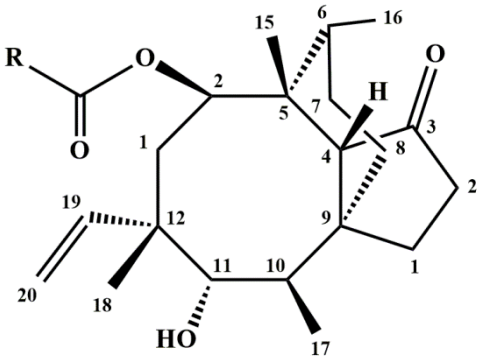


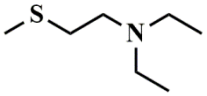
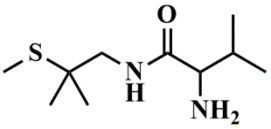
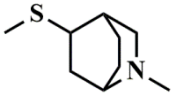
	Pleuromutilin	Tiamulin	Valnemulin	Retapamulin
R	—OH			

Figure S1 Chemical structures of the pleuromutilins

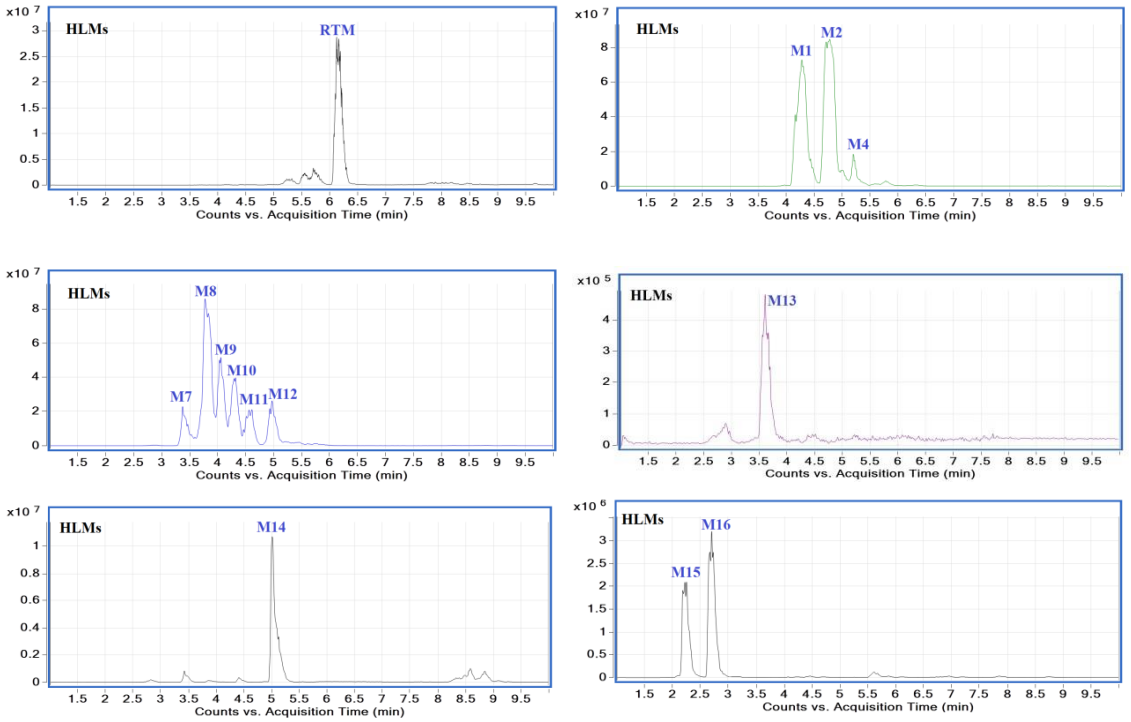


Figure S2 Accurate extracted ion chromatograms (EICs) of retapamulin and its metabolites after incubation with human liver microsomes.

Table S3 Summary of metabolites of RTP detected in *in vivo* and *in vitro*

NO.	Description	Composition	$[M+H]^+$ (*m/z*)	Error (ppm)	Corresponding mass errors (ppm)
M0	RTP	$C_{30}H_{48}NO_4S^+$	518.32986	0.40	0.77
M1	8α-OH-RTP	$C_{30}H_{48}NO_5S^+$	534.32477	0.06	0.11
M2	RTP+O	$C_{30}H_{48}NO_5S^+$	534.32477	0.12	0.22
M3	RTP+O	$C_{30}H_{48}NO_5S^+$	534.32477	0.43	0.80
M4	RTP+O	$C_{30}H_{48}NO_5S^+$	534.32477	0.51	0.95
M5	RTP+O	$C_{30}H_{48}NO_5S^+$	534.32477	0.36	0.67
M6	Sulfoxide RTP	$C_{30}H_{48}NO_5S^+$	534.32477	0.34	0.64
M7	RTP+2O	$C_{30}H_{48}NO_6S^+$	550.31969	0.32	0.58
M8	RTP+2O	$C_{30}H_{48}NO_6S^+$	550.31969	0.32	0.58
M9	RTP+2O	$C_{30}H_{48}NO_6S^+$	550.31969	0.41	0.75
M10	RTP+2O	$C_{30}H_{48}NO_6S^+$	550.31969	0.52	0.94
M11	RTP+2O	$C_{30}H_{48}NO_6S^+$	550.31969	0.36	0.65
M12	RTP+2O	$C_{30}H_{48}NO_6S^+$	550.31969	0.07	0.13
M13	RTP+3O	$C_{30}H_{48}NO_7S^+$	566.31460	0.51	0.90
M14	N-deethly-RTP	$C_{29}H_{46}NO_4S^+$	504.31421	0.03	0.06
M15	N-deethly-RTP+O	$C_{29}H_{46}NO_5S^+$	520.30912	0.02	0.04
M16	N-deethly-RTP+O	$C_{29}H_{46}NO_5S^+$	520.30912	0.04	0.08

The $[M+H]^+$ (*m/z*) values were calculated from the proposed structural formulae. The Error (ppm) is the difference between the calculated and observed *m/z* values.