Supplementary Information

Text S1: Supplementary material and methods

Pharmacokinetics study with novobiocin. 6 male FVB mice were divided into two groups. Triptolide (0.25mg/kg) (group 1) and mixture of triptolide(0.25mg/kg) and novobiocin(100mg/kg)(group 2) were orally administered. Under isoflurane anesthesia, blood was collected from left jugular vein at 5, 10, 15, 30, 60, 120min and centrifuged at 4°C and 1000 x g for 5 min to obtain plasma.

Figure legends of Supplementary figures

Fig.S1 Triptolide did not induce obvious toxicity in liver (A&B), kidney(C&D), epididymis (E&F) and spleen (G&H). Triptolide(0.125, 0.25mg/kg) was orally administered for 15 days. All the data are presented as the mean ± S.D.; n = 6.

Fig.S2. Triptolide could not be effluxed by MDR1 or MRP2-expressed MDCKII cells.
(A) Mock, MDR1 and BCRP MDCKII cells were incubated with triptolide (5μM) for 5, 15 and 45min. (B) Mock, MRP2 and BCRP MDCKII cells were incubated with triptolide (5μM) for 15, 30 and 60min. All the data are presented as the mean ± S.D.; n = 3.

Fig.S3. Novobiocin increased plasma content of triptolide in male FVB mice. (A) the time profiles of plasma concentration. Novobiocin (100mg/kg) was orally co-administered with triptolide (0.25mg/kg) for once. (B) Pharmacokinetic parameters of triptolide after oral administration of triptolide and novobiocin. All the data are presented as the mean ± S.D.; n = 4.

Fig.S4. **Triptolide dose-dependently caused cell-selective testis injury**. Administration of triptolide (0.0625-0.5mg/kg) for 60days.

Fig.S5. Comparison of plasma distribution of triptolide between wild-type and $Bcrp^{-/-}$ mice at steady state. Triptolide was infused intravenously at a dose rate of 200ng/min/kg. All the data are presented as the mean ± S.D.; n=3.

Fig. S1

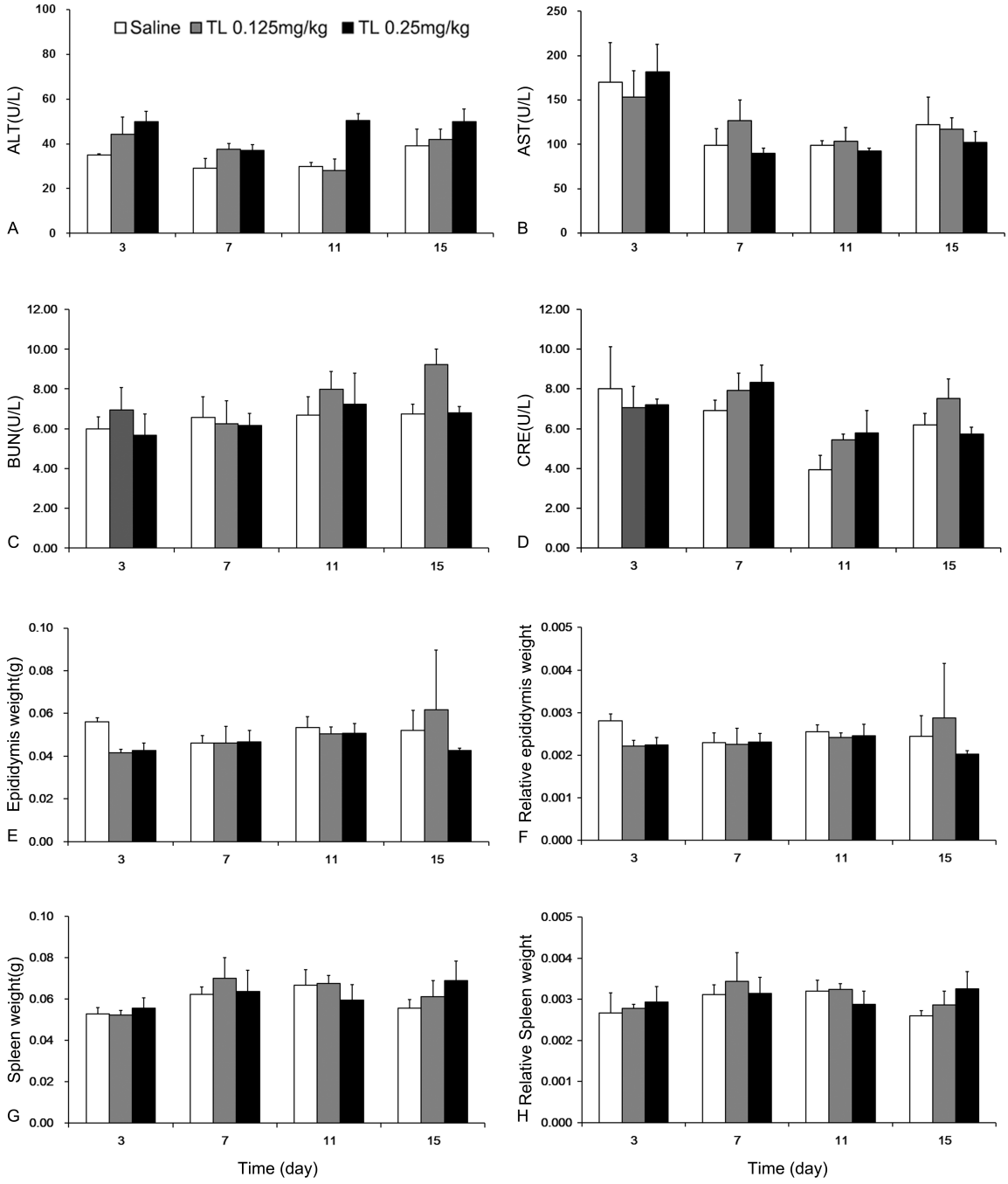

Saline
TL 0.125mg/kg
TL 0.25mg/kg
ALT(U/L)
AST(U/L)
BUN(U/L)
CRE(U/L)
Epididymis weight(g)
Relative epididymis weight
Spleen weight(g)
Relative Spleen weight
A
B
C
D
E
F
G
H
Time (day)
Time (day)

Fig. S2

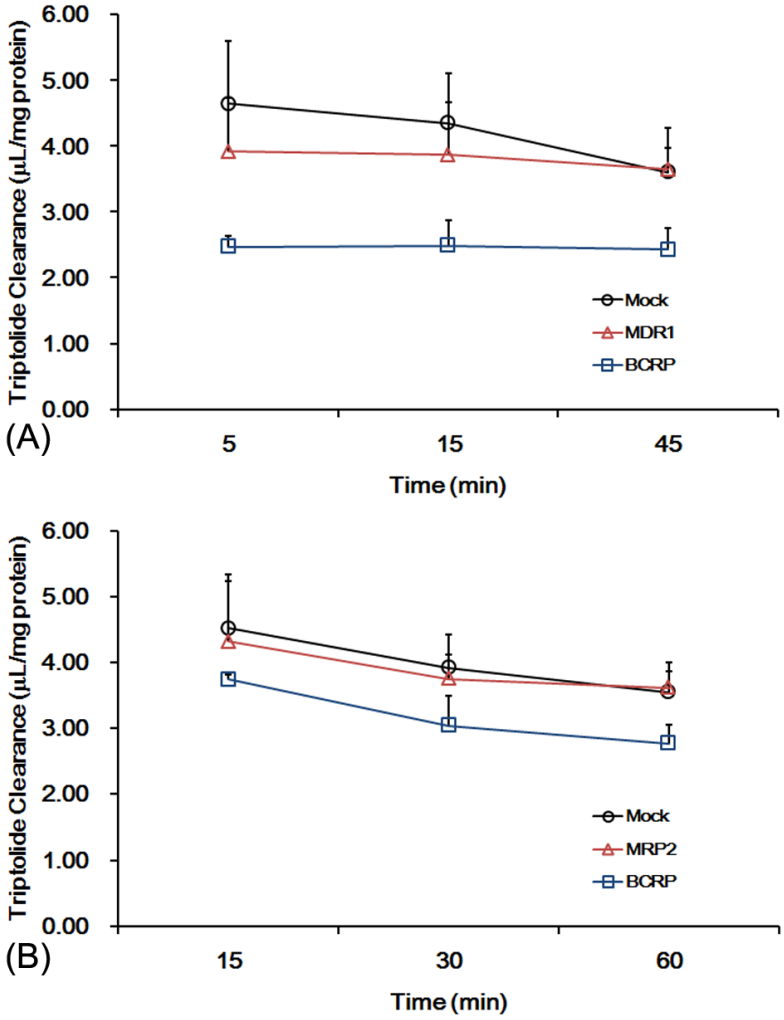

Triptolide Clearance (μL/mg protein)
6.00
5.00
4.00
3.00
2.00
1.00
0.00
Mock
MDR1
BCRP
(A)
5
15
45
Time (min)
Triptolide Clearance (μL/mg protein)
6.00
5.00
4.00
3.00
2.00
1.00
0.00
Mock
MRP2
BCRP
(B)
15
30
60
Time (min)

Fig. S3

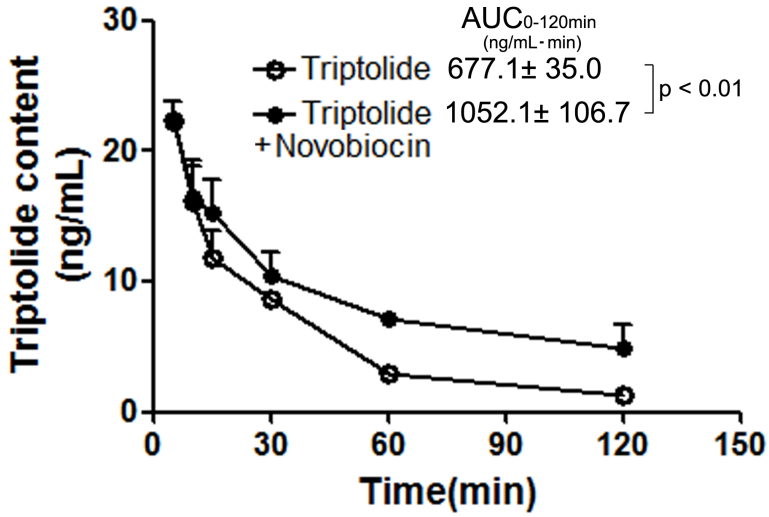


Fig.S4

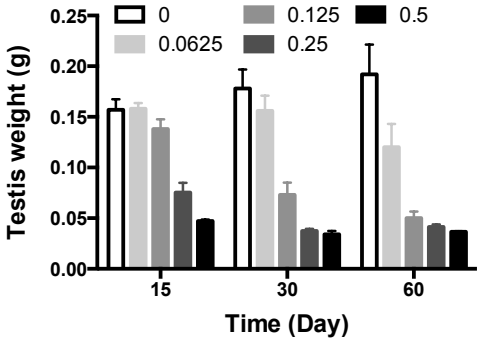
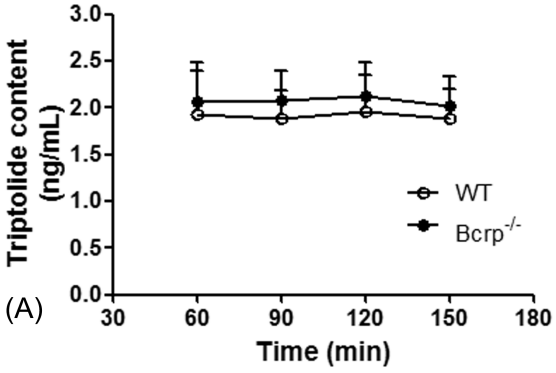


Fig.S5



(A)