Drug Metabolism and Disposition

Assessment of the Biotransformation of Low Turnover Drugs in the HμREL® Human Hepatocyte Coculture Model

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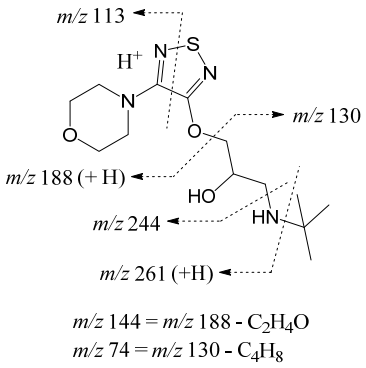
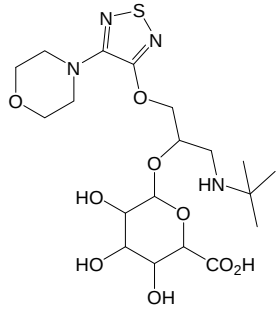
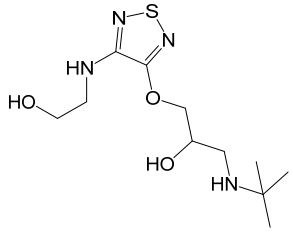
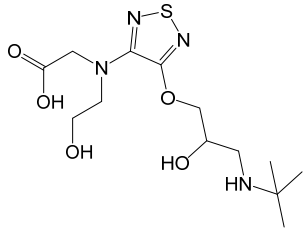
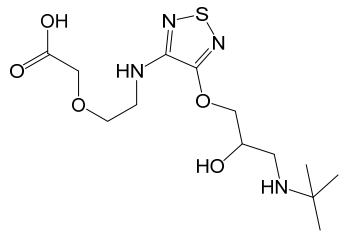
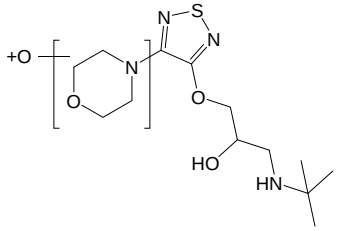
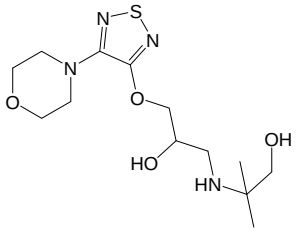
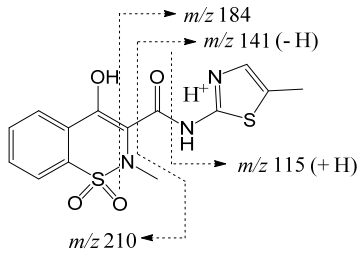
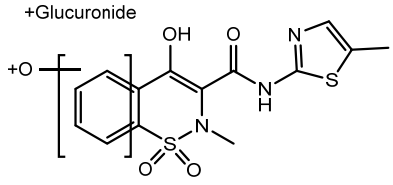
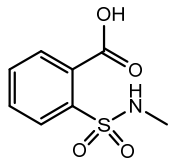
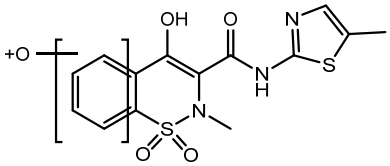
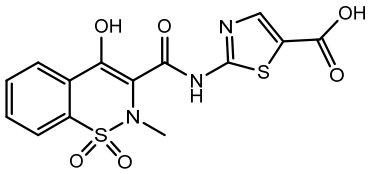
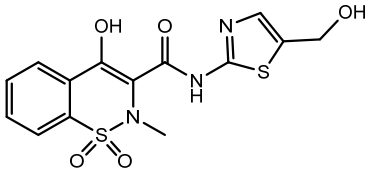
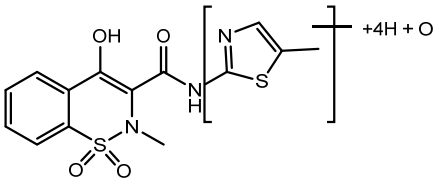
Supplemental Table 1. Fragmentation of Parent Drug and Key Fragment Ions of Metabolites.

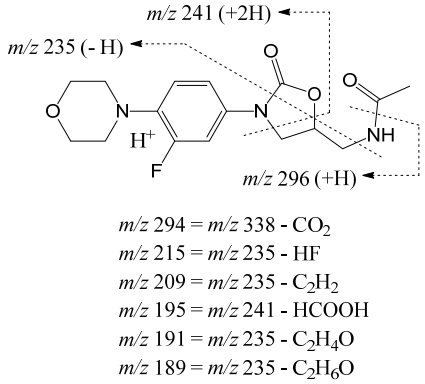
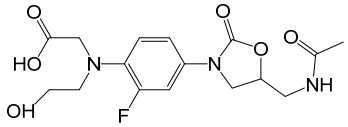
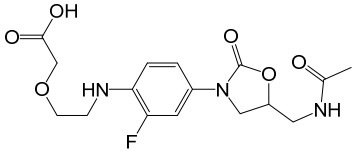
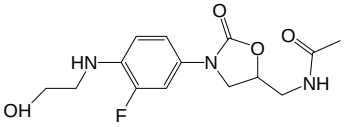
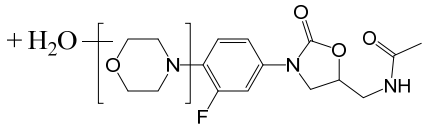
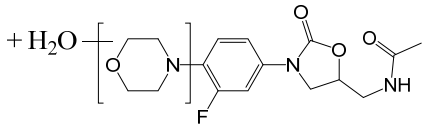
Compound/Metabolite	Metabolite	$[M + H]^+$ (*m/z*)	Fragment Ions (MS^2)
Timolol 	Parent Drug	317.1638	261, **244**, 243, 188, 144, 130, 113, 74
	**T1**, Tim + Gluc	493.1955	437, 420, 401, 339, 317, 306, 303, 261, **244**, 243, 188, 186, 130, 74
	**T2,** Tim – C_2H_2	291.1485	235, 218, 217, **162**, 144, 130, 74
	**T3,** Tim + 2O (a)	349.1536	293, 276, 275, 247, 220, 202, 176, **174**, 158, 144, 130, 86, 74

Compound/Metabolite	Metabolite	$[M + H]^+$ (*m/z*)	Fragment Ions (MS^2)
	**T4,** Tim + 2O (b)	349.1537	293, 276, 275, 220, 202, 174, **144**, 130, 103, 74
	**T5,** Tim + O (a)	333.1592	259, 242, 241, 198, **186**, 130, 74
	**T6**, Tim + O (b)	333.1589	261, **244**, 243, 188, 146, 144, 113, 74
Meloxicam 	Parent Drug	352.0417	265, 210, 184, 141, **115**, 88
	**M1**, Melox + O + Gluc	544.0679	368, 342, 341, 203, 202, 141, **115**

Compound/Metabolite	Metabolite	$[M + H]^+$	Fragment Ions

		(*m/z*)	(MS^2)
	**M2**, Melox Cleavage	216.0323	**198**, 185, 121
	**M3**, Melox + O	368.0368	141, **115**
	**M4**, Melox-COOH	382.0154	214, 171, **145**, 127, 101
	**M5**, Melox-OH	368.0362	210, 200, 157, 139, **131**, 127, 113, 101
	**M6**, Melox + 4H + O	372.0676	255, 238, 210, **135**, 118, 117, 76

Compound/Metabolite	Metabolite	$[M + H]^+$ (*m/z*)	Fragment Ions (MS^2)

Linezolid  	Parent Drug	338.1505	**296**, 294, 252, 241, 235, 215, 209, 195, 191, 189, 148
	**L1**, Lin + 2O (a)	370.1403	328, **324**, 311, 310, 282, 267, 238, 221, 181, 177
	**L2**, Lin + 2O (b)	370.1404	**328**, 282, 273, 267, 252, 241, 227, 222, 197, 191, 165, 163, 151, 139, 137, 103
	**L3**, Lin – C_2H_2	312.1352	**270**, 252, 225, 223, 215, 209, 197, 191, 183, 169, 164, 151, 139
	**L4**, Lin + H_2O (a)	356.1611	338, 314, 311, 296, 294, 280, 270, **267**, 253, 235, 213, 208
	**L5**, Lin + H_2O (b)	356.1614	314, **252**, 222, 200, 191

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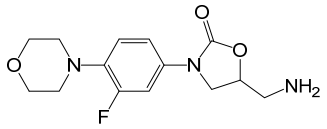
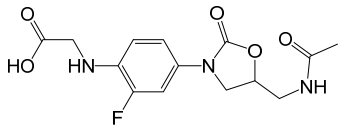
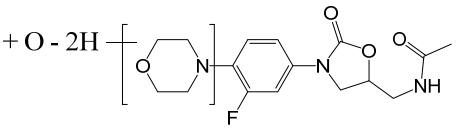
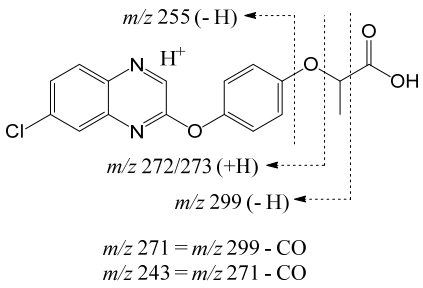
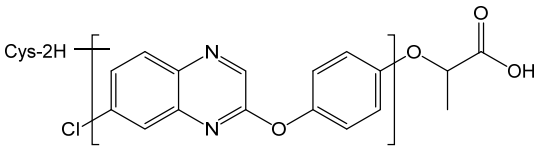
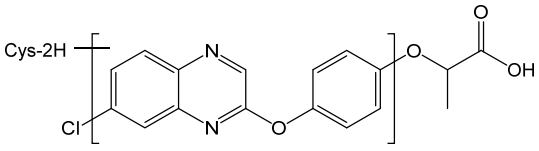
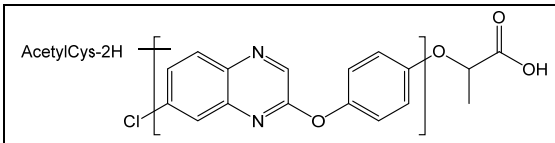
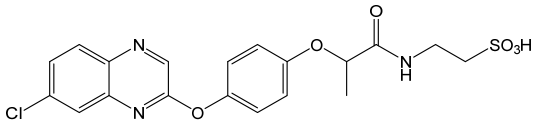
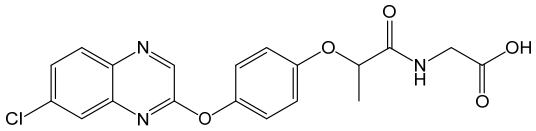
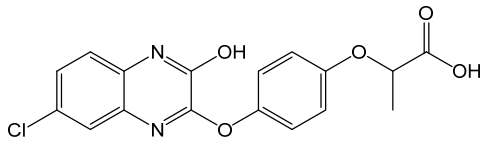
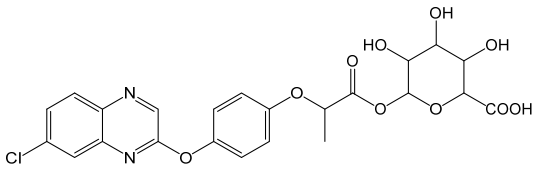
	**L6**, Lin – C_2H_2O	296.1402	252, 209, 200, **195**
	**L7**, Lin + 2O – C_2H_4O	326.1147	284, **238**, 225, 223, 197, 183, 177, 164, 163, 151, 139
	**L8**, Lin + O – 2H	352.1300	**324**, 310, 282, 223
XK469 	Parent Drug	345.0632	**299**, 273, 272, 271, 255, 244, 243, 181, 121, 91
	**X1**, XK469-Cys-2H (a)	464.0670	428, 382, 377, **375**, 356, 347, 331, 329, 275
	**X2**, XK469-Cys-2H (b)	464.0668	**447**, 419, 401, 389, 375, 374, 356, 329, 301

Compound/Metabolite	Metabolite	$[M + H]^+$ (*m/z*)	Fragment Ions (MS^2)
	X3, XK469-AcetylCys-	506.0775	447, 419, 418,

	2H		401, **377**, 331, 304, 305, 130
	**X4**, XK469-Taur	452.0668	327, **299**, 273, 272, 271, 243, 236, 152, 126
	**X5**, XK469-Gly	402.0844	327, **299**, 273, 272, 271, 243, 236, 207
	**X6**, XK469-OH	361.0580	**315**, 297, 289, 288, 287, 271, 260, 259, 231, 224, 223, 121
	**X-Gluc**, XK469-Gluc	521.0946	345, **299**, 273, 272, 271