

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig 6A_CYP2D6 inhibition assays_Endoxifen_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
Endoxifen (metabolite)			Endoxifen (metabolite)		
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
D_Test Iscador P 10 mg_500 µg/mL	3.60616E-05	89.1	D_Test Iscador P 10 mg_500 µg/mL	7.21398E-06	43.8
D_Test Iscador P 10 mg_100 µg/mL	4.13965E-05	102.3	D_Test Iscador P 10 mg_100 µg/mL	1.95476E-05	118.6
D_Test Iscador P 10 mg_10 µg/mL	3.78969E-05	93.6	D_Test Iscador P 10 mg_10 µg/mL	1.96541E-05	119.3
D_Test Iscador P 10 mg_5 µg/mL	3.54045E-05	87.5	D_Test Iscador P 10 mg_5 µg/mL	2.17025E-05	131.7
D_Test Iscador P 10 mg_1 µg/mL	4.22246E-05	104.3	D_Test Iscador P 10 mg_1 µg/mL	1.6304E-05	98.9
D_Test Iscador P 10 mg_0.1 µg/mL	3.68969E-05	91.2	D_Test Iscador P 10 mg_0.1 µg/mL	2.15621E-05	130.8
	Peak Area Ratio	metabolite vs NC		Peak Area Ratio	metabolite vs NC
D_Test Iscador Qu 5 mg_500 µg/mL	4.25015E-05	105.0	D_Test Iscador Qu 5 mg_500 µg/mL	1.72586E-05	104.7
D_Test Iscador Qu 5 mg_100 µg/mL	5.1676E-05	127.7	D_Test Iscador Qu 5 mg_100 µg/mL	1.83713E-05	111.5
D_Test Iscador Qu 5 mg_10 µg/mL	3.53096E-05	87.2	D_Test Iscador Qu 5 mg_10 µg/mL	1.98354E-05	120.4
D_Test Iscador Qu 5 mg_5 µg/mL	4.17018E-05	103.0	D_Test Iscador Qu 5 mg_5 µg/mL	1.81764E-05	110.3
D_Test Iscador Qu 5 mg_1 µg/mL	4.16317E-05	102.8	D_Test Iscador Qu 5 mg_1 µg/mL	2.45853E-05	149.2
D_Test Iscador Qu 5 mg_0.1 µg/mL	4.21081E-05	104.0	D_Test Iscador Qu 5 mg_0.1 µg/mL	1.89268E-05	114.9
	Peak Area Ratio	metabolite vs NC		Peak Area Ratio	metabolite vs NC
D_Test Iscador M 5 mg_500 µg/mL	3.91586E-05	96.7	D_Test Iscador M 5 mg_500 µg/mL	1.63952E-05	99.5
D_Test Iscador M 5 mg_100 µg/mL	3.74561E-05	92.5	D_Test Iscador M 5 mg_100 µg/mL	2.07329E-05	125.8
D_Test Iscador M 5 mg_10 µg/mL	3.95348E-05	97.7	D_Test Iscador M 5 mg_10 µg/mL	1.65889E-05	100.7
D_Test Iscador M 5 mg_5 µg/mL	4.38595E-05	108.4	D_Test Iscador M 5 mg_5 µg/mL	1.72681E-05	104.8
D_Test Iscador M 5 mg_1 µg/mL	3.88095E-05	95.9	D_Test Iscador M 5 mg_1 µg/mL	1.50332E-05	91.2
D_Test Iscador M 5 mg_0.1 µg/mL	4.29956E-05	106.2	D_Test Iscador M 5 mg_0.1 µg/mL	2.04076E-05	123.8
	Peak Area Ratio	metabolite vs NC		Peak Area Ratio	metabolite vs NC
D_Negative Control 1-1_no inhibitors	4.4456E-05	109.8	D_Negative Control 1-1_no inhibitors	1.6213E-05	98.4
D_Negative Control 1-2_no inhibitors	4.05463E-05	100.2	D_Negative Control 1-2_no inhibitors	1.60233E-05	97.2
D_Negative Control 1-3_no inhibitors	3.64346E-05	90.0	D_Negative Control 1-3_no inhibitors	1.7201E-05	104.4
D_Negative Control 2_no inhibitors/no microsomes	0.00	0.00	D_Negative Control 2_no inhibitors/no microsomes	0.00	0.00
D_Negative Control 3_no inhibitors/no microsomes/no NADPH	0.00	0.00	D_Negative Control 3_no inhibitors/no microsomes/no NADPH	0.00	0.00
Average Negative controls	4.0479E-05		Average Negative controls	1.64791E-05	100

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Assay III			Mean	SD	SE
Endoxifen (metabolite)					
		%			
	Peak Area Ratio	metabolite			
D_Test Iscador P 10 mg_500 µg/mL	3.43457E-05	77.2	70.0	23.5	13.56
D_Test Iscador P 10 mg_100 µg/mL	4.3534E-05	97.9	106.2	10.9	6.32
D_Test Iscador P 10 mg_10 µg/mL	4.39669E-05	98.8	103.9	13.6	7.83
D_Test Iscador P 10 mg_5 µg/mL	6.68009E-05	150.2	123.1	32.2	18.60
D_Test Iscador P 10 mg_1 µg/mL	5.69661E-05	128.0	110.4	15.5	8.94
D_Test Iscador P 10 mg_0.1 µg/mL	4.5065E-05	101.3	107.8	20.6	11.91
C	Peak Area Ratio	metabolite vs NC			
D_Test Iscador Qu 5 mg_500 µg/mL	4.31629E-05	97.0	102.2	4.53	2.62
D_Test Iscador Qu 5 mg_100 µg/mL	4.22026E-05	94.9	111.3	16.4	9.47
D_Test Iscador Qu 5 mg_10 µg/mL	4.77204E-05	107.3	105.0	16.7	9.64
D_Test Iscador Qu 5 mg_5 µg/mL	5.78444E-05	130.0	114.4	14.0	8.06
D_Test Iscador Qu 5 mg_1 µg/mL	4.89721E-05	110.1	120.7	24.9	14.39
D_Test Iscador Qu 5 mg_0.1 µg/mL	5.33684E-05	120.0	112.9	8.14	4.70
C	Peak Area Ratio	metabolite vs NC			
D_Test Iscador M 5 mg_500 µg/mL	4.31235E-05	96.9	97.7	1.54	0.89
D_Test Iscador M 5 mg_100 µg/mL	4.88613E-05	109.8	109.4	16.6	9.61
D_Test Iscador M 5 mg_10 µg/mL	4.32642E-05	97.2	98.5	1.86	1.08
D_Test Iscador M 5 mg_5 µg/mL	4.40275E-05	99.0	104.0	4.74	2.74
D_Test Iscador M 5 mg_1 µg/mL	4.14447E-05	93.2	93.4	2.34	1.35
D_Test Iscador M 5 mg_0.1 µg/mL	4.46695E-05	100.4	110.2	12.2	7.05
C	Peak Area Ratio	metabolite vs NC			
0_Negative Control 1-1_no inhibitor	4.64481E-05	104.4	104.2	5.72	3.30
0_Negative Control 1-2_no inhibitor	4.40081E-05	98.9	98.8	1.47	0.85
0_Negative Control 1-3_no inhibitor	4.30115E-05	96.7	97.0	7.19	4.15
0_Negative Control 2_no inhibitors/no microsomes	1.86875E-05	42.0	14.00	24.3	14.00
0_Negative Control 3_no inhibitors/no microsomes	2.24818E-05	50.5	16.84	29.2	16.84
Average Negative controls	4.44892E-05	100	100.0	0.0	0.000

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig 6B_CYP3A4-5 inhibition assays_Endoxifen_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
Endoxifen (metabolite)	Peak Area Ratio	% metabolite vs NC	Endoxifen (metabolite)	Peak Area Ratio	% metabolite vs NC
TE_Test Iscador P 10 mg_500 µg/mL	3.57113E-05	86.5	TE_Test Iscador P 10 mg_500 µg/mL	3.23578E-05	81.0
TE_Test Iscador P 10 mg_100 µg/mL	3.88185E-05	94.0	TE_Test Iscador P 10 mg_100 µg/mL	5.11774E-05	128.2
TE_Test Iscador P 10 mg_10 µg/mL	4.17151E-05	101.0	TE_Test Iscador P 10 mg_10 µg/mL	4.85964E-05	121.7
TE_Test Iscador P 10 mg_5 µg/mL	4.87448E-05	118.0	TE_Test Iscador P 10 mg_5 µg/mL	4.59791E-05	115.1
TE_Test Iscador P 10 mg_1 µg/mL	3.89346E-05	94.3	TE_Test Iscador P 10 mg_1 µg/mL	4.74794E-05	118.9
TE_Test Iscador P 10 mg_0.1 µg/mL	4.90767E-05	118.8	TE_Test Iscador P 10 mg_0.1 µg/mL	5.41175E-05	135.5
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Test Iscador Qu 5 mg_500 µg/mL	-	-	TE_Test Iscador Qu 5 mg_500 µg/mL	4.97212E-05	124.5
TE_Test Iscador Qu 5 mg_100 µg/mL	4.10534E-05	99.4	TE_Test Iscador Qu 5 mg_100 µg/mL	5.1219E-05	128.3
TE_Test Iscador Qu 5 mg_10 µg/mL	3.93644E-05	95.3	TE_Test Iscador Qu 5 mg_10 µg/mL	5.27174E-05	132.0
TE_Test Iscador Qu 5 mg_5 µg/mL	4.49849E-05	108.9	TE_Test Iscador Qu 5 mg_5 µg/mL	4.35692E-05	109.1
TE_Test Iscador Qu 5 mg_1 µg/mL	3.72907E-05	90.3	TE_Test Iscador Qu 5 mg_1 µg/mL	4.93094E-05	123.5
TE_Test Iscador Qu 5 mg_0.1 µg/mL	4.29758E-05	104.1	TE_Test Iscador Qu 5 mg_0.1 µg/mL	4.38854E-05	109.9
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Test Iscador M 5 mg_500 µg/mL	3.63107E-05	87.9	TE_Test Iscador M 5 mg_500 µg/mL	3.58424E-05	89.8
TE_Test Iscador M 5 mg_100 µg/mL	5.08802E-05	123.2	TE_Test Iscador M 5 mg_100 µg/mL	4.80585E-05	120.3
TE_Test Iscador M 5 mg_10 µg/mL	4.07728E-05	98.7	TE_Test Iscador M 5 mg_10 µg/mL	-	-
TE_Test Iscador M 5 mg_5 µg/mL	4.42298E-05	107.1	TE_Test Iscador M 5 mg_5 µg/mL	4.17972E-05	104.7
TE_Test Iscador M 5 mg_1 µg/mL	-	-	TE_Test Iscador M 5 mg_1 µg/mL	-	107.7
TE_Test Iscador M 5 mg_0.1 µg/mL	3.65532E-05	88.5	TE_Test Iscador M 5 mg_0.1 µg/mL	-	-
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Negative Control 1-1_no inhibitors	4.21314E-05	102.0	TE_Negative Control 1-1_no inhibitors	3.92572E-05	98.3
TE_Negative Control 1-2_no inhibitors	4.17027E-05	101.0	TE_Negative Control 1-2_no inhibitors	3.73476E-05	93.5
TE_Negative Control 1-3_no inhibitors	4.00693E-05	97.0	TE_Negative Control 1-3_no inhibitors	4.31965E-05	108.2
TE_Negative Control 2_no inhibitors/no microsomes	0.00	0.00	Negative Control 2_no inhibitors/no microsomes	0.00	0.00
Negative Control 3_no inhibitors/no microsomes/no NAI	0.00	0.00	Negative Control 3_no inhibitors/no microsomes/no NAI	0.00	0.00
Average Negative controls	0.00004130	100	Average Negative controls	0.00003993	100.0

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Assay III			Mean	SD	SE
Endoxifen (metabolite)					
	Peak Area Ratio	% metabolite vs NC			
TE_Test Iscador P 10 mg_500 µg/mL	3.71197E-05	85.0	84.2	2.81	1.62
TE_Test Iscador P 10 mg_100 µg/mL	4.35216E-05	99.7	107.3	18.3	10.57
TE_Test Iscador P 10 mg_10 µg/mL	4.46759E-05	102.3	108.3	11.6	6.69
TE_Test Iscador P 10 mg_5 µg/mL	4.48841E-05	102.8	112.0	8.1	4.67
TE_Test Iscador P 10 mg_1 µg/mL	5.41371E-05	124.0	112.4	15.9	9.17
TE_Test Iscador P 10 mg_0.1 µg/mL	4.81502E-05	110.3	121.5	12.8	7.42
	Peak Area Ratio	% metabolite vs NC			
TE_Test Iscador Qu 5 mg_500 µg/mL	5.39596E-05	123.6	124.0	0.7	0.47
TE_Test Iscador Qu 5 mg_100 µg/mL	4.9582E-05	113.5	113.7	14.4	8.33
TE_Test Iscador Qu 5 mg_10 µg/mL	5.04966E-05	115.6	114.3	18.4	10.62
TE_Test Iscador Qu 5 mg_5 µg/mL	5.41894E-05	124.1	114.0	8.7	5.03
TE_Test Iscador Qu 5 mg_1 µg/mL	5.85422E-05	134.1	115.9	22.8	13.18
TE_Test Iscador Qu 5 mg_0.1 µg/mL	4.97191E-05	113.9	109.3	4.9	2.85
	Peak Area Ratio	% metabolite vs NC			
TE_Test Iscador M 5 mg_500 µg/mL	4.28273E-05	98.1	91.9	5.4	3.12
TE_Test Iscador M 5 mg_100 µg/mL	5.0164E-05	114.9	119	4.2	2.44
TE_Test Iscador M 5 mg_10 µg/mL	4.28707E-05	98.2	98.4	0.4	0.27
TE_Test Iscador M 5 mg_5 µg/mL	-	-	106	1.7	1.21
TE_Test Iscador M 5 mg_1 µg/mL	5.05595E-05	115.8	112	5.7	4.04
TE_Test Iscador M 5 mg_0.1 µg/mL	4.45102E-05	101.9	95.2	9.5	6.71
	Peak Area Ratio	% metabolite vs NC			
TE_Negative Control 1-1_no inhibitors	4.35539E-05	99.7	100.0	1.87	1.08
TE_Negative Control 1-2_no inhibitors	4.43937E-05	101.7	98.7	4.51	2.60
TE_Negative Control 1-3_no inhibitors	4.3061E-05	98.6	101.3	6.03	3.48
Negative Control 2_no inhibitors/no microsomes	0.00	0.00	0.00	0.00	0.00
Negative Control 3_no inhibitors/no microsomes/n	0.00	0.00	0.00	0.00	0.00
Average Negative controls	4.36695E-05	100	100	0.00	0.00

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig S1_CYP2D6 inhibition assays_Dextrorphan_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
Dextrorphan (metabolite)	Peak Area Ratio	% metabolite vs NC	Dextrorphan (metabolite)	Peak Area Ratio	% metabolite vs NC
D_Test Iscador P 10 mg_500 µg/mL	0.014208097	94.4	D_Test Iscador P 10 mg_500 µg/mL	0.011565397	67.5
D_Test Iscador P 10 mg_100 µg/mL	0.015814367	105.1	D_Test Iscador P 10 mg_100 µg/mL	0.016361201	95.6
D_Test Iscador P 10 mg_10 µg/mL	0.015028411	99.8	D_Test Iscador P 10 mg_10 µg/mL	0.01626224	95.0
D_Test Iscador P 10 mg_5 µg/mL	0.01486649	98.8	D_Test Iscador P 10 mg_5 µg/mL	0.017125527	100.0
D_Test Iscador P 10 mg_1 µg/mL	0.015336473	101.9	D_Test Iscador P 10 mg_1 µg/mL	0.017291943	101.0
D_Test Iscador P 10 mg_0.1 µg/mL	0.014776322	98.2	D_Test Iscador P 10 mg_0.1 µg/mL	0.015527767	90.7
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
D_Test Iscador Qu 5 mg_500 µg/mL	0.013341404	88.6	D_Test Iscador Qu 5 mg_500 µg/mL	0.012937646	75.6
D_Test Iscador Qu 5 mg_100 µg/mL	0.013205066	87.7	D_Test Iscador Qu 5 mg_100 µg/mL	0.014724655	86.0
D_Test Iscador Qu 5 mg_10 µg/mL	0.015431764	102.5	D_Test Iscador Qu 5 mg_10 µg/mL	0.013770358	80.4
D_Test Iscador Qu 5 mg_5 µg/mL	0.013335287	88.6	D_Test Iscador Qu 5 mg_5 µg/mL	0.016662382	97.3
D_Test Iscador Qu 5 mg_1 µg/mL	0.012561886	83.5	D_Test Iscador Qu 5 mg_1 µg/mL	0.015424235	90.1
D_Test Iscador Qu 5 mg_0.1 µg/mL	0.013288851	88.3	D_Test Iscador Qu 5 mg_0.1 µg/mL	0.016091145	94.0
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
D_Test Iscador M 5 mg_500 µg/mL	0.011586939	77.0	D_Test Iscador M 5 mg_500 µg/mL	0.013112596	76.6
D_Test Iscador M 5 mg_100 µg/mL	0.013301942	88.4	D_Test Iscador M 5 mg_100 µg/mL	0.013860267	80.9
D_Test Iscador M 5 mg_10 µg/mL	0.014062342	93.4	D_Test Iscador M 5 mg_10 µg/mL	0.01305638	76.3
D_Test Iscador M 5 mg_5 µg/mL	0.014895997	99.0	D_Test Iscador M 5 mg_5 µg/mL	0.014397467	84.1
D_Test Iscador M 5 mg_1 µg/mL	0.013970371	92.8	D_Test Iscador M 5 mg_1 µg/mL	0.013754865	80.3
D_Test Iscador M 5 mg_0.1 µg/mL	0.014813049	98.4	D_Test Iscador M 5 mg_0.1 µg/mL	0.0139601	81.5
		% metabolite vs NC			% metabolite vs NC
D_Negative Control 1-1_no inhibitors	0.015269822	101.4	D_Negative Control 1-1_no inhibitors	0.016992498	99.2
D_Negative Control 1-2_no inhibitors	0.015064957	100.1	D_Negative Control 1-2_no inhibitors	0.016852928	98.4
D_Negative Control 1-3_no inhibitors	0.014820281	98.5	D_Negative Control 1-3_no inhibitors	0.01752154	102.3
D_Negative Control 2_no inhibitors/no microsomes	7.94889E-05	0.53	D_Negative Control 2_no inhibitors/no microsomes	7.84442E-05	0.46
D_Negative Control 3_no inhibitors/no microsomes	6.36886E-05	0.42	D_Negative Control 3_no inhibitors/no microsomes	4.97233E-05	0.29
		% metabolite vs NC			% metabolite vs NC
Average Negative controls	0.015051687		Average Negative controls	0.017122322	100

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Assay III			Mean	SD	SE
Dextrorphan (metabolite)					
	Peak Area Ratio	% metabolite vs NC			
D_Test Iscador P 10 mg_500 µg/mL	0.141899671	91.7	84.5	14.8	8.53
D_Test Iscador P 10 mg_100 µg/mL	0.152889254	98.8	99.8	4.84	2.79
D_Test Iscador P 10 mg_10 µg/mL	0.157569351	101.8	98.9	3.52	2.03
D_Test Iscador P 10 mg_5 µg/mL	0.157739425	101.9	100.2	1.59	0.92
D_Test Iscador P 10 mg_1 µg/mL	0.15607049	100.8	101.2	0.57	0.33
D_Test Iscador P 10 mg_0.1 µg/mL	0.163160198	105.4	98.1	7.37	4.25
	Peak Area Ratio	% metabolite vs NC			
D_Test Iscador Qu 5 mg_500 µg/mL	0.152076673	98.3	87.5	11.39	6.58
D_Test Iscador Qu 5 mg_100 µg/mL	0.157943709	102.1	91.9	8.81	5.09
D_Test Iscador Qu 5 mg_10 µg/mL	0.163418313	105.6	96.2	13.73	7.93
D_Test Iscador Qu 5 mg_5 µg/mL	0.157926864	102.0	96.0	6.82	3.94
D_Test Iscador Qu 5 mg_1 µg/mL	0.14513121	93.8	89.1	5.23	3.02
D_Test Iscador Qu 5 mg_0.1 µg/mL	0.156292574	101.0	94.4	6.36	3.67
	Peak Area Ratio	% metabolite vs NC			
D_Test Iscador M 5 mg_500 µg/mL	0.148206864	95.8	83.1	10.96	6.33
D_Test Iscador M 5 mg_100 µg/mL	0.149782759	96.8	88.7	7.92	4.57
D_Test Iscador M 5 mg_10 µg/mL	0.155753751	100.6	90.1	12.53	7.23
D_Test Iscador M 5 mg_5 µg/mL	0.147654642	95.4	92.8	7.77	4.49
D_Test Iscador M 5 mg_1 µg/mL	0.150028031	96.9	90.0	8.65	4.99
D_Test Iscador M 5 mg_0.1 µg/mL	0.15322061	99.0	93.0	9.92	5.73
		% metabolite vs NC			
0_Negative Control 1-1_no inhibitor	0.151833594	98.1	99.6	1.70	0.98
0_Negative Control 1-2_no inhibitor	0.148491204	95.9	98.2	2.09	1.20
0_Negative Control 1-3_no inhibitor	0.163975889	106.0	102.2	3.74	2.16
0_Negative Control 2_no inhibitors/no micros	0.010673354	6.90	2.63	3.70	2.13
0_Negative Control 3_no inhibitors/no micros	0.009634672	6.23	2.31	3.39	1.96
		% metabolite vs NC			
Average Negative controls	0.154766896	100	100.0	0.0	0.00

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig S2_CYP2D6 inhibition assays by Quinidin_Endoxifen_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
Endoxifen (metabolite)			Endoxifen (metabolite)		
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
D_Positive Control_Quinidine 100 uM	0.00	0.00	D_Positive Control_Quinidine 100 uM	0.00	0.00
D_Positive Control_Quinidine 10 uM	2.01993E-05	49.9	D_Positive Control_Quinidine 10 uM	6.51387E-06	39.5
D_Positive Control_Quinidine 5 uM	2.20493E-05	54.5	D_Positive Control_Quinidine 5 uM	7.6237E-06	46.3
D_Positive Control_Quinidine 2 uM	2.51806E-05	62.2	D_Positive Control_Quinidine 2 uM	8.07856E-06	49.0
D_Positive Control_Quinidine 1 uM	2.55626E-05	63.2	D_Positive Control_Quinidine 1 uM	9.69827E-06	58.9
D_Positive Control_Quinidine 0.1 uM	2.84574E-05	70.3	D_Positive Control_Quinidine 0.1 uM	1.38156E-05	83.8
D_Negative Control 1-1_no inhibitors	4.4456E-05	109.8	D_Negative Control 1-1_no inhibitors	1.6213E-05	98.4

Assay III			Mean	SD	SE
Endoxifen (metabolite)					
	Peak Area Ratio	% metabolite vs NC			
D_Positive Control_Quinidine 100 uM	7.35921E-06	16.5	5.51	9.55	5.51
D_Positive Control_Quinidine 10 uM	1.15879E-05	26.0	38.5	12.0	6.91
D_Positive Control_Quinidine 5 uM	2.17554E-05	48.9	49.9	4.19	2.42
D_Positive Control_Quinidine 2 uM	2.33783E-05	52.5	54.6	6.83	3.94
D_Positive Control_Quinidine 1 uM	2.52793E-05	56.8	59.6	3.23	1.87
D_Positive Control_Quinidine 0.1 uM	3.95828E-05	89.0	81.0	9.64	5.57
D_Negative Control 1-1_no inhibitors	4.64481E-05	104.4	104.2	5.72	3.30

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig S3_CYP2D6 inhibition assays by Quinidine_Dextrorphan_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
Endoxifen (metabolite)			Endoxifen (metabolite)		
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
D_Positive Control_Quinidine 100 uM	0.000212752	1.41	D_Positive Control_Quinidine 100 uM	0.000274118	1.60
D_Positive Control_Quinidine 10 uM	0.000683177	4.54	D_Positive Control_Quinidine 10 uM	0.000820142	4.79
D_Positive Control_Quinidine 5 uM	0.00114825	7.63	D_Positive Control_Quinidine 5 uM	0.001265521	7.39
D_Positive Control_Quinidine 2 uM	0.002349049	15.6	D_Positive Control_Quinidine 2 uM	0.002366089	13.8
D_Positive Control_Quinidine 1 uM	0.003780586	25.1	D_Positive Control_Quinidine 1 uM	0.004402311	25.7
D_Positive Control_Quinidine 0.1 uM	0.010918579	72.5	D_Positive Control_Quinidine 0.1 uM	0.013487882	78.8
D_Negative Control 1-1_no inhibitors	0.015269822	101.4	D_Negative Control 1-1_no inhibitors	0.016992498	99.2

Assay III			Mean	SD	SE
Endoxifen (metabolite)					
	Peak Area Ratio	% metabolite vs NC			
D_Positive Control_Quinidine 100 uM	0.006682118	4.32	2.44	1.63	0.938
D_Positive Control_Quinidine 10 uM	0.01072527	6.93	5.42	1.31	0.759
D_Positive Control_Quinidine 5 uM	0.014205437	9.18	8.07	0.97	0.560
D_Positive Control_Quinidine 2 uM	0.023559882	15.2	14.9	0.94	0.543
D_Positive Control_Quinidine 1 uM	0.039926759	25.8	25.5	0.37	0.214
D_Positive Control_Quinidine 0.1 uM	0.12451359	80.5	77.3	4.17	2.407
D_Negative Control 1-1_no inhibitors	0.151833594	98.1	99.6	1.70	0.982

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig S4_CYP3A4-5 inhibition assays_6BetaHT_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
6BHT (metabolite)			6BHT (metabolite)		
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Test Iscador P 10 mg_500 µg/mL	0.00918256	70.3	TE_Test Iscador P 10 mg_500 µg/mL	0.008947753	36.0
TE_Test Iscador P 10 mg_100 µg/mL	0.011075095	84.8	TE_Test Iscador P 10 mg_100 µg/mL	0.018450672	74.3
TE_Test Iscador P 10 mg_10 µg/mL	0.018078525	138.4	TE_Test Iscador P 10 mg_10 µg/mL	-	-
TE_Test Iscador P 10 mg_5 µg/mL	0.019729599	151.0	TE_Test Iscador P 10 mg_5 µg/mL	0.011266651	45.4
TE_Test Iscador P 10 mg_1 µg/mL	-	-	TE_Test Iscador P 10 mg_1 µg/mL	0.021306142	85.8
TE_Test Iscador P 10 mg_0.1 µg/mL	-	-	TE_Test Iscador P 10 mg_0.1 µg/mL	0.02855527	114.9
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Test Iscador Qu 5 mg_500 µg/mL	0.00320392	24.5	TE_Test Iscador Qu 5 mg_500 µg/mL	0.006491894	26.1
TE_Test Iscador Qu 5 mg_100 µg/mL	0.006875019	52.6	TE_Test Iscador Qu 5 mg_100 µg/mL	0.007022276	28.3
TE_Test Iscador Qu 5 mg_10 µg/mL	0.01305385	99.9	TE_Test Iscador Qu 5 mg_10 µg/mL	-	-
TE_Test Iscador Qu 5 mg_5 µg/mL	-	-	TE_Test Iscador Qu 5 mg_5 µg/mL	0.02154394	86.7
TE_Test Iscador Qu 5 mg_1 µg/mL	0.013564209	103.8	TE_Test Iscador Qu 5 mg_1 µg/mL	0.016468292	66.3
TE_Test Iscador Qu 5 mg_0.1 µg/mL	-	-	TE_Test Iscador Qu 5 mg_0.1 µg/mL	0.018371759	74.0
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Test Iscador M 5 mg_500 µg/mL	0.007739921	59.2	TE_Test Iscador M 5 mg_500 µg/mL	0.009047538	36.4
TE_Test Iscador M 5 mg_100 µg/mL	0.006545399	50.1	TE_Test Iscador M 5 mg_100 µg/mL	0.010206931	41.1
TE_Test Iscador M 5 mg_10 µg/mL	-	-	TE_Test Iscador M 5 mg_10 µg/mL	-	-
TE_Test Iscador M 5 mg_5 µg/mL	0.007768031	59.5	TE_Test Iscador M 5 mg_5 µg/mL	-	-
TE_Test Iscador M 5 mg_1 µg/mL	0.013688362	104.8	TE_Test Iscador M 5 mg_1 µg/mL	0.021213463	85.4
TE_Test Iscador M 5 mg_0.1 µg/mL	0.013350574	102.2	TE_Test Iscador M 5 mg_0.1 µg/mL	-	-
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Negative Control 1-1_no inhibitors	0.012655482	96.9	TE_Negative Control 1-1_no inhibitors	-	-
TE_Negative Control 1-2_no inhibitors	-	-	TE_Negative Control 1-2_no inhibitors	-	-
TE_Negative Control 1-3_no inhibitors	0.013476017	103.1	TE_Negative Control 1-3_no inhibitors	0.02484259	-
TE_Negative Control 2_no inhibitors/no microsomes	0.00	0.00	TE_Negative Control 2_no inhibitors/no microsomes	0.00	0.00
TE_Negative Control 3_no inhibitors/no microsomes/no P	0.00	0.00	TE_Negative Control 3_no inhibitors/no microsomes/no P	0.00	0.00
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
		0			
Average Negative controls	0.01306575	100	Average Negative controls	0.02484259	100.0

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Assay III			Mean	SD	SE
6BHT (metabolite)					
	Peak Area Ratio	% metabolite vs NC			
TE_Test Iscador P 10 mg_500 µg/mL	0.054987651	55.5	53.9	17.19	9.92
TE_Test Iscador P 10 mg_100 µg/mL	-	-	79.5	7.42	5.25
TE_Test Iscador P 10 mg_10 µg/mL	0.060730912	61.3	100	54.48	38.5
TE_Test Iscador P 10 mg_5 µg/mL	0.098856935	99.8	98.7	52.83	30.5
TE_Test Iscador P 10 mg_1 µg/mL	-	-	85.8	-	-
TE_Test Iscador P 10 mg_0.1 µg/mL	0.104865961	105.9	110	6.41	4.53
	Peak Area Ratio	% metabolite vs NC			
TE_Test Iscador Qu 5 mg_500 µg/mL	0.034597475	34.9	28.5	5.60	3.23
TE_Test Iscador Qu 5 mg_100 µg/mL	0.047440611	47.9	42.9	12.91	7.46
TE_Test Iscador Qu 5 mg_10 µg/mL	0.068221993	68.9	84.4	21.94	15.5
TE_Test Iscador Qu 5 mg_5 µg/mL	0.073969412	74.7	80.7	8.51	6.02
TE_Test Iscador Qu 5 mg_1 µg/mL	0.097044188	98.0	89.4	20.19	11.7
TE_Test Iscador Qu 5 mg_0.1 µg/mL	-	-	74.0	-	-
	Peak Area Ratio	% metabolite vs NC			
TE_Test Iscador M 5 mg_500 µg/mL	0.057689422	58.2	51.3	12.9	7.45
TE_Test Iscador M 5 mg_100 µg/mL	0.052339284	52.8	48.0	6.2	3.55
TE_Test Iscador M 5 mg_10 µg/mL	0.058158691	58.7	58.7	-	-
TE_Test Iscador M 5 mg_5 µg/mL	-	-	59.5	-	-
TE_Test Iscador M 5 mg_1 µg/mL	-	-	95.1	13.7	9.69
TE_Test Iscador M 5 mg_0.1 µg/mL	0.083094595	83.9	93.0	12.9	9.14
	Peak Area Ratio	% metabolite vs NC			
E_Negative Control 1-1_no inhibitor	0.089878988	90.7	93.8	4.32	3.06
E_Negative Control 1-2_no inhibitor	-	-	-	-	-
E_Negative Control 1-3_no inhibitor	0.108213975	109.3	106.2	4.32	2.50
ative Control 2_no inhibitors/no mic	0.00	0.00	0.0	0.00	0.00
ontrol 3_no inhibitors/no microsom	0.00	0.00	0.0	0.00	0.00
	Peak Area Ratio	% metabolite vs NC			
Average Negative controls	0.099046481	100	100.0	0.00	0.00

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig S5_CYP3A4-5 inhibition assays by Ketoconazole_Endoxifen_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
Endoxifen (metabolite)			Endoxifen (metabolite)		
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Positive Control_KETOCONAZOLE 100 uM	1.54127E-06	3.73	TE_Positive Control_KETOCONAZOLE 100 uM	0.00	0.00
TE_Positive Control_KETOCONAZOLE 10 uM	7.62948E-06	18.5	TE_Positive Control_KETOCONAZOLE 10 uM	4.26237E-06	10.67
TE_Positive Control_KETOCONAZOLE 5 uM	1.02207E-05	24.7	TE_Positive Control_KETOCONAZOLE 5 uM	-	-
TE_Positive Control_KETOCONAZOLE 2 uM	1.1345E-05	27.5	TE_Positive Control_KETOCONAZOLE 2 uM	1.52932E-05	38.30
TE_Positive Control_KETOCONAZOLE 1 uM	1.62545E-05	39.4	TE_Positive Control_KETOCONAZOLE 1 uM	2.38592E-05	59.7
TE_Positive Control_KETOCONAZOLE 0.1 uM	4.00021E-05	96.9	TE_Positive Control_KETOCONAZOLE 0.1 uM	-	-

Assay III			Mean	SD	SE
Endoxifen (metabolite)					
	Peak Area Ratio	% metabolite vs NC			
TE_Positive Control_KETOCONAZOLE 100 uM	0.00	0.00	1.24	2.15	1.244
TE_Positive Control_KETOCONAZOLE 10 uM	5.39611E-06	12.36	13.8	4.10	2.370
TE_Positive Control_KETOCONAZOLE 5 uM	9.03534E-06	20.69	22.7	2.87	2.028
TE_Positive Control_KETOCONAZOLE 2 uM	1.68183E-05	38.5	34.8	6.31	3.646
TE_Positive Control_KETOCONAZOLE 1 uM	2.18172E-05	50.0	49.7	10.20	5.888
TE_Positive Control_KETOCONAZOLE 0.1 uM	-	-	96.9	-	-

Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)-Endoxifen and Cytochrome P450 3A4/5 and 2D6 *in vitro*

Data Fig S6_CYP3A4-5 inhibition assays by Ketoconazole_6BetaHT_Metabolite_Mean of 3 assays_SD_SE

Assay I			Assay II		
Endoxifen (metabolite)			Endoxifen (metabolite)		
	Peak Area Ratio	% metabolite vs NC		Peak Area Ratio	% metabolite vs NC
TE_Positive Control_KETOCONAZOLE 100 uM	0.000544197	4.17	TE_Positive Control_KETOCONAZOLE 100 uM	0.00	0.00
TE_Positive Control_KETOCONAZOLE 10 uM	0.000649502	4.97	TE_Positive Control_KETOCONAZOLE 10 uM	0.00	0.00
TE_Positive Control_KETOCONAZOLE 5 uM	0.001170492	8.96	TE_Positive Control_KETOCONAZOLE 5 uM	0.000928438	4.77
TE_Positive Control_KETOCONAZOLE 2 uM	0.001259259	9.64	TE_Positive Control_KETOCONAZOLE 2 uM	0.001192394	6.13
TE_Positive Control_KETOCONAZOLE 1 uM	0.002362481	18.08	TE_Positive Control_KETOCONAZOLE 1 uM	0.002148023	11.04
TE_Positive Control_KETOCONAZOLE 0.1 uM	0.005440135	41.64	TE_Positive Control_KETOCONAZOLE 0.1 uM	-	-

Assay III			Mean	SD	SE
Endoxifen (metabolite)					
	Peak Area Ratio	% metabolite vs NC			
TE_Positive Control_KETOCONAZOLE 100 uM	0.003171883	3.20	2.46	2.18	1.259
TE_Positive Control_KETOCONAZOLE 10 uM	0.004942901	4.99	3.32	2.88	1.660
TE_Positive Control_KETOCONAZOLE 5 uM	0.002599058	2.62	5.45	3.22	1.860
TE_Positive Control_KETOCONAZOLE 2 uM	-	-	7.88	2.48	1.756
TE_Positive Control_KETOCONAZOLE 1 uM	0.015401216	15.55	14.89	3.57	2.061
TE_Positive Control_KETOCONAZOLE 0.1 uM	0.047996546	48.46	45.05	4.82	3.411