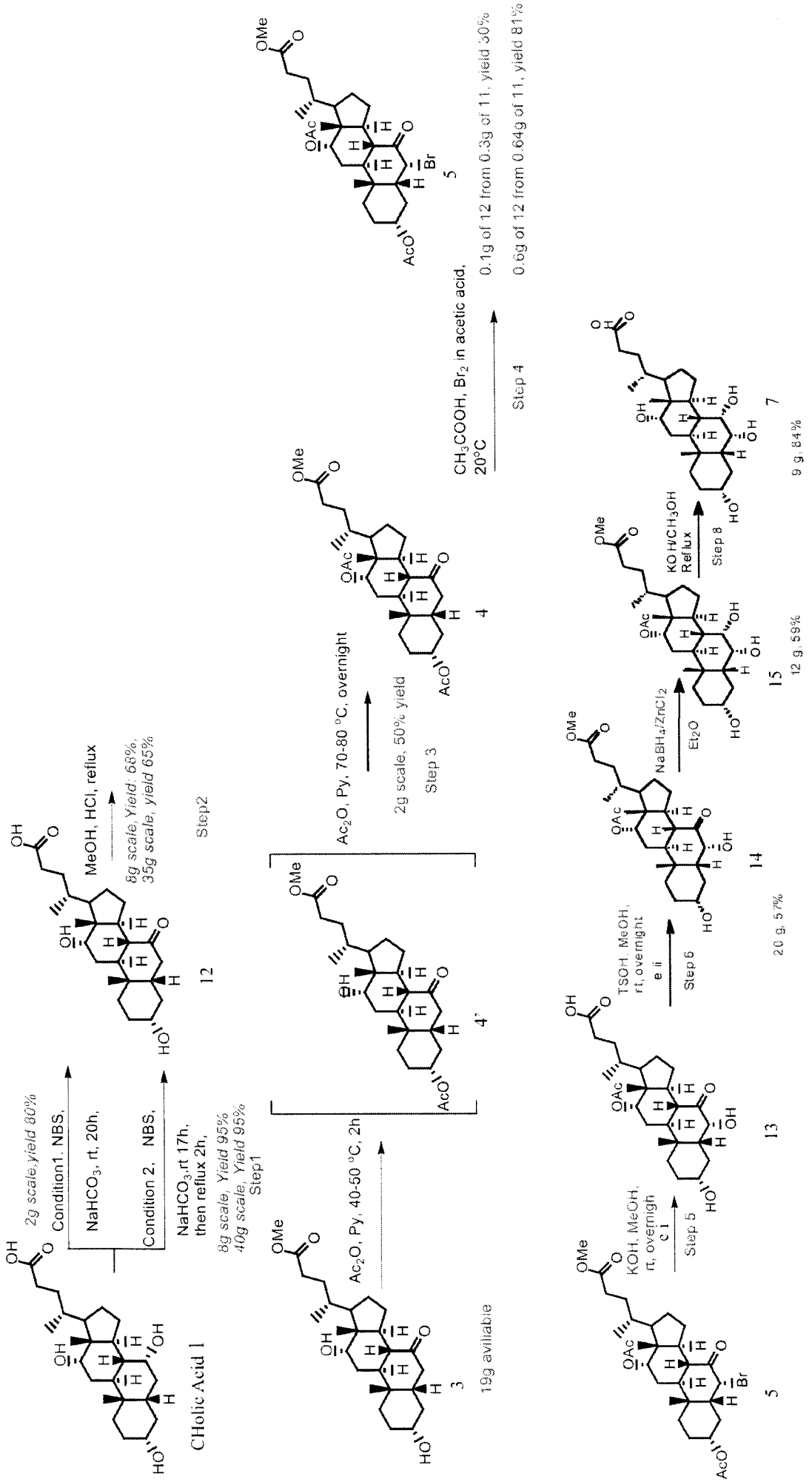

CHolic Acid 1
2g scale, yield 80%
Condition1. NBS,
NaHCO3, rt, 20h,
Condition 2, NBS,
NaHCO3,rt 17h,
then reflux 2h,
8g scale, Yield 95%
40g scale, Yield 95%
Step1
MeOH, HCl, reflux
8g scale, Yield: 68%,
35g scale, yield 65%
Step2
12
19g avilable
3
Ac2O, Py, 40-50 °C, 2h
4'
Ac2O, Py, 70-80 °C, overnight
2g scale, 50% yield
Step 3
4
CH3COOH, Br2 in acetic acid,
20°C
Step 4
5
0.1g of 12 from 0.3g of 11, yield 30%
0.6g of 12 from 0.64g of 11, yield 81%
KOH, MeOH,
rt, overnigh
c i
Step 5
13
TSOH, MeOH,
rt, overnight
e ii
Step 6
14
20 g, 57%
NaBH4/ZnCl2
Et2O
15
12 g, 59%
KOH/CH3OH
Reflux
Step 8
7
9 g, 84%

Fig. 10

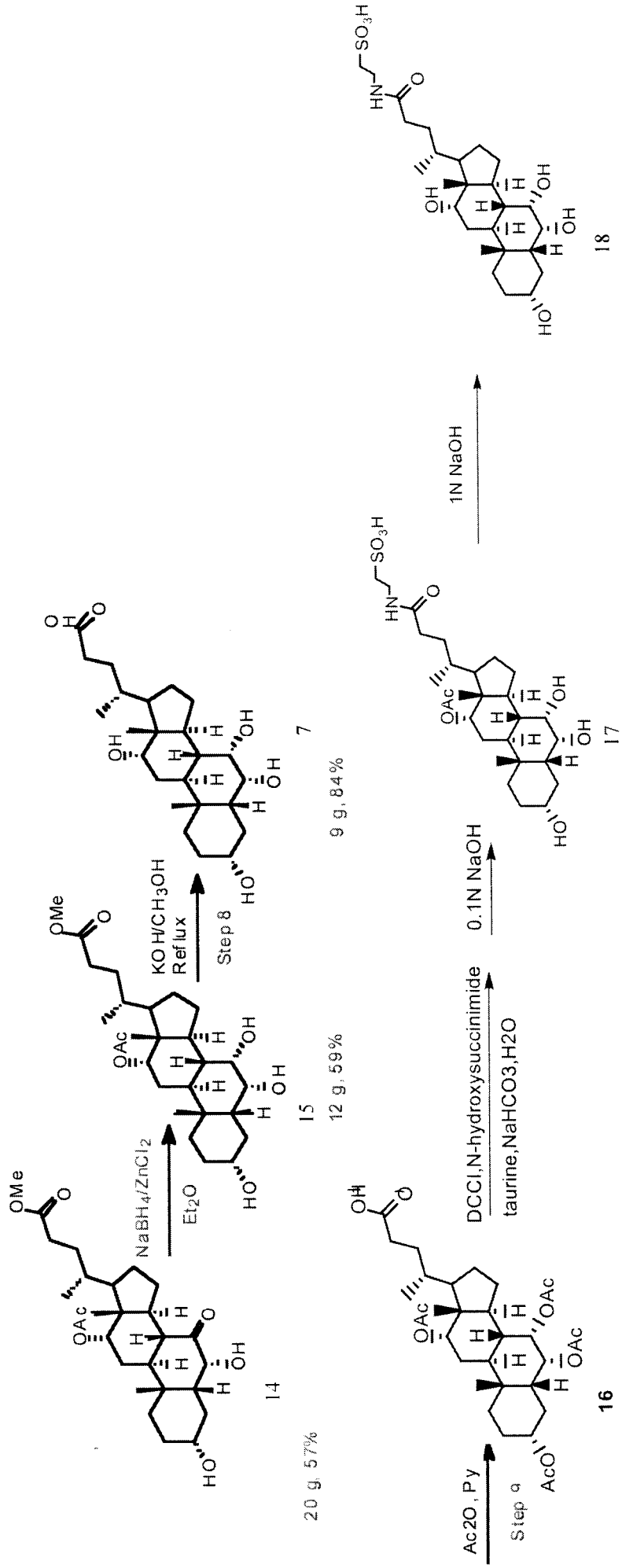

Ac2O, Py
Step a
20 g, 57%
14
NaBH4/ZnCl2
Et2O
12 g, 59%
15
KOH/CH3OH
Reflux
Step 8
9 g, 84%
7
DCCI,N-hydroxysuccinimide
taurine,NaHCO3,H2O
0.1N NaOH
1N NaOH
16
17
18

Fig. 11

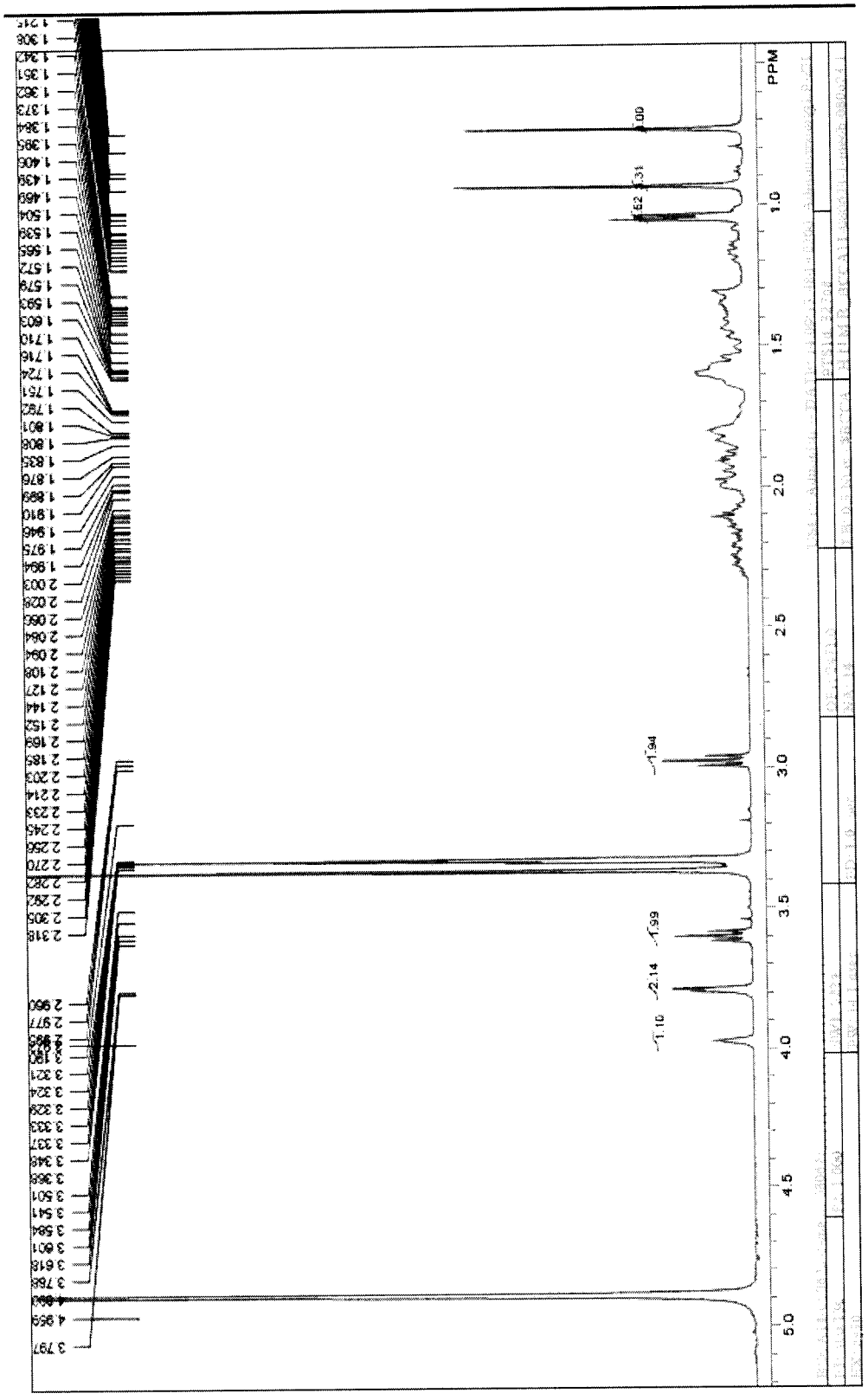
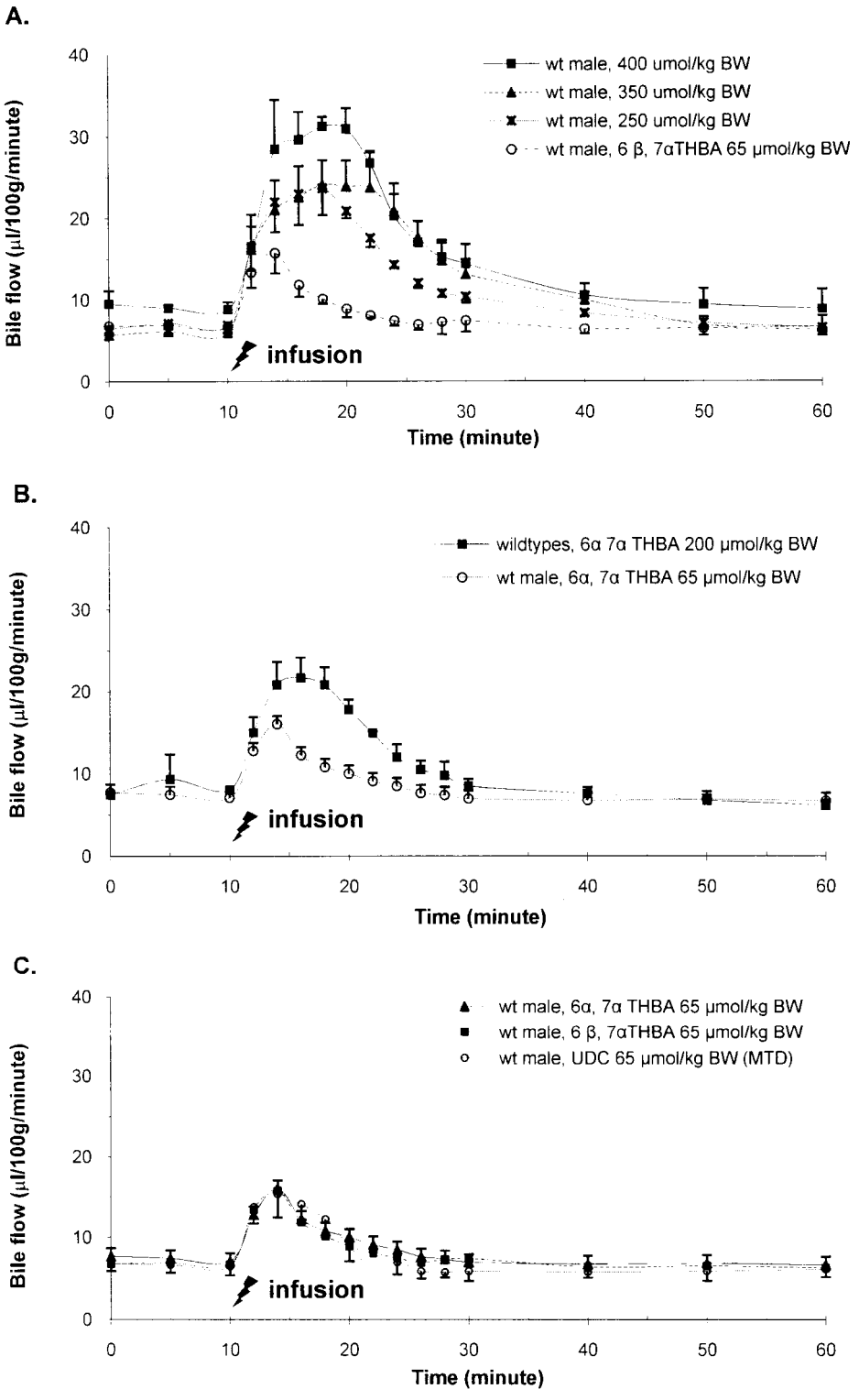


Fig. 12


A.
wt male, 400 umol/kg BW
wt male, 350 umol/kg BW
wt male, 250 umol/kg BW
wt male, 6 β, 7αTHBA 65 μmol/kg BW
Bile flow (μl/100g/minute)
infusion
Time (minute)
B.
wildtypes, 6α 7α THBA 200 μmol/kg BW
wt male, 6α, 7α THBA 65 μmol/kg BW
Bile flow (μl/100g/minute)
infusion
Time (minute)
C.
wt male, 6α, 7α THBA 65 μmol/kg BW
wt male, 6 β, 7αTHBA 65 μmol/kg BW
wt male, UDC 65 μmol/kg BW (MTD)
Bile flow (μl/100g/minute)
infusion
Time (minute)