Spectroscopic data ofsynthesized compounds

3,7-dimethyl-1-[(6*E*)-5-oxo-7-(6-methoxynaphthyl)hept-6-en-1-yl]-3,7-dihydro-1*H*-purine-2,6-diones(mPTF1)

IR (KBr, cm^{-1}): 2946(-C-H stretch of CH_3), 1697(-C=O), 1662,1621(-C= N stretch), 1549 and 1483, 1458 (C=C).

^{1}H-NMR (Solvent DMSO,δ ppm): 1.6(bs, 4H, -CH_2-CH_2-), 2.74(2H, appeared as singlet instead of triplet),3.42(s, 3H, NCH_3), 3.85-3.95 (8H, broad singlet, here three protons of -OCH_3, three protons ofNCH_3 and two protons of aliphatic chain-CH_2- merged together and appeared as broad singlet), 6.95**(**d, 1H, *J*=16Hz, α,β-unsaturated system), 7.19**(**d, 1H, *J*=12Hz, naphthyl ring), 7.20(d, 1H, *J*=8 Hz, naphthyl ring), 7.35(d, 1H, *J*=8 Hz, naphthyl ring), 7.71**(**d, 1H, *J*=16Hz, α,β-unsaturated system),7.83(s, 1H, C_5-H of naphthyl ring), 7.85(d, 1H, *J*=12 Hz, naphthyl ring), 7.98(1H, s, imidazole ring) 8.13(s, 1H, C_1-H of naphthyl ring); LC-MS, [M^+], (m/z): 447(M+1, 96),

3,7-dimethyl-1-[(6*E*)-5-oxo-7-(2-methoxy-5-bromophenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*-purine-2,6-diones (mPTF2)

IR (KBr, cm^{-1}): 2931 & 2866(-C-H stretch of –CH_2-, CH_3), 1698(-C=O), 1658,1609(-C= N stretch), 1551 and 1485, 1454(C=C).

^{1}H-NMR (Solvent DMSO,δ ppm): 1.6(bs, 4H, -CH_2-CH_2-), 2.66(2H, appeared as broad singlet instead of triplet),3.29(s, 3H, NCH_3),3.41(s, 3H, NCH_3),3.88(s, 3H, OCH_3), 3.85(bs, 2H, -CH_2-), 6.90 **(**d, 1H, *J*=16Hz, α,β-unsaturated system), 6.98**(**d, 1H, *J*=8.8Hz, C_3-H of phenyl), 7.67**(**d, 1H, *J*=16Hz, α,β-unsaturated system), 7.47(d, 1H, *J*=8.8Hz, C_3-H of phenyl), 7.79(d, 1H, *J*=2.4 Hz, coupling of C_6-H with C_4-Hof phenyl ring), 7.90(1H, s, imidazole ring); LC-MS, [M^+], (m/z): 477(M+2, 75),

3,7-dimethyl-1-[(6*E*)-5-oxo-7-(3,4-dimethoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*-purine-2,6-diones (mPTF5)

IR (KBr, cm^{-1}): 3072(-Ar-H stretch), 2969, 2946 & 2893(-C-H stretch of-CH_2-, CH_3), 1703,1686(-C=O), 1662,1589(-C= N stretch), 1550 and 1491, 1458(C=C).

^{1}H-NMR (Solvent $CDCl_3$, δ ppm): 1.75(bs, 4H, -CH_2-CH_2-), 2.72(2H, appeared as broad singlet instead of triplet),3.57(s, 3H, NCH_3),3.84(s, 3H, NCH_3),3.89(s, 3H, OCH_3),3.98(s, 3H, OCH_3), 4.06(bs, 2H, -CH_2-),6.70 **(**d, 1H, *J*=16Hz, α,β-unsaturated system),

6.45**(**d, 1H, *J*=2.4Hz, coupling of C_2-H with C_6-H of phenyl ring), 6.52(dd, 1H, C_5-H of phenyl), 7.44**(**d, 1H, *J*=8.4, C6-H of phenyl ring), 7.82**(**d, 1H, *J*=16Hz, α,β-unsaturated system),7.49(1H, s, imidazole ring); LC-MS, [M^+], (m/z): 427(M+1, 80),

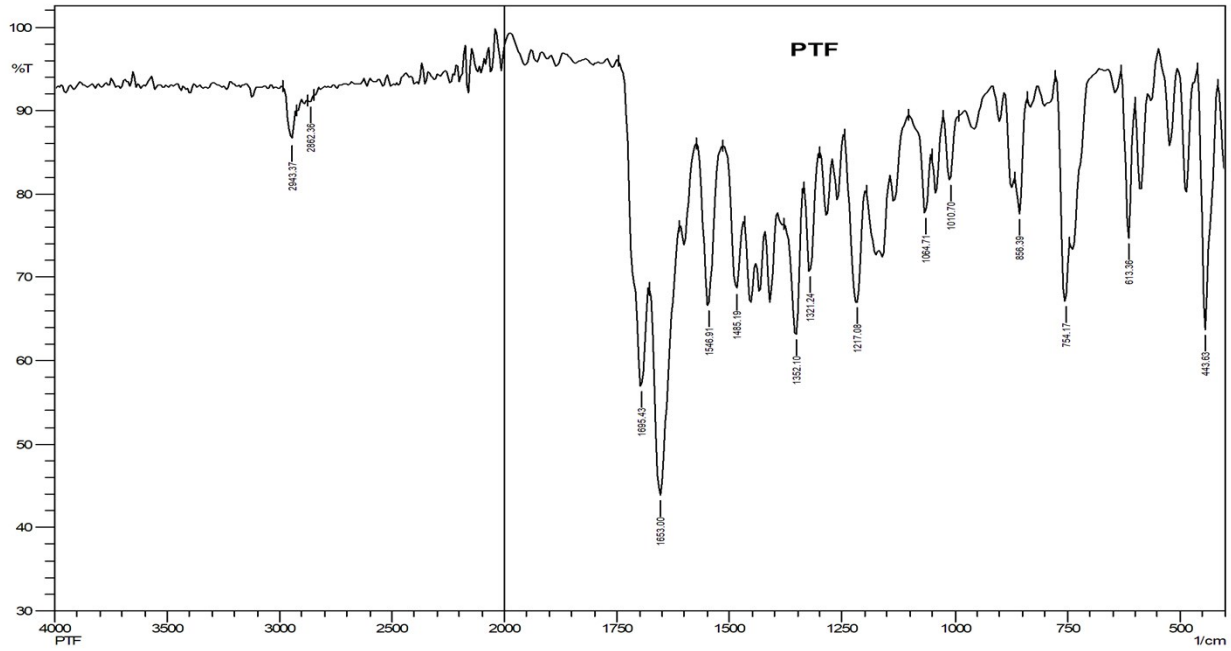
3,7-dimethyl-1-[(6*E*)-5-oxo-7-(4-methoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF6)

IR (KBr, cm^{-1}): 3086& 3040(-Ar-H stretch), 2949, 2877 & 2837(-C-H stretch of-CH_2-, CH_3), 1697(-C=O), 1632,1601(-C= N stretch), 1571 and 1550(C=C).

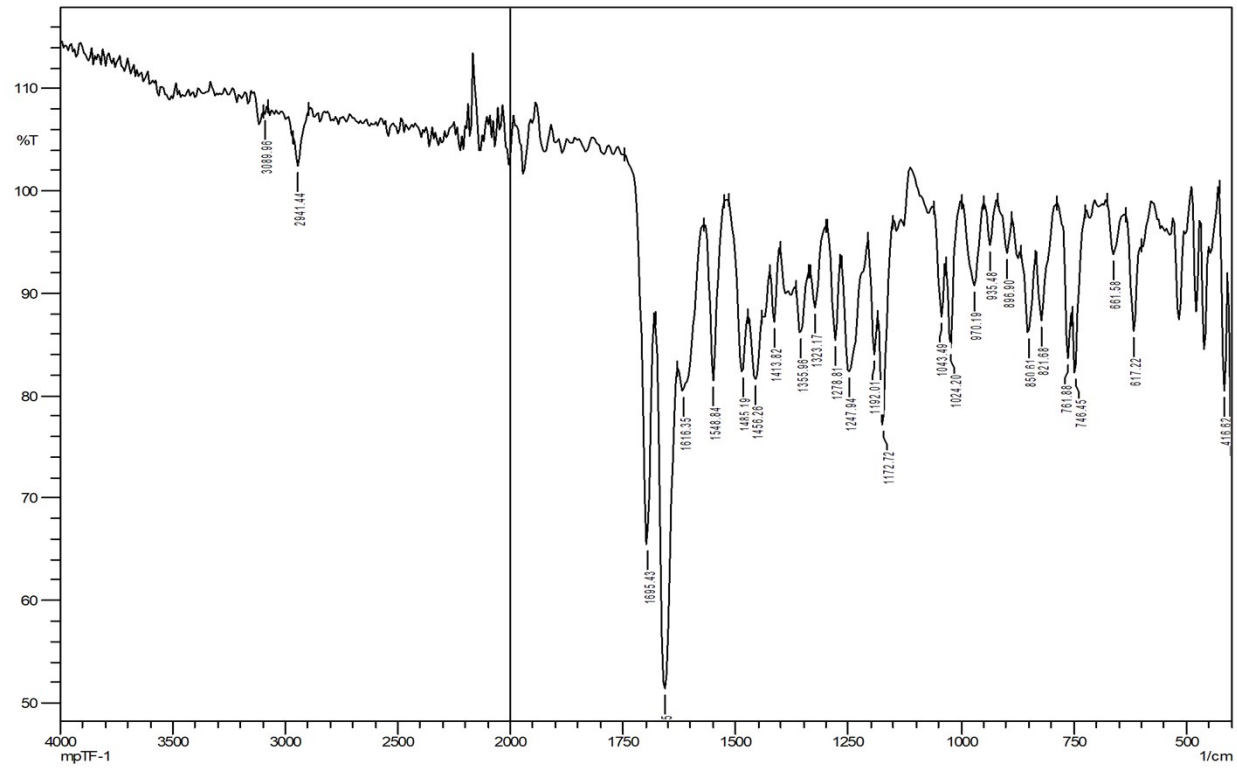
^{1}H-NMR (Solvent $CDCl_3$, δ ppm): 1.76(bs, 4H, -CH_2-CH_2-), 2.73(2H, appeared as broad singlet instead of triplet),3.59(s, 3H, NCH_3),3.86(s, 3H, NCH_3),4.00(s, 3H, OCH_3), 4.07(bs, 2H, -CH_2-), 6.65 **(**d, 1H, *J*=16Hz, α,β-unsaturated system),

6.93**(**d, 2H, *J*=28.8Hz, 4-methoxyphenyl), 7.2**(**d, 2H, *J*=7.2Hz, 4-methoxyphenyl), 7.53**(**d, 1H, *J*=16Hz, α,β-unsaturated system),7.56(s, 1H,, imidazole ring); LC-MS, [M^+], (m/z): 497(M+1, 75), 498(M+2, 26),

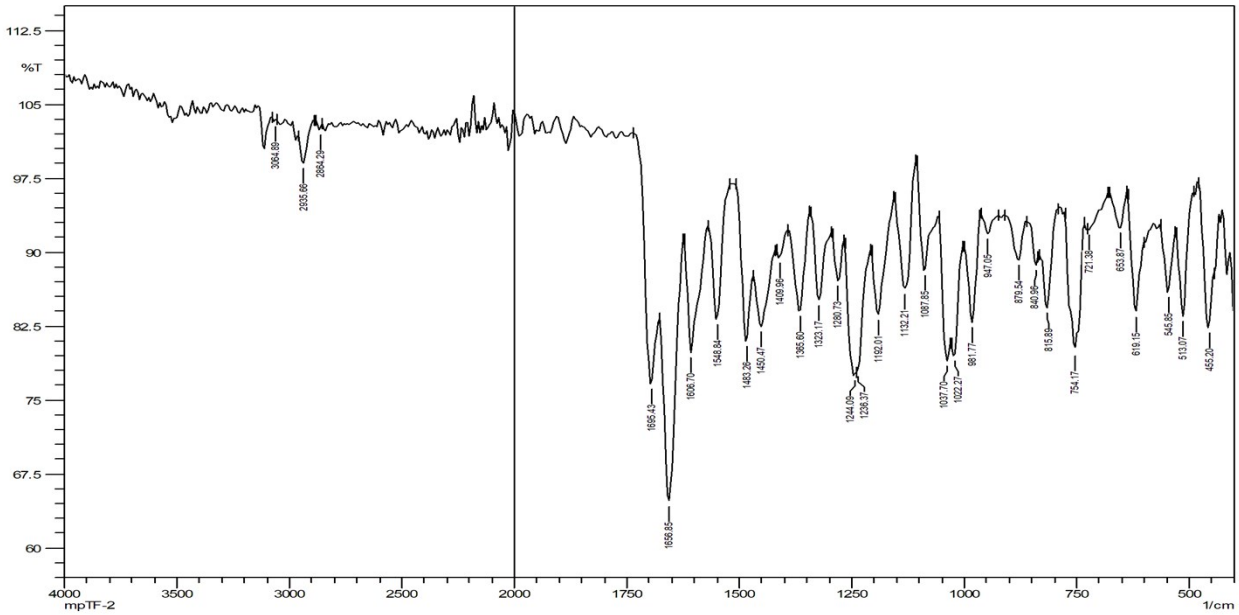
1. **FTIR – Spectrum of Pentoxifylline (PTF)**



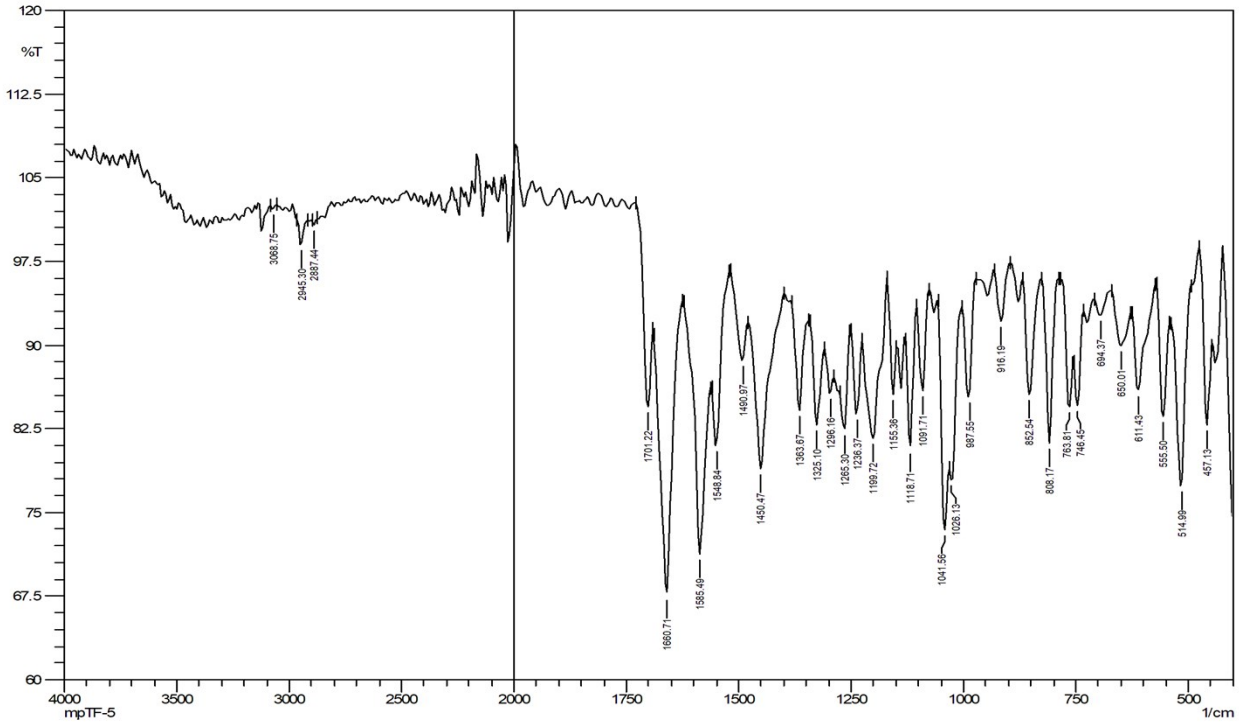
2. **FTIR – Spectrum of Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(6-methoxynaphthyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones(mPTF1)**



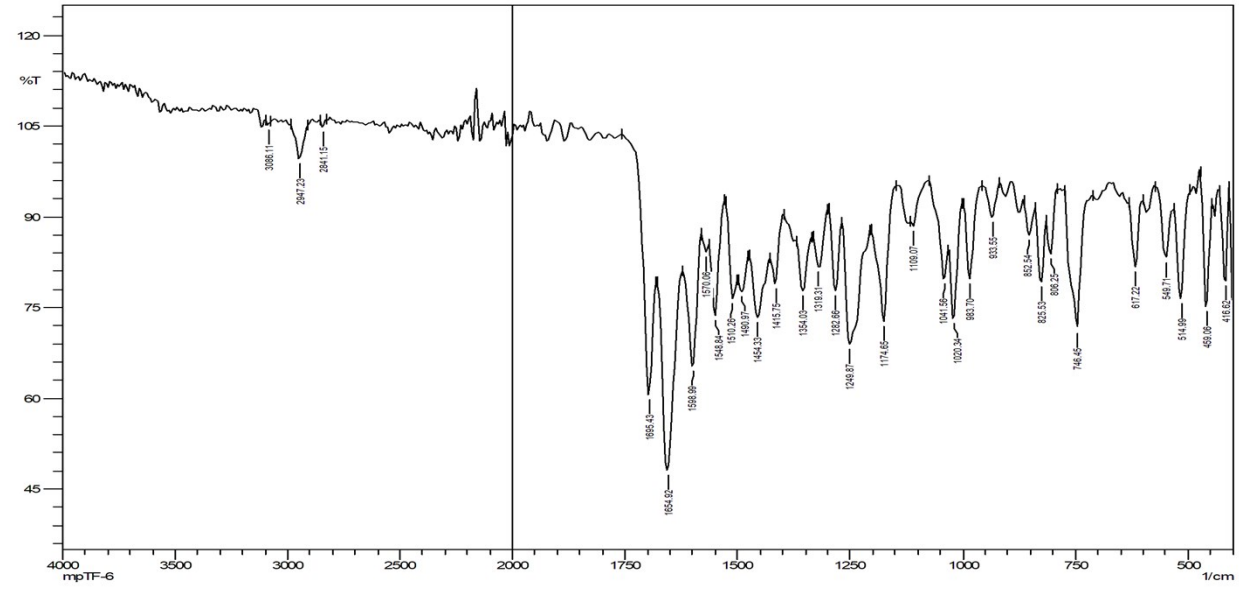
3. FTIR – Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(2-methoxy-5-bromophenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF2)



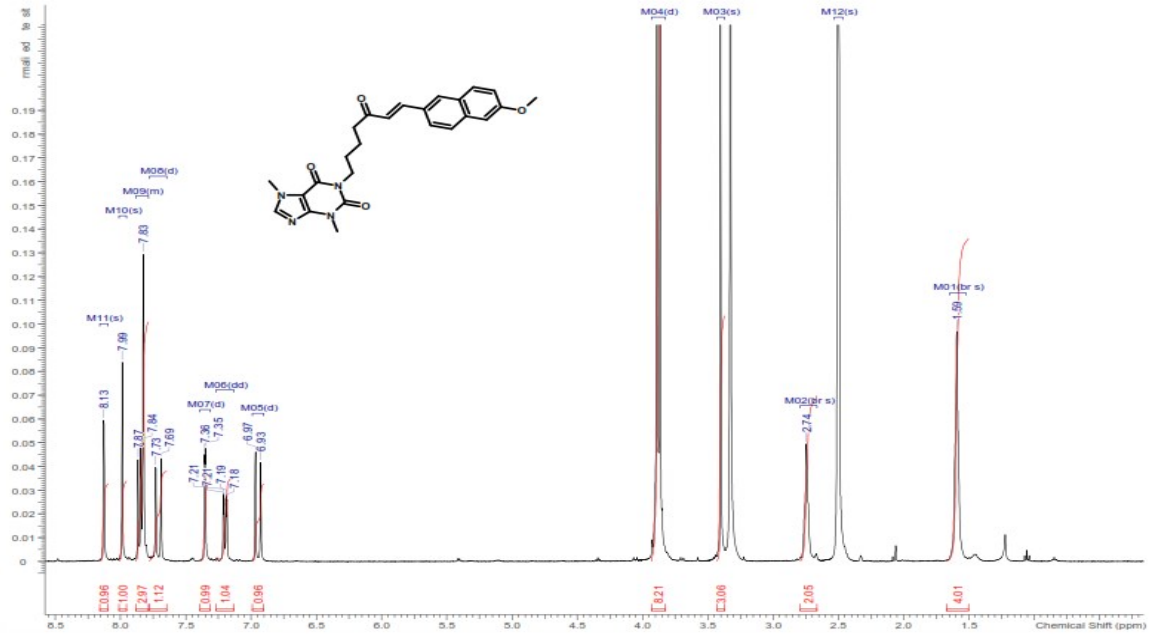
4. FTIR – Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(3,4-dimethoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF5)



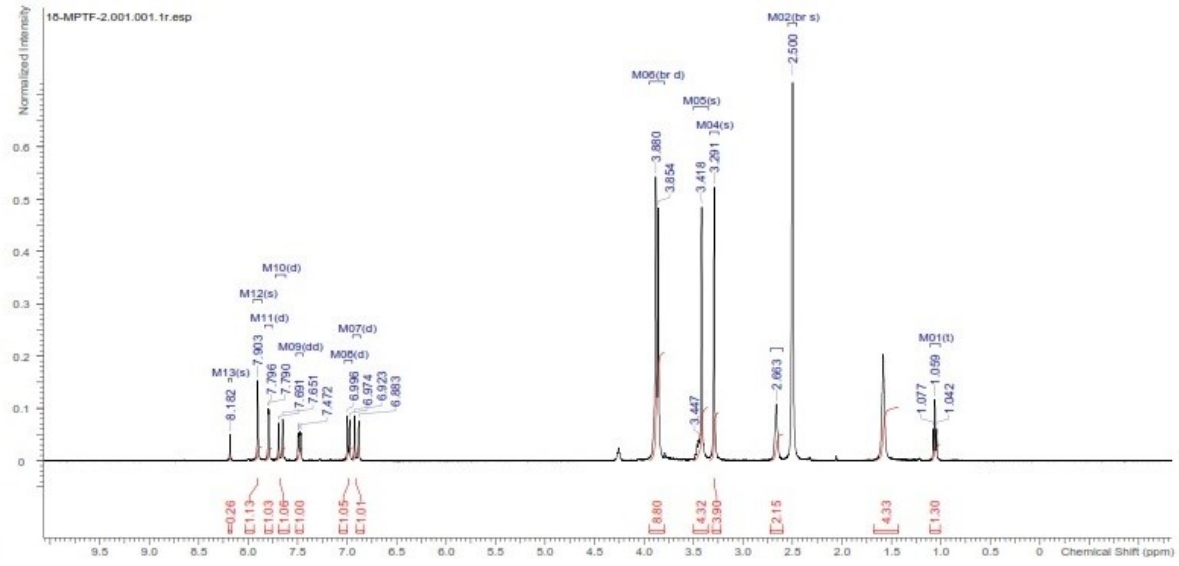
5. FTIR – Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(4-methoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF6)



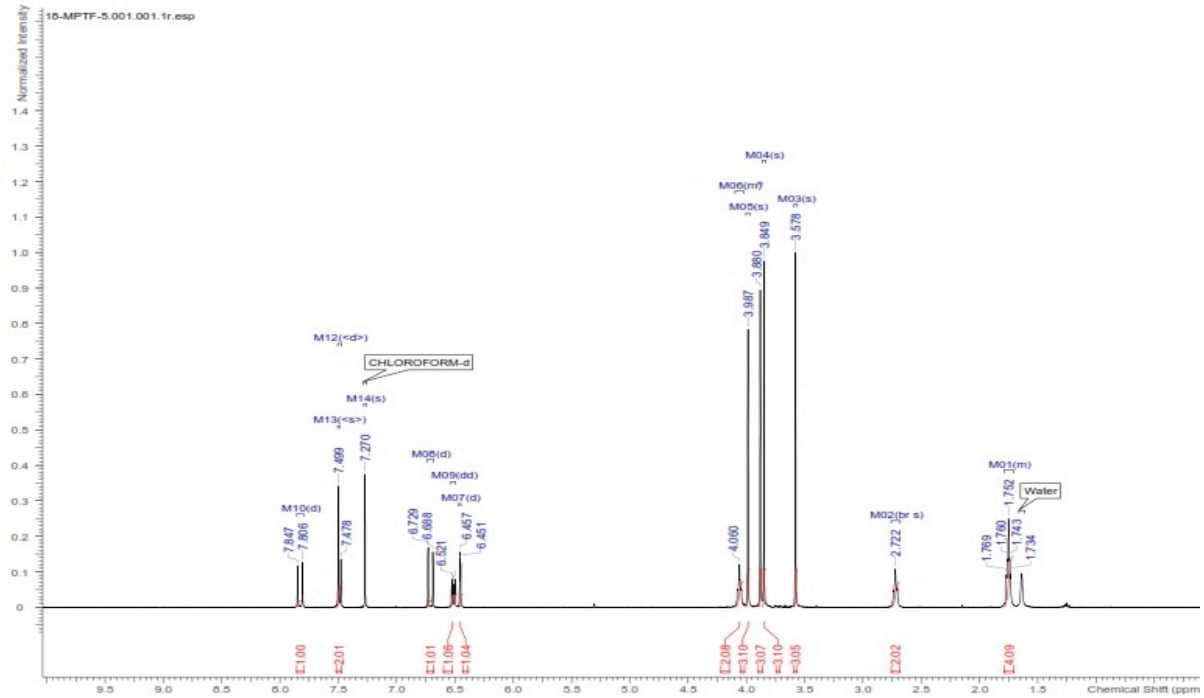
6. 1H-NMR Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(6-methoxynaphthyl)hept-6-en-1-yl]-3,7-dihydro-1*H*-purine-2,6-diones(mPTF1)



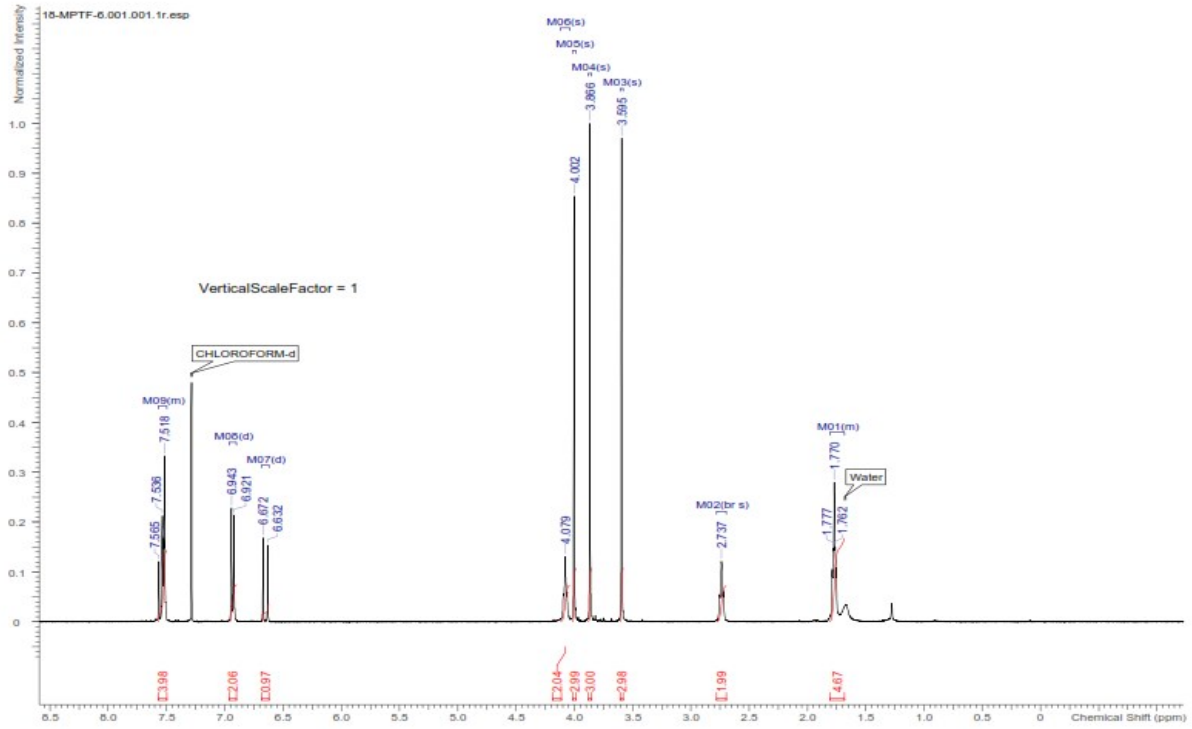
7. 1H-NMR Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(2-methoxy-5-bromophenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF2)



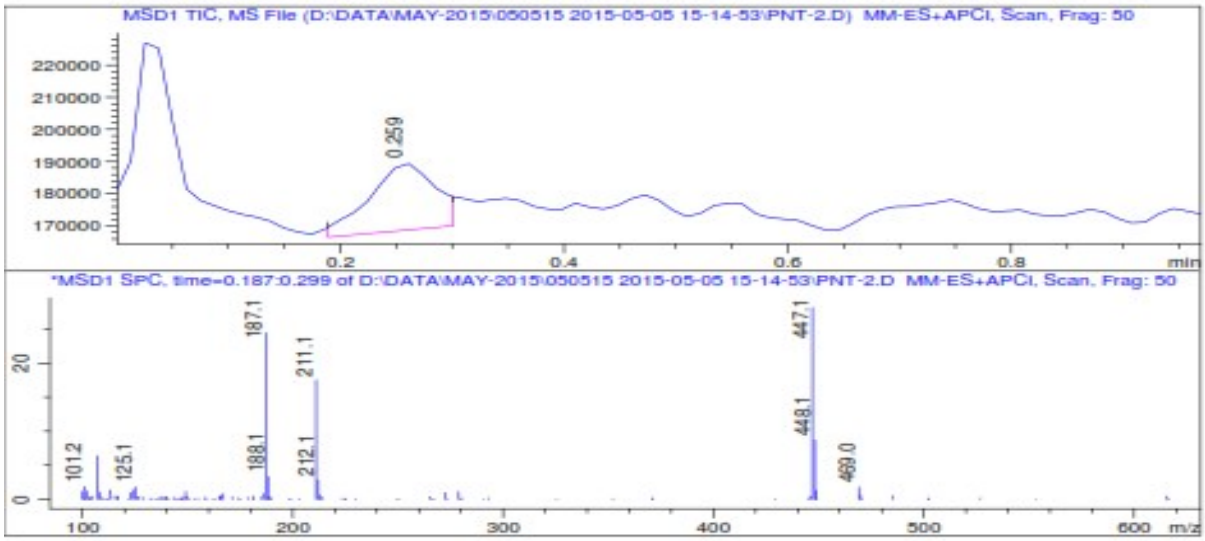
8. **1H-NMR Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(3,4-dimethoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF5)**



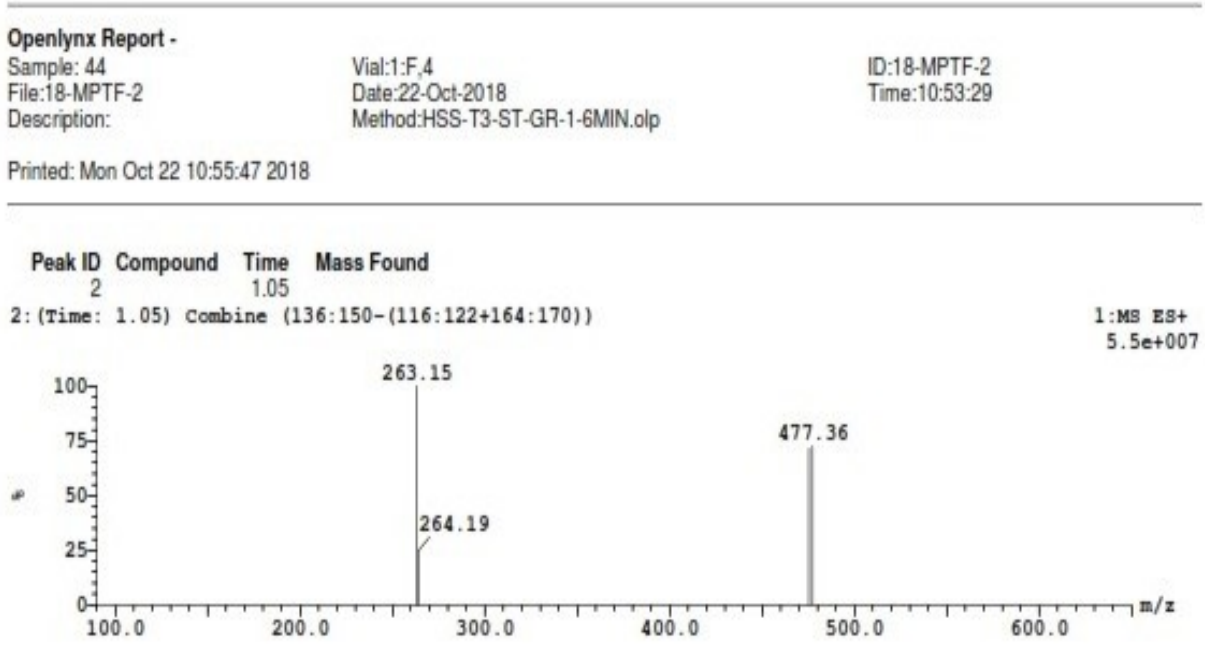
9. **1H-NMR Spectrum of FTIR – Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(4-methoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF6)**



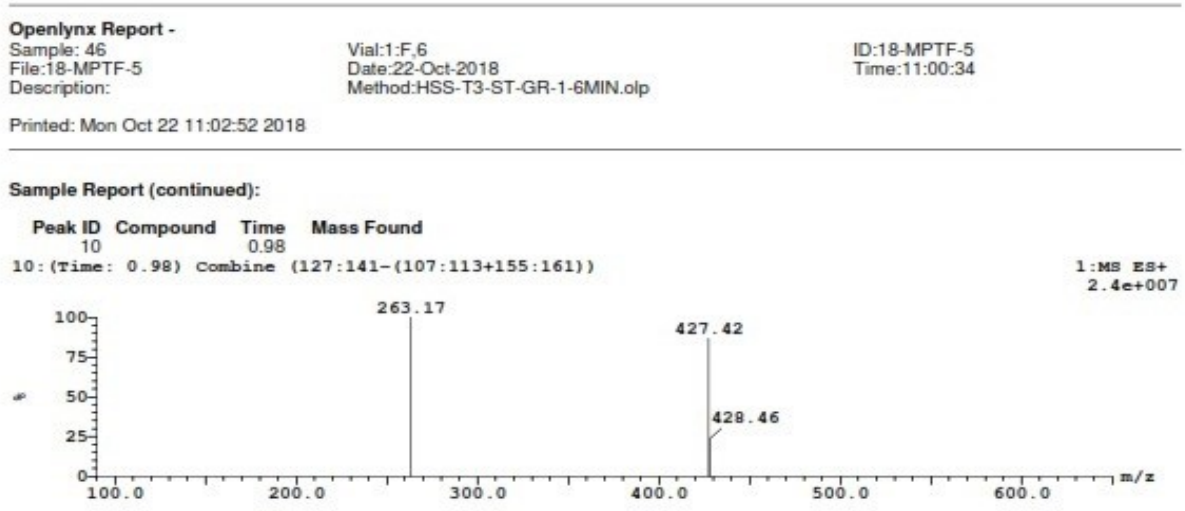
10. LC-Mass–Spectrum of Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(6-methoxynaphthyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones(mPTF1)



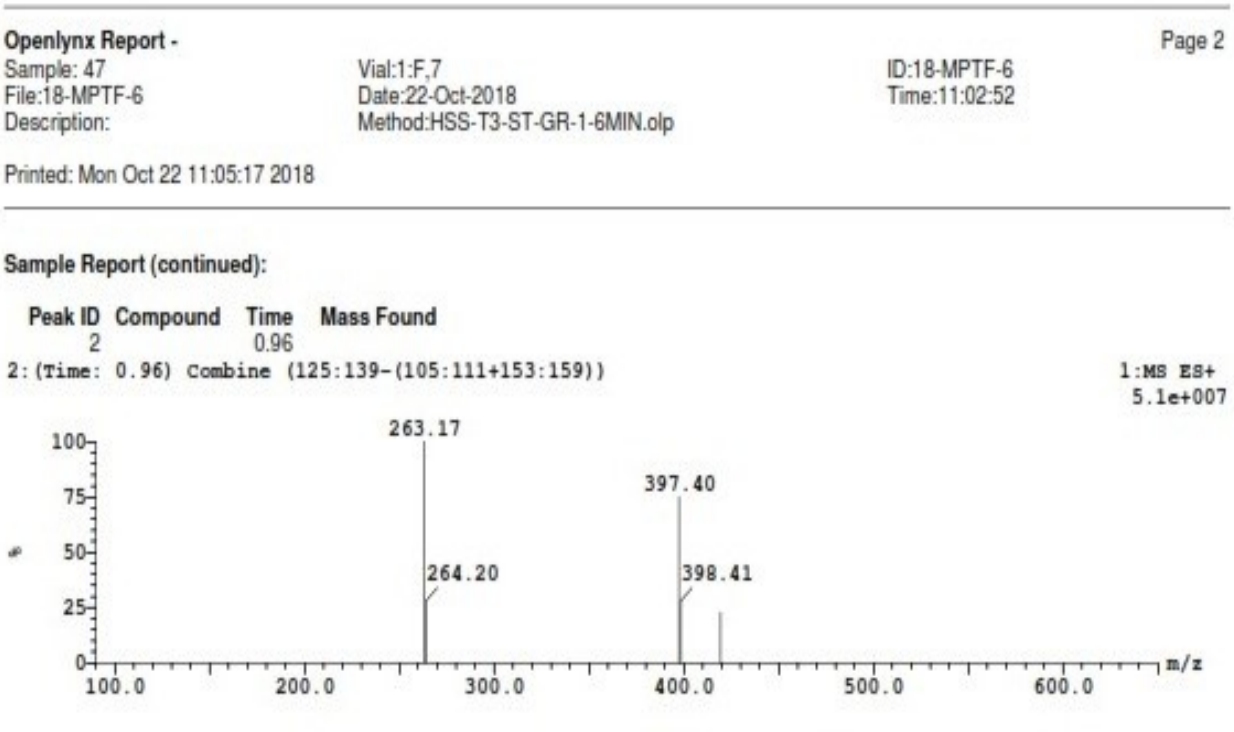
11. LC-Mass–Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(2-methoxy-5-bromophenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF2)



12. LC-Mass–Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(3,4-dimethoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF5)



13. LC-Mass–Spectrum of FTIR – Spectrum of 3,7-dimethyl-1-[(6*E*)-5-oxo-7-(4-methoxyphenyl)hept-6-en-1-yl]-3,7-dihydro-1*H*- purine-2,6-diones (mPTF6)



Supplementary Table 1: Physicochemical and ADMET properties of PTF and mPTF1 retrieved from admetSAR 2.0.

S. Table 1A: Physicochemical properties

	PTF	**mPTF1**
AlogP	0.19	3.05
H-Bond Acceptor	7	8
H-Bond Donor	0	0
Rotatable Bonds	5	8

S. Table 1B: ADMET properties

	PTF		mPTF1	
	Value	***Probability***	***Value***	***Probability***
ADMET predicted profile - classification				
Human Intestinal Absorption	+	0.9743	+	0.9268
Caco-2	+	0.5866	-	0.7321
Blood Brain Barrier	+	0.9942	+	0.9840
Human oral bioavailability	-	0.7714	-	0.5286
Subcellular localization	Mitochondria	0.7430	Mitochondria	0.7903
OATP2B1 inhibitor	-	0.8604	-	0.8562
OATP1B1 inhibitor	+	0.9413	+	0.9157
OATP1B3 inhibitor	+	0.9480	+	0.9266
MATE1 inhibitor	-	0.9800	-	0.9600
OCT2 inhibitor	+	0.5250	-	0.5140
BSEP inhibitor	-	0.9405	+	0.9447
P-glycoprotein inhibitor	-	0.6262	+	0.8717
P-glycoprotein substrate	-	0.7267	-	0.6057
CYP3A4 substrate	-	0.5540	+	0.6015
CYP2C9 substrate	-	1.0000	-	0.6193
CYP2D6 substrate	-	0.8849	-	0.8642
CYP3A4 inhibition	-	0.9827	-	0.6609
CYP2C9 inhibition	-	0.9518	-	0.8436
CYP2C19 inhibition	-	0.9313	-	0.7430
CYP2D6 inhibition	-	0.9430	-	0.9726
CYP1A2 inhibition	+	0.9107	+	0.6447
CYP inhibitory promiscuity	-	0.9010	+	0.6352
UGT catelyzed	-	0.0000	-	0.0000
Carcinogenicity (binary)	-	0.8857	-	0.7956
Carcinogenicity (trinary)	Non-required	0.7023	Non-required	0.6370
Eye corrosion	-	0.9899	-	0.9897
Eye irritation	-	0.9780	-	0.9765
Ames mutagenesis	-	0.7400	-	0.6400
Human either-a-go-go inhibition	+	0.8312	+	0.9565
micronuclear	+	0.7500	+	0.7300
Hepatotoxicity	+	0.5750	+	0.6250
Acute Oral Toxicity (c)	III	0.8132	III	0.7444
Estrogen receptor binding	-	0.8681	+	0.6089
Androgen receptor binding	-	0.7272	+	0.7691
Thyroid receptor binding	-	0.5214	+	0.6495
Glucocorticoid receptor binding	-	0.4643	+	0.7579
Aromatase binding	-	0.7638	+	0.5479
PPAR gamma	-	0.6274	+	0.5460
Honey bee toxicity	-	0.5769	-	0.5000
Biodegradation	+	0.5250	-	0.8500
Crustacean aquatic toxicity	-	0.5500	+	0.5100
Fish aquatic toxicity	-	0.5354	+	0.6910
ADMET predicted profile --- Regressions				
	Value	***Unit***	***Value***	***Unit***

Water solubility	-2.315	logS	-3.068	logS
Plasma protein binding	0.515	100%	0.951	100%
Acute Oral Toxicity	2.424	kg/mol	2.534	kg/mol
Tetrahymena pyriformis	1.216	pIGC50 (ug/L)	1.691	pIGC50 (ug/L)

Supplementary Table 2: Physicochemical, pharmacokinetic, and druglikeness predictions retrieved from SwissADME.

		PTF	mPTF1
Physicochemical Properties	Formula	$C_{13}H_{18}N_4O_3$	$C_{25}H_{26}N_4O_4$
	Molecular weight	278.31 g/mol	446.50 g/mol
	Num. heavy atoms	20	33
	Num. arom. heavy atoms	9	19
	Fraction Csp3	0.54	0.28
	Molar Refractivity	76.27	129.88
	TPSA	78.89 Å²	88.12 Å²
Lipophilicity	Log $P_{o/w}$ (iLOGP)	2.49	4.07
	Log $P_{o/w}$ (XLOGP3)	0.29	3.60
	Log $P_{o/w}$ (WLOGP)	0.19	2.94
	Log $P_{o/w}$ (MLOGP)	0.40	2.20
	Log $P_{o/w}$ (SILICOS-IT)	0.83	3.71
	Consensus Log $P_{o/w}$	0.84	3.30
Water Solubility	Log *S* (ESOL)	-1.75	-4.77
	Solubility	4.94e+00 mg/ml ; 1.77e-02 mol/l	7.51e-03 mg/ml ; 1.68e-05 mol/l
	Class	Very soluble	Moderately soluble
	Log *S* (Ali)	-1.51	-5.14
	Solubility	8.62e+00 mg/ml ; 3.10e-02 mol/l	3.25e-03 mg/ml ; 7.29e-06 mol/l
	Class	Very soluble	Moderately soluble
	Log *S* (SILICOS-IT)	-2.23	-6.14
	Solubility	1.63e+00 mg/ml ; 5.86e-03 mol/l	3.26e-04 mg/ml ; 7.31e-07 mol/l
	Class	Soluble	Poorly soluble
Pharmacokinetics	GI absorption	High	High
	BBB permeant	No	No
	P-gp substrate	No	No
	CYP1A2 inhibitor	No	No

	CYP2C19 inhibitor	No	Yes
	CYP2C9 inhibitor	No	Yes
	CYP2D6 inhibitor	No	No
	CYP3A4 inhibitor	No	Yes
	Log K_p (skin permeation)	-7.79 cm/s	-6.47 cm/s
Druglikeness	Lipinski	Yes; 0 violation	Yes; 0 violation
	Ghose	Yes	Yes
	Veber	Yes	Yes
	Egan	Yes	Yes
	Muegge	Yes	Yes
	Bioavailability Score	0.55	0.55
Medicinal Chemistry	PAINS (Pan Assay Interference Structures)	0 alert	0 alert
	Brenk	0 alert	1 alert: michael_acceptor_1
	Leadlikeness	Yes	No; 3 violations: MW>350, Rotors>7, XLOGP3>3.5
	Synthetic accessibility [1 (very easy to 10 (very difficult)]	2.44	3.33

Supplementary Table 3. ADMET properties of PTF and mPTF1 retrieved from pkCSM.

		PTF	mPTF1	
Property	**Model Name**	**Predicted Value**	**Predicted Value**	**Unit**
Absorption	Water solubility	-1.686	-3.201	Numeric (log mol/L)
	Caco2 permeability	1.45	1.223	Numeric (log Papp in 10^{-6} cm/s)
	Intestinal absorption (human)	91.086	100	Numeric (% Absorbed)
	Skin Permeability	-2.737	-2.735	Numeric (log Kp)
	P-glycoprotein substrate	Yes	Yes	Categorical (Yes/No)
	P-glycoprotein I inhibitor	No	Yes	Categorical (Yes/No)
	P-glycoprotein II inhibitor	No	Yes	Categorical (Yes/No)

Distribution	VDss (human)	0.205	0.32	Numeric (log L/kg)
	Fraction unbound (human)	0.673	0.205	Numeric (Fu)
	BBB permeability	-1.135	-1.414	Numeric (log BB)
	CNS permeability	-3.058	-2.808	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	No	Categorical (Yes/No)
	CYP3A4 substrate	No	Yes	Categorical (Yes/No)
	CYP1A2 inhibitor	No	No	Categorical (Yes/No)
	CYP2C19 inhibitor	No	Yes	Categorical (Yes/No)
	CYP2C9 inhibitor	No	Yes	Categorical (Yes/No)
	CYP2D6 inhibitor	No	No	Categorical (Yes/No)
	CYP3A4 inhibitor	No	Yes	Categorical (Yes/No)
Excretion	Total Clearance	0.693	0.823	Numeric (log ml/min/kg)
	Renal OCT2 substrate	No	Yes	Categorical (Yes/No)
Toxicity	AMES toxicity	Yes	No	Categorical (Yes/No)
	Max. tolerated dose (human)	0.687	0.432	Numeric (log mg/kg/day)
	hERG I inhibitor	No	No	Categorical (Yes/No)
	hERG II inhibitor	No	Yes	Categorical (Yes/No)
	Oral Rat Acute Toxicity (LD50)	2.644	2.696	Numeric (mol/kg)
	Oral Rat Chronic Toxicity (LOAEL)	1.538	1.101	Numeric (log mg/kg_bw/day)
	Hepatotoxicity	Yes	No	Categorical (Yes/No)
	Skin Sensitisation	No	No	Categorical (Yes/No)
	T. Pyriformis toxicity	0.285	0.285	Numeric (log ug/L)
	Minnow toxicity	1.343	-3.404	Numeric (log mM)