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Enhancement of metformin bioavailability by *Tinospora cordifolia* extracts: Insights into pharmacokinetic interactions

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Supplementary Figures

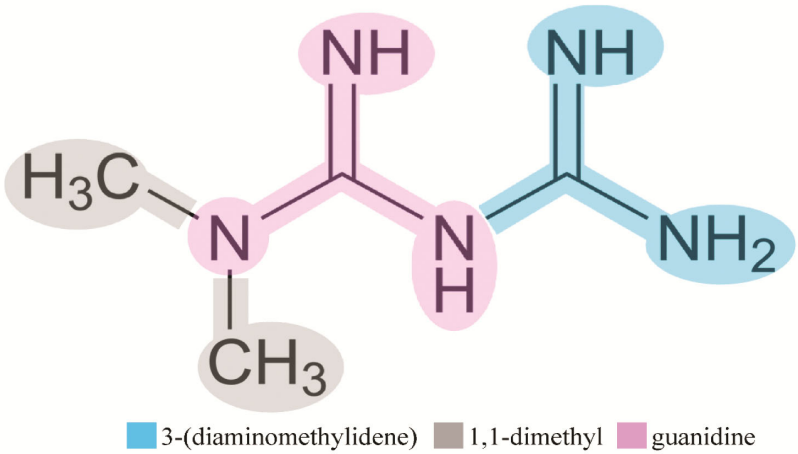

Fig. S1 — 2D Chemical structures of metformin {Abbreviation: MET; IPUAC Name: 3-(diaminomethylidene)-1,1-dimethylguanidine; SMILE: CN(C)C(=N)N=C(N)N and PubChem CID: 4091} with highlighted sub-structures.

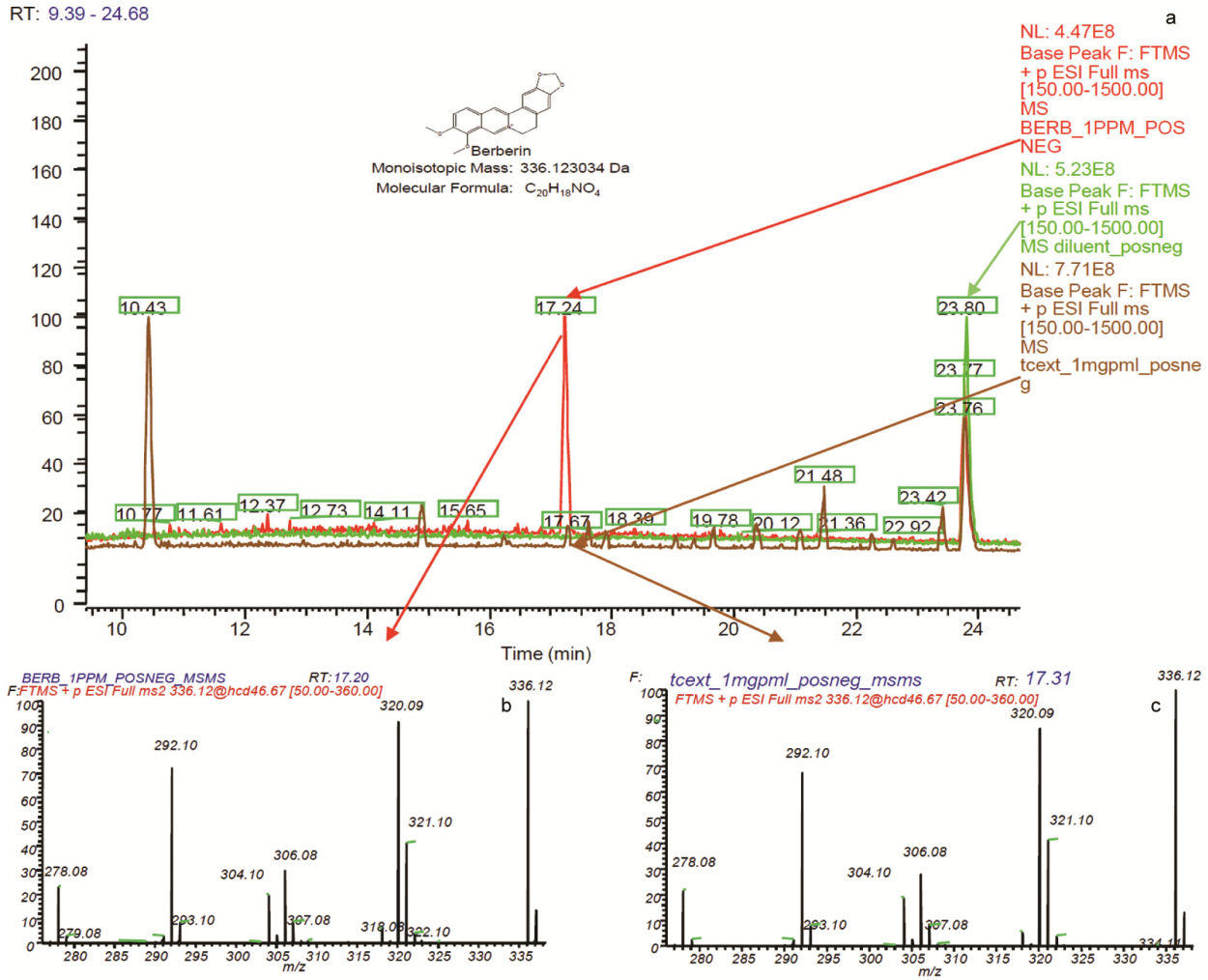

Fig. S2 — Overplayed chromatograms of berberine standard, TCE, and Diluent; a) Overlaid base peak chromatogram of 1 µg/mL berberine standard(red), base peak chromatogram of 1 mg/mL TCE(Brown), base peak chromatogram of Diluent, b) Product ion spectra for Berberine standard, and c) Product ion spectra for berberine in TCE.

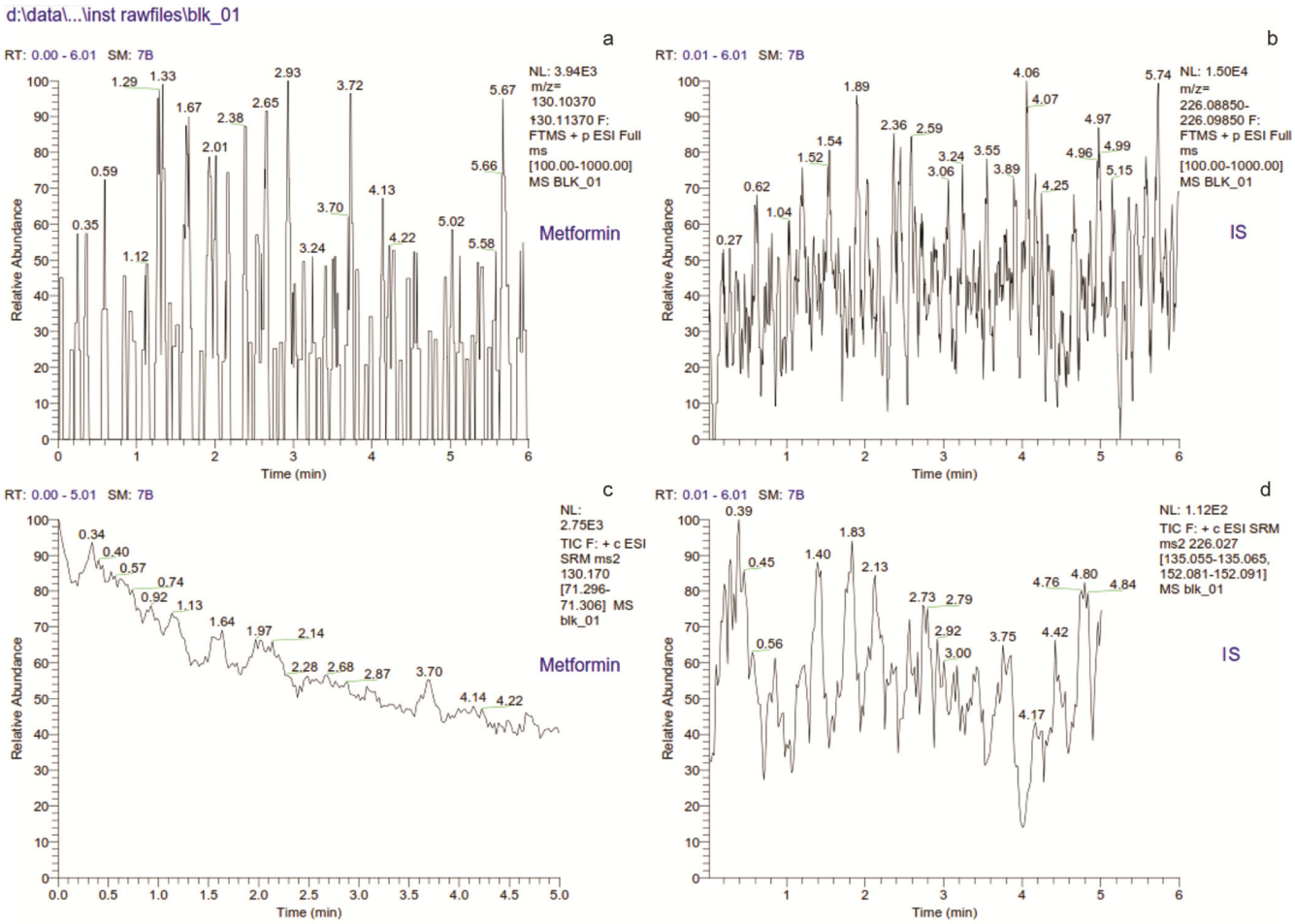

Fig. S3 — Representative blank plasma chromatograms of specificity for analysis of MET in rat plasma; a) HRMS chromatogram for MET, b) HRMS chromatogram for IS, c) SRM chromatogram for metformin, and d) SRM chromatogram for IS.

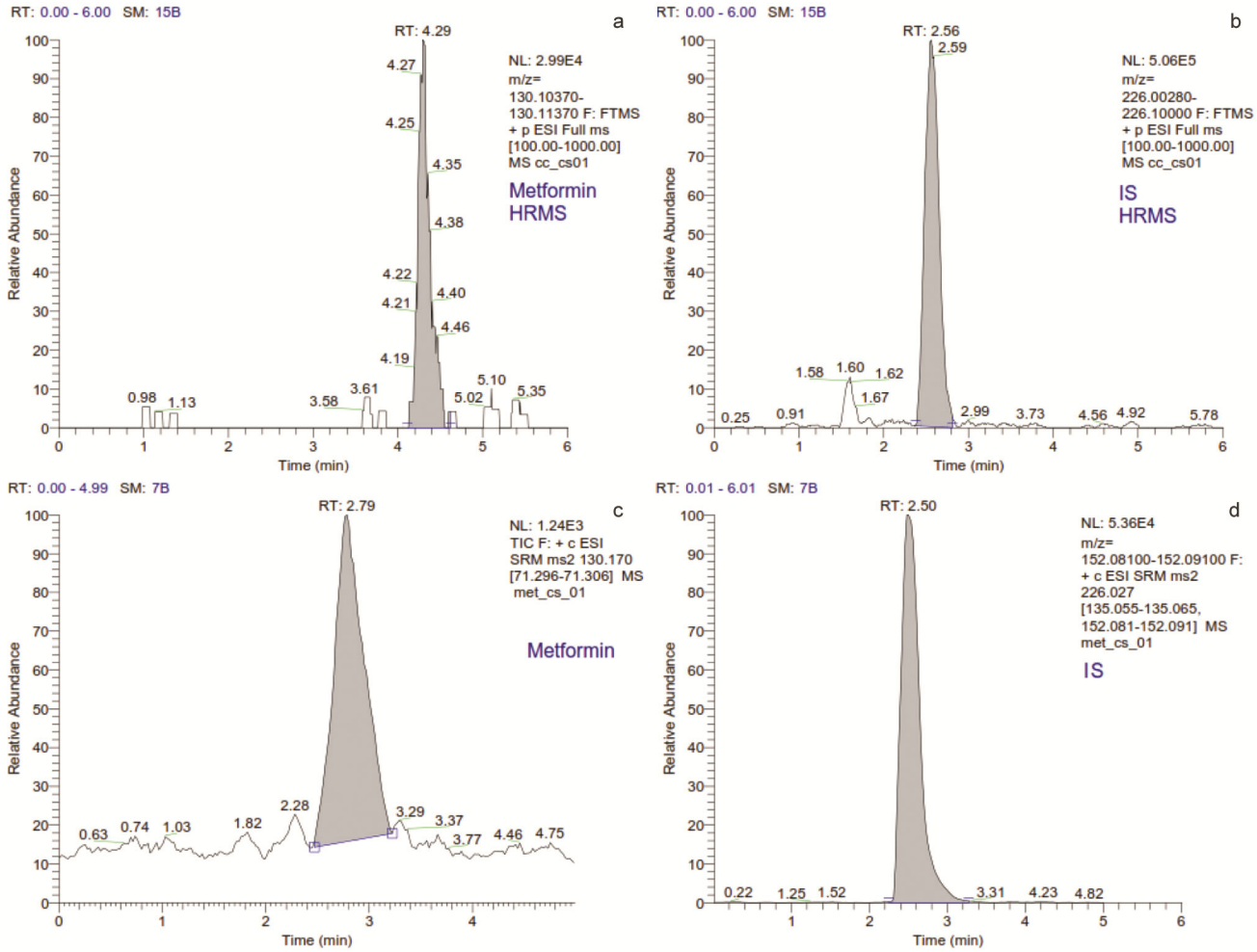

Fig. S4 — Representative blank plasma chromatograms for specificity; a) HRMS chromatogram for MET, b) HRMS chromatogram for IS, c) SRM chromatogram for MET, and d) SRM chromatogram for IS.

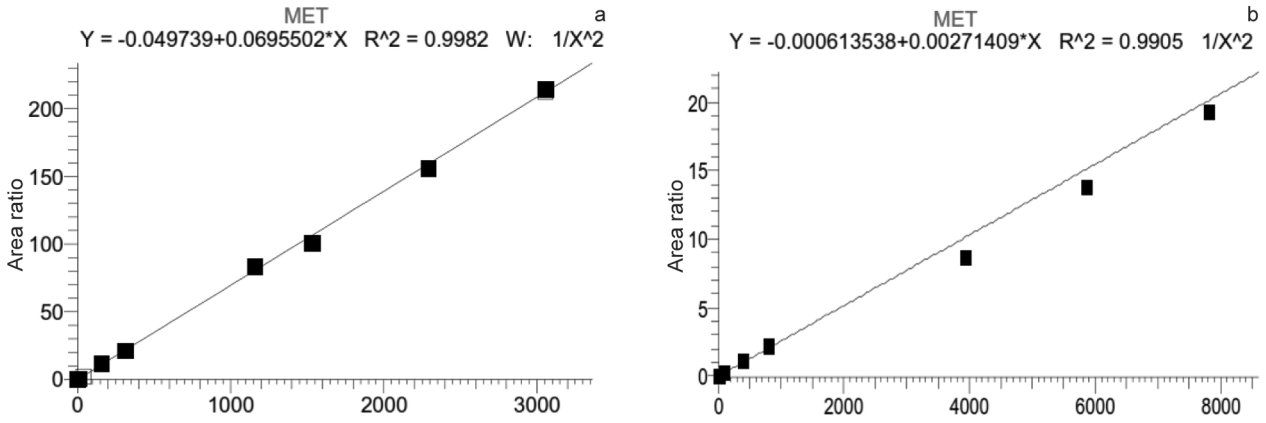

Fig. S5 — Calibration curves of MET in rat plasma; a) Calibration curve for a single dose study (HRMS), and b) multiple dose study Triple quadrupole.

Supplementary Tables

Table S1 — Details of nitrogen containing phytoconstituents of TCE collected from published resources. (MW: Molecular Weight)

Title	PubChem CID	Generic Name	IUPAC Name	SMILES	MW
M02	305	Choline	2-hydroxyethyl(trimethyl)azanium	OCC[N+](C)(C)C	104.17
M37	2353	Berberine	16,17-dimethoxy-5,7-dioxa-13-azoniapentacyclo[11.8.0.02,10.04,8.015,20]henicosa-1(13),2,4(8),9,14,16,18,20-octaene	COc1c(OC)ccc(c2)c1c[n+](CC3)c2c(c4)c3cc(c45)OCO5	336.4
M41	3999	(+)-Magnoflorine Iodide	2,10-dimethoxy-6,6-dimethyl-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinolin-6-ium-1,11-diol	C[N+]1(C)CCc(cc(c2O)OC)c3[C@@H]1Cc(c4c23)ccc(c4O)OC	342.4
M30	4840	Piperidine, 1-(5-(1,3-benzodioxol-5-yl)-1-oxo-2,4-pentadienyl)-	5-(1,3-benzodioxol-5-yl)-1-piperidin-1-ylpenta-2,4-dien-1-one	C1CCCCN1C(=O)/C=C/C=C/c(c2)ccc(c23)OCO3	285.34
M44	5417	Rotundine	2,3,9,10-tetramethoxy-6,8,13,13a-tetrahydro-5H-isoquinolino[2,1-b]isoquinoline	COc1c(OC)ccc(c12)C[C@@H]3c4c(CCN3C2)cc(OC)c(c4)OC	355.4
M01	13387	1-Methyl-2-pyrrolidinone	1-methylpyrrolidin-2-one	CN1CCCC1=O	99.13
M43	19009	Palmatine/ Berbericinine	2,3,9,10-tetramethoxy-5,6-dihydroisoquinolino[2,1-b]isoquinolin-7-ium	COc1c(OC)ccc(c12)cc3c4c(CC[n+]3c2)cc(OC)c(c4)OC	352.4
M39	48704	Luteanine	1,2,10-trimethoxy-6-methyl-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinolin-11-ol	COc1c(OC)cc(CCN2C)c3[C@@H]2Cc(c4c13)ccc(c4O)OC	341.4
M38	72323	Jatrorrhizine	2,9,10-trimethoxy-5,6-dihydroisoquinolino[2,1-b]isoquinolin-7-ium-3-ol	COc1c(OC)ccc(c12)cc3c4c(CC[n+]3c2)cc(O)c(c4)OC	338.4
M40	111119	(+/-)-Corydine	2,10,11-trimethoxy-6-methyl-5,6,6a,7-tetrahydro-4H-dibenzo[de,g]quinolin-1-ol	CN1CCc(cc(c2O)OC)c3[C@@H]1Cc(c4c23)ccc(OC)c4OC	341.4
M34	125213	N-feruloyltyramine; Moupinamide	3-(4-hydroxy-3-methoxyphenyl)-N-[2-(4-hydroxyphenyl)ethyl]prop-2-enamide	c1cc(O)c(OC)cc1\C=C\C(=O)NCCc2ccc(O)cc2	313.3
M35	550072	Dasycarpidan-1-methanol, acetate (ester)	(16-ethyl-15-methyl-9,15-diazatetracyclo[10.3.1.02,10.03,8]hexadeca-2(10),3,5,7-tetraen-11-yl)methyl acetate	C1CN(C)[C@@H]2[C@H](CC)[C@H]1[C@@H](COC(=O)C)c(c2c34)[nH]c3cccc4	326.4
M42	4622630	Tembetarine	1-[(3-hydroxy-4-methoxyphenyl)methyl]-6-methoxy-2,2-dimethyl-3,4-dihydro-1 H-isoquinolin-2-ium-7-ol	COc(cc1)c(O)cc1C[C@H]2[N+](C)(C)CCc(c23)cc(c(c3)O)OC	344.4
M33	23251787	N-Formylannonaine	3,5-dioxa-11-azapentacyclo[10.7.1.02,6.08,20.014,19]icosa-1(20),2(6),7,14,16,18-hexaene-11-carbaldehyde	C1CN(C=O)[C@@H]2Cc(cccc3)c3c4c2c1cc(c45)OCO5	293.3

Table S2 — Details of predicted metabolites of fourteen phytoconstituents of TCE. (MW: Molecular Weight).

Title	SMILES	PubChem CID	Common Name	MW
MET001	O=CC[N+](C)(C)C	249	betaine aldehyde	102.157
MET002	O=C(O)C[N+](C)(C)C	248	TRIMETHYL GLYCINE	118.156
MET003	O=C(O)[C@@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			252.29
MET004	O=CCC[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			264.345
MET005	O=C(O)/C=C/[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			278.328
MET006	O=C(O)CC[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			280.344
MET007	O=C[C@@H](C1=O)C[C@H]2[N+](C)(C)CCc(c2c13)cc(c3O)OC			290.339
MET008	O=C(O)CC(=O)[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			294.327
MET009	Oc1c(O)ccc(c12)cc3c4c(cc(O)c(c4)O)CC[n+]3c2	443768	2,3,9,10-Tetrahydroxyberberine	296.302
MET010	O=C(O)C[C@@H](O)[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			296.343
MET011	O=C(O)[C@@H](C1=O)C[C@@H]2[N+](C)(C)CCc(c2c13)cc(c3O)OC			306.338
MET012	COc1c(O)ccc(c12)cc3[n+](c2)CCC=4C3=CC(=O)C(=O)C4			308.313
MET013	COc(c1O)ccc(c12)cc3[n+](c2)CCC=4C3=CC(=O)C(=O)C4			308.313
MET014	O1COc(c12)cc3c(c2)c4[n+](CC3)cc5c(c4)ccc(O)c5O	68426959	SCHEMBL2882394	308.313
MET015	COc1c(O)ccc(c12)cc3c4c(cc(O)c(c4)O)CC[n+]3c2	147339878	9-Methoxy-5,6-dihydroisoquinolino[2,1-b]isoquinolin-7-ium-2,3,10-triol	310.329
MET016	COc(c1)c(O)cc(CC[n+]2c3)c1c2cc(c34)ccc(O)c4O			310.329
MET017	COc(c(c1)O)cc(CC[n+]2c3)c1c2cc(c34)ccc(O)c4O			310.329
MET018	COc(c1O)ccc(c12)cc3c4c(cc(O)c(c4)O)CC[n+]3c2	68071758	SCHEMBL10233793	310.329
MET019	C[N+]1(C)CCC2=CC(=O)C(=O)C3=C2[C@H]1Cc(c34)ccc(O)c4O			312.345
MET020	Oc1c(O)cc(c2c13)CC[N+](C)(C)[C@H]2CC4=C3C(=O)C(=O)C=C4			312.345
MET021	c1cc(O)c(O)cc1C[C@H]2[N+](C)(C)CCC(C2=3)=CC(=O)C(=O)C3			314.361
MET022	C[N+]1(C)CCc(cc(O)c2O)c3[C@H]1Cc(c4c23)ccc(O)c4O			314.361
MET023	C1=CC(=O)C(=O)C=C1C[C@H]2[N+](C)(C)CCc(c23)cc(O)c(c3)O			314.361
MET024	O=C(O)CC1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(O)c3O			316.289
MET025	c1cc(O)c(O)cc1C[C@H]2[N+](C)(C)CCc(c23)cc(O)c(c3)O	3246432	NCIStruc1_001546	316.377
MET026	COc1c(O)ccc(c2)c1c[n+](CC3)c2c(c4)c3cc(c45)OCO5	3084288	Thalifendine	322.34
MET027	COc(c1O)ccc(c2)c1c[n+](CC3)c2c(c4)c3cc(c45)OCO5	72704	Berberrubine	322.34
MET028	COc1c(OC)ccc(c12)cc3[n+](c2)CCC=4C3=CC(=O)C(=O)C4			322.34
MET029	O1COc(c12)cc3c(c2)c4[n+](C[C@H]3O)cc5c(c4)ccc(O)c5O			324.312
MET030	COc(c1O)ccc(c12)cc3c4c(CC[n+]3c2)cc(O)c(c4)OC	12304702	SCHEMBL16804539	324.356
MET031	COc1c(O)ccc(c12)cc3c4c(CC[n+]3c2)cc(O)c(c4)OC	157159	2,9-Dimethoxy-5,6-dihydroisoquinolino[2,1-b]isoquinolin-7-ium-3,10-diol	324.356
MET032	COc(c1)c(OC)cc(CC[n+]2c3)c1c2cc(c34)ccc(O)c4O			324.356
MET033	COc(c1O)ccc(c12)cc3c4c(cc(c(c4)O)OC)CC[n+]3c2	14191590	2,9-Dihydroxy-3,10-Dimethoxy-5,6-Dihydroisoquino[3,2-A]isoquinolinium	324.356
MET034	COc1c(O)ccc(c12)cc3c4c(cc(c(c4)O)OC)CC[n+]3c2	10358881	stepharanine	324.356
MET035	COc1c(OC)ccc(c12)cc3c4c(cc(O)c(c4)O)CC[n+]3c2	363209	Demethyleneberberine	324.356
MET036	c1cc(O)c(OC)c(c2)c1cc3[n+]2CCc(c34)c(O)c(O)c(c4)O			326.328

MET037	COc1c(O)ccc(c12)cc3c4c(cc(O)c(c4)O)[C@H](O)C[n+]3c2			326.328
MET038	COc(c1)c(O)cc([C@H](O)C[n+]2c3)c1c2cc(c34)ccc(O)c4O			326.328
MET039	COc(c1)c(O)c(O)c(c12)CC[n+]3c2cc4c(c3)c(O)c(O)cc4			326.328
MET040	COc(cc1)c(O)c(c2)c1cc3[n+]2CCc(c34)c(O)c(O)c(c4)O			326.328
MET041	COc(c1O)ccc(c12)cc3c4c(cc(O)c(c4)O)[C@H](O)C[n+]3c2			326.328
MET042	COc(c1O)cc(c2c13)CC[N+](C)(C)[C@H]2CC4=C3C(=O)C(=O)C=C4			326.372
MET043	C[N+]1(C)CCC2=CC(=O)C(=O)C3=C2[C@@H]1Cc(c34)ccc(c4O)OC			326.372
MET044	C1=CC(=O)C(=O)C=C1C[C@H]2[N+](C)(C)CCc(c23)cc(c(c3)O)OC			328.388
MET045	C[N+]1(C)CCc(cc(c2O)OC)c3[C@H]1Cc(c4c23)ccc(O)c4O			328.388
MET046	COc(cc1)c(O)cc1C[C@H]2[N+](C)(C)CCC(C2=3)=CC(=O)C(=O)C3			328.388
MET047	C[N+]1(C)CCc(cc(O)c2O)c3[C@H]1Cc(c4c23)ccc(c4O)OC			328.388
MET048	O=C(O)CC1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(O)c3OC			330.316
MET049	O=C(O)CC1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(c3O)OC			330.316
MET050	c1cc(O)c(O)cc1C[C@H]2[N+](C)(C)CCc(c23)cc(c(c3)O)OC			330.404
MET051	COc(cc1)c(O)cc1C[C@H]2[N+](C)(C)CCc(c23)cc(O)c(c3)O			330.404
MET052	O=C(O)CC1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(O)c3O			332.288
MET053	C[N+]1(C)CCC(CC(=O)O)=C(C2=O)[C@H]1Cc(c23)ccc(c3O)OC			332.376
MET054	O=C(O)/C(O)=C/C=C/C[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			334.392
MET055	O=C(O)C(=O)C/C=C/C[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC			334.392
MET056	COc1c(O)ccc(c2)c1c[n+](C[C@H]3O)c2c(c4)c3cc(c45)OCO5			338.339
MET057	COc(c1O)ccc(c2)c1c[n+](C[C@H]3O)c2c(c4)c3cc(c45)OCO5			338.339
MET058	COc1c(OC)ccc(c12)cc3c4c(CC[n+]3c2)cc(O)c(c4)OC	72323	Jatrorrhizine	338.383
MET059	COc1c(O)ccc(c12)cc3c4c(CC[n+]3c2)cc(OC)c(c4)OC	3083983	Dehydrocorydalmine	338.383
MET060	COc1c(OC)ccc(c12)cc3c4c(cc(c(c4)O)OC)CC[n+]3c2	72310	Columbamine	338.383
MET061	COc(c1O)ccc(c12)cc3c4c(CC[n+]3c2)cc(OC)c(c4)OC	10547386	PALMATRUBINE	338.383
MET062	COc1c(O)ccc(c12)cc3c4c([C@H](O)C[n+]3c2)cc(O)c(c4)OC			340.355
MET063	COc(c1O)ccc(c12)cc3c4c([C@H](O)C[n+]3c2)cc(O)c(c4)OC			340.355
MET064	c1cc(O)c(OC)c(c2)c1cc3[n+]2CCc(c34)c(O)c(O)c(c4)OC			340.355
MET065	COc1c(O)ccc(c12)cc3c4c(cc(c(c4)O)OC)[C@@H](O)C[n+]3c2			340.355
MET066	COc(c1)c(OC)cc([C@@H](O)C[n+]2c3)c1c2cc(c34)ccc(O)c4O			340.355
MET067	COc(c1O)ccc(c12)cc3c4c(cc(c(c4)O)OC)[C@@H](O)C[n+]3c2			340.355
MET068	COc(cc1)c(OC)c(c2)c1cc3[n+]2CCc(c34)c(O)c(O)c(c4)O			340.355
MET069	COc1c(OC)ccc(c12)cc3c4c(cc(O)c(c4)O)[C@H](O)C[n+]3c2			340.355
MET070	COc(c1)c(O)c(O)c(c12)CC[n+]3c2cc4c(c3)c(O)c(cc4)OC			340.355
MET071	O=C(O)/C(O)=C/C1=C(C=O)CC[n+](c2)c1cc(c23)ccc(O)c3OC			342.327
MET072	O=C(O)/C(O)=C/C1=C(C=O)CC[n+](c2)c1cc(c23)ccc(c3O)OC			342.327
MET073	C1C[N@+]([O-])(C)[C@H]2[C@H](CC)[C@@H]1[C@@H](COC(=O)C)c(c2c34)[nH]c3cccc4			342.439
MET074	O=C(O)CC1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(OC)c3OC			344.343
MET075	O=C(O)CC1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(O)c3OC			346.315
MET076	O=C(O)CC1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(c3O)OC			346.315
MET077	O=C(O)CC(CC1)=C(C(=O)O)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC			350.391
MET078	C1CC(C(=O)O)=C(CC(=O)O)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC			350.391

MET079	O=C(O)CC(CC1)=C[C@@H]([N+]1(C)C)Cc(c2C(=O)O)ccc(c2O)OC	350.391
MET080	COc1c(OC)ccc(c2)c1c[n+](C[C@H]3O)c2c(c4)c3cc(c45)OCO5	352.366
MET081	O=C(O)C(=O)C[C@@H](O)CC[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC	352.407
MET082	COc1c(OC)ccc(c12)cc3c4c([C@H](O)C[n+]3c2)cc(O)c(c4)OC	354.382
MET083	COc(cc1)c(OC)c(c2)c1cc3[n+]2CCc(c34)c(O)c(O)c(c4)OC	354.382
MET084	COc1c(O)ccc(c12)cc3c4c([C@@H](O)C[n+]3c2)cc(OC)c(c4)OC	354.382
MET085	COc1c(OC)ccc(c12)cc3c4c(cc(c(c4)O)OC)[C@@H](O)C[n+]3c2	354.382
MET086	COc(c1O)ccc(c12)cc3c4c([C@H](O)C[n+]3c2)cc(OC)c(c4)OC	354.382
MET087	O=C(O)/C(O)=C/C1=C(C=O)CC[n+](c2)c1cc(c23)ccc(OC)c3OC	356.354
MET088	C[N@+]1([O-])CCc(cc(c2O)OC)c3[C@H]1Cc(c4c23)ccc(OC)c4OC	357.406
MET089	COc1c(OC)cc(CC[N@@+]2([O-])C)c3[C@H]2Cc(c4c13)ccc(c4O)OC	357.406
MET090	O=C(O)[C@@H](O)C(=O)/C=C/1C(=O)CC[n+](c2)c1cc(c23)ccc(O)c3OC	358.326
MET091	O=C(O)/C(O)=C(O)/C=C/1C(=O)CC[n+](c2)c1cc(c23)ccc(O)c3OC	358.326
MET092	O=C(O)/C(O)=C/C1=C(C=O)[C@H](O)C[n+](c2)c1cc(c23)ccc(O)c3OC	358.326
MET093	O=C(O)/C(O)=C/C1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(O)c3OC	358.326
MET094	O=C(O)C(=O)CC1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(O)c3OC	358.326
MET095	O=C(O)[C@@H](O)C(=O)/C=C/1C(=O)CC[n+](c2)c1cc(c23)ccc(c3O)OC	358.326
MET096	O=C(O)/C(O)=C(O)/C=C/1C(=O)CC[n+](c2)c1cc(c23)ccc(c3O)OC	358.326
MET097	O=C(O)/C(O)=C/C1=C(C=O)[C@H](O)C[n+](c2)c1cc(c23)ccc(c3O)OC	358.326
MET098	O=C(O)/C(O)=C/C1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(c3O)OC	358.326
MET099	O=C(O)C(=O)CC1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(c3O)OC	358.326
MET100	C[N+]1(C)CCc(cc(c2O)OC)c3[C@@H]1[C@H](O)c(c4c23)ccc(c4O)OC	358.414
MET101	C[N+]1(C)CCc2cc(OC)c(O)c(c2[C@]13O)c4c(C3)ccc(c4O)OC	358.414
MET102	C[N+]1(C)C[C@@H](O)c(cc(c2O)OC)c3[C@H]1Cc(c4c23)ccc(c4O)OC	358.414
MET103	C1C[N@+]([O])(C)[C@H]2[C@H](CC)[C@@H]1[C@@H](COC(=O)C)c(c2c34)[nH]c3cc(O)cc4	358.438
MET104	O=C(O)CC1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(OC)c3OC	360.342
MET105	O=C(O)/C(O)=C/C=C(/C1=O)C[C@@H]2[N+](C)(C)CCc(c2c13)cc(c3O)OC	360.386
MET106	O=C(O)C(=O)C/C=C(/C1=O)C[C@H]2[N+](C)(C)CCc(c2c13)cc(c3O)OC	360.386
MET107	C[N+]1(C)CCC(C=O)=C(C\2=C(O)\C(=O)O)[C@@H]1Cc(c23)ccc(c3O)OC	360.386
MET108	C[N+]1(C)CCC(\C=C(O)\C(=O)O)=C(C2=O)[C@H]1Cc(c23)ccc(c3O)OC	360.386
MET109	C[N+]1(C)CCC(CC(=O)C(=O)O)=C(C2=O)[C@H]1Cc(c23)ccc(c3O)OC	360.386
MET110	COc(cc1)c(O)c(O)c1C[C@H]2[N+](C)(C)CCc(c23)cc(c(c3)O)OC	360.43
MET111	COc(cc1)c(O)cc1[C@H](O)[C@H]2[N+](C)(C)CCc(c23)cc(c(c3)O)OC	360.43
MET112	COc(cc1)c(O)cc1C[C@@]2(O)[N+](C)(C)CCc(c23)cc(c(c3)O)OC	360.43
MET113	COc(cc1)c(O)cc1C[C@H]2[N+](C)(C)CCc(c23)cc(OC)c(O)c3O	360.43
MET114	COc(cc1)c(O)cc1C[C@H]2[N+](C)(C)C[C@H](O)c(c23)cc(c(c3)O)OC	360.43
MET115	O=C(O)[C@H](O)C(=O)/C=C/c([n+](c1)CCC(=O)O)cc(c12)ccc(O)c2O	362.314
MET116	O=C(O)/C(O)=C/C=C(\C=O)C[C@H]1[N+](C)(C)CCc(c12)cc(c(c2)O)OC	362.402
MET117	O=C(O)/C(O)=C/C(=C(C=O)CC1)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC	362.402
MET118	O=C(O)/C(O)=C/C(CC1)=C(C=O)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC	362.402
MET119	COc1c(OC)ccc(c12)cc3c4c([C@@H](O)C[n+]3c2)cc(OC)c(c4)OC	368.409

MET120	COc(cc1)c(OC)c(C2)c1C[C@@H]([N@+]23[O-])c4c(CC3)cc(OC)c(c4)OC	154831453	(7R,13aR)-2,3,9,10-tetramethoxy-7-oxido-6,8,13,13a-tetrahydro-5H-isoquinolino[2,1-b]isoquinolin-7-ium	371.433
MET121	O=C(O)[C@@H](O)C(=O)/C=C/1C(=O)CC[n+](c2)c1cc(c23)ccc(OC)c3OC			372.353
MET122	O=C(O)/C(O)=C(O)/C=C/1C(=O)CC[n+](c2)c1cc(c23)ccc(OC)c3OC			372.353
MET123	O=C(O)/C(O)=C/C1=C(C=O)[C@H](O)C[n+](c2)c1cc(c23)ccc(OC)c3OC			372.353
MET124	O=C(O)/C(O)=C/C1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(OC)c3OC			372.353
MET125	O=C(O)C(=O)CC1=C(C(=O)O)CC[n+](c2)c1cc(c23)ccc(OC)c3OC			372.353
MET126	O=C(O)/C(O)=C/C1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(O)c3OC			374.325
MET127	O=C(O)C(=O)CC1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(O)c3OC			374.325
MET128	O=C(O)/C(O)=C/C1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(c3O)OC			374.325
MET129	O=C(O)C(=O)CC1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(c3O)OC			374.325
MET130	O=C(O)[C@@H](O)C(=O)/C=C/c([n+](c1)CCC(=O)O)cc(c12)ccc(O)c2OC			376.341
MET131	O=C(O)[C@@H](O)C(=O)/C=C/c([n+](c1)CCC(=O)O)cc(c12)ccc(c2O)OC			376.341
MET132	C[N+]1(C)CCC(C(=O)O)=C(C\2=C(O)\C(=O)O)[C@@H]1Cc(c23)ccc(c3O)OC			376.385
MET133	C[N+]1(C)CCC(C(=O)O)=C([C@H]2C(=O)C(=O)O)[C@@H]1Cc(c23)ccc(c3O)OC			376.385
MET134	O=C(O)C(=O)C[C@@H](O)[C@H](C1=O)C[C@@H]2[N+](C)(C)CCc(c2c13)cc(c3O)OC			378.401
MET135	O=C(O)/C(O)=C/C(CC1)=C(C(=O)O)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC			378.401
MET136	O=C(O)C(=O)CC(CC1)=C(C(=O)O)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC			378.401
MET137	O=C(O)/C(O)=C/C(=C(C(=O)O)CC1)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC			378.401
MET138	O=C(O)C(=O)CC(=C(C(=O)O)CC1)[C@@H]([N+]1(C)C)Cc2cc(O)c(cc2)OC			378.401
MET139	O=C(O)/C(O)=C/C1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(OC)c3OC			388.352
MET140	O=C(O)C(=O)CC1=C(C(=O)O)[C@H](O)C[n+](c2)c1cc(c23)ccc(OC)c3OC			388.352
MET141	O=C(O)[C@@H](O)C(=O)/C=C/c([n+](c1)CCC(=O)O)cc(c12)ccc(OC)c2OC			390.368

Table S3 — Molecular docking and MM/GBSA analysis of nitrogen containing phytoconstituents of TCE against human OCT1, OCT2 and OCT3 proteins. All energy terms are in kcal/mol standard unit. (ND: Not Docked, XP: Extra Precision; GScore: Glide's Docking Score; HB: Hydrogen Bond; LE: Ligand Efficiency; ΔG_{Bind}: Gibb's binding free energy).

Title	PubChem CID	Generic Name	XP GScore			XP HB			XP LE			ΔG_{Bind}			ΔG_{Bind} HB			ΔG_{Bind} LE		
			OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3
Ref	92305 39484 5753	Verapamil [OCT1] Cyperquat [OCT2] Corticosterone [OCT3]	-6.15	-8.12	-8.36	-0.44	0.00	-0.77	-0.19	-0.63	-0.33	-43.12	-26.92	-68.11	2.45	0.06	-1.34	-1.31	-2.07	-2.72
T01	4091	Metformin (Control)	-3.34	-5.06	-2.79	-1.71	-0.67	-0.90	-0.37	-0.47	-0.31	-183.05	-34.09	-71.74	-15.48	-5.93	-2.73	-20.34	-3.79	-7.97
M01	13387	1-Methyl-2-pyrrolidinone	-4.30	-3.35	-2.91	-0.70	-0.70	-0.28	-0.61	-0.48	-0.42	47.64	19.22	-115.15	-0.75	2.05	-0.95	6.81	2.75	-16.45
M02	305	Choline	-6.05	-6.18	-2.70	-0.75	-0.35	-1.00	-0.86	-0.88	-0.39	17.43	-52.66	-161.38	0.60	-1.16	-7.07	2.49	-7.52	-23.06
M30	4840	Piperin	-7.58	-8.60	-5.98	0.00	-0.50	0.00	-0.36	-0.41	-0.29	18.84	-173.25	-78.46	4.92	-6.02	-8.26	0.90	-8.25	-3.74
M33	23251787	N-Formylannonaine	-6.50	ND	-8.18	0.00	-	-0.35	-0.30	-	-0.37	93.94	-	-115.46	12.59	-	1.06	4.27	-	-5.25
M34	125213	N-feruloyltyramine; Moupinamide	-9.16	-8.55	-7.96	-1.63	-0.67	-0.93	-0.40	-0.32	-0.34	-19.54	-70.98	-110.38	1.19	-6.83	-8.36	-0.85	-3.09	-4.80
M35	550072	Dasycarpidan-1-methanol, acetate (ester)	-10.24	-8.32	-9.76	-0.30	-0.12	0.00	-0.43	-0.27	-0.41	-44.84	-114.01	-168.57	0.88	-9.56	-11.85	-1.87	-4.75	-7.02

M37	2353	Berberine	-10.55	-11.37	-7.32	-0.70	-0.56	0.00	-0.42	-0.46	-0.29	5.90	-194.20	-254.37	7.63	-13.01	-11.18	0.24	-7.77	-10.18
M38	72323	Jatrorrhizine	-8.50	-12.52	-7.70	-0.64	-0.48	-0.96	-0.34	-0.50	-0.31	-53.81	-96.29	-200.73	2.75	0.37	-0.83	-2.15	-3.85	-8.03
M39	48704	Luteanine	-6.64	ND	-7.62	-1.36	-	-0.48	-0.26	-	-0.30	-46.62	-	-107.48	-1.80	-	-4.82	-1.87	-	-4.30
M40	111119	(+/-)-Corydine	-7.36	ND	-7.90	-0.96	-	-0.48	-0.23	-	-0.31	-36.72	-	-135.49	-0.76	-	-5.76	-1.47	-	-5.42
M41	3999	(+)-Magnoflorine Iodide	-7.43	ND	-11.09	-0.48	-	-0.96	-0.25	-	-0.43	-83.96	-	-216.81	-3.44	-	-14.13	-3.36	-	-8.67
M42	4622630	Tembetarine	-12.36	-11.61	-10.50	-1.14	-0.70	-0.96	-0.49	-0.46	-0.42	-51.96	9.49	-125.02	-1.20	1.93	-4.54	-2.08	0.38	-5.00
M43	19009	Palmatine/Berbericinine	-8.06	-10.92	-6.78	-0.20	-0.51	0.00	-0.31	-0.42	-0.26	-14.43	-216.29	-199.09	6.29	-5.37	1.61	-0.56	-8.32	-7.66
M44	5417	Rotundine	-9.44	-3.83	-9.09	-0.51	0.00	0.00	-0.36	-0.10	-0.35	-20.63	-99.33	-251.03	1.13	-2.84	-14.58	-0.79	-3.82	-9.66

Table S4 — Molecular docking and MM/GBSA analysis of cationic metabolites of nitrogen containing phytoconstituents of TCE against human OCT1, OCT2 and OCT3 proteins. All energy terms are in kcal/mol standard unit. (ND: Not Docked, XP: Extra Precision; GScore: Glide's Docking Score; HB: Hydrogen Bond; LE: Ligand Efficiency; ΔGBind: Gibb's binding free energy)

Title	XP GScore			XP HBond			XP LE			ΔGBind			ΔGBind HB			ΔGBind LE		
	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3	OCT1	OCT2	OCT3
MET001	-5.76	-6.02	-2.58	0.00	0.00	-0.35	-0.82	-0.86	-0.37	205.04	-48.16	-120.25	19.24	-0.45	-4.03	29.29	-6.88	-17.179
MET002	-5.45	-5.94	-2.32	0.00	-0.13	0.00	-0.68	-0.74	-0.29	77.70	-37.08	-180.09	5.61	2.94	-13.82	9.71	-4.636	-22.511
MET003	-10.35	-8.00	-4.76	-1.14	-0.51	-1.07	-0.58	-0.45	-0.26	-14.32	-146	-96.17	0.71	-10.26	0.42	-0.80	-8.111	-5.343
MET004	-10.69	-11.73	-8.64	-1.09	-0.48	-1.18	-0.56	-0.62	-0.45	-66.67	129.47	-140.98	-7.43	10.86	-11.06	-3.51	6.814	-7.42
MET005	-10.20	-9.14	-8.91	-1.18	-0.96	-0.71	-0.51	-0.46	-0.45	226.84	-16.8	-41.84	16.99	-1.84	-2.11	11.34	-0.84	-2.092
MET006	-10.96	-10.88	-9.08	-1.16	-0.83	-1.37	-0.55	-0.54	-0.45	30.84	28.87	-156.66	1.06	5.18	-10.29	1.54	1.444	-7.833
MET007	-8.83	-11.50	-9.64	-0.48	-0.48	-0.86	-0.41	-0.53	-0.43	-35.29	-129.42	-138.52	-1.93	1.6	1.96	-1.68	-6.163	-6.596
MET008	-9.60	-11.20	-8.20	-1.10	-0.48	-1.86	-0.46	-0.53	-0.39	-70.47	-20.92	-67.32	-2.00	-3.93	1.01	-3.36	-0.996	-3.206
MET009	-9.36	-9.86	-10.06	-1.61	-1.44	-2.40	-0.43	-0.45	-0.46	52.48	-23.49	-116.55	6.65	-7.1	-1.79	2.39	-1.068	-5.298
MET010	-11.25	-12.17	-9.95	-1.29	-0.96	-1.14	-0.54	-0.58	-0.47	-5.23	22.01	-38.39	-3.09	-2.27	0.97	-0.25	1.048	-1.828
MET011	-6.11	-10.69	-9.33	-0.48	-0.68	-0.48	-0.28	-0.49	-0.42	-18.83	-70.01	-103.62	-1.74	-0.3	-8.1	-0.86	-3.182	-4.71
MET012	-8.66	-12.91	-8.14	-1.02	-0.60	-0.92	-0.37	-0.52	-0.31	13.20	-49.05	-191.46	6.84	1.79	-1.23	0.57	-2.133	-8.324
MET013	-7.72	-6.40	-7.08	-0.70	0.00	0.00	-0.34	-0.28	-0.31	-30.86	-61.12	-188.21	1.10	1.28	-6.37	-1.34	-2.657	-8.183
MET014	-9.01	-9.50	-7.61	-0.51	-0.54	-0.96	-0.39	-0.41	-0.33	-59.11	-90.92	-184.3	-4.93	-5.53	-4.86	-2.57	-3.953	-8.013
MET015	-12.48	-12.95	-10.94	-2.50	-1.52	-2.40	-0.49	-0.53	-0.47	-18.31	5.56	-177.07	1.94	4.53	-5.86	-0.80	0.242	-7.699
MET016	-8.93	-9.62	-8.79	-1.18	-1.03	-0.96	-0.39	-0.42	-0.38	-13.15	-160.18	-97.66	4.15	-5.23	-4.66	-0.57	-6.964	-4.246
MET017	-8.90	-10.11	-8.17	-1.37	-0.96	-1.44	-0.39	-0.44	-0.36	-4.70	-33.99	-184.07	0.33	-0.34	-5.04	-0.20	-1.478	-8.003
MET018	-8.65	-9.52	-7.62	-1.77	-0.96	-1.12	-0.38	-0.41	-0.33	-83.92	66.81	16.15	-10.11	8.54	-3.35	-3.65	2.905	0.702
MET019	-6.72	-7.84	-8.94	0.00	-0.48	-0.48	-0.29	-0.34	-0.39	-63.17	1.15	-58.47	-1.08	1.67	-12.82	-2.75	0.05	-2.542
MET020	-8.61	ND	-10.97	-1.51		-1.64	-0.33		-0.40	-28.19		-164.36	-0.63		-8	-1.23		-7.146
MET021	-13.10	-11.52	-10.69	-2.01	-1.06	-1.24	-0.57	-0.50	-0.47	-38.74	-11.15	-16.59	0.26	-0.31	2.7	-1.68	-0.485	-0.721
MET022	-10.19	-12.15	-12.71	-2.32	-2.88	-2.40	-0.42	-0.50	-0.49	-18.35	-11.65	-22.88	1.72	-4.54	-1.75	-0.80	-0.507	-0.995
MET023	-11.55	-10.72	-12.21	-1.95	-0.96	-1.62	-0.42	-0.47	-0.53	111.99	-16.5	-57.57	8.75	-0.31	-2.61	4.87	-0.717	-2.503
MET024	-7.95	-7.26	-5.98	-1.01	-0.48	-0.65	-0.35	-0.32	-0.26	38.47	-136.46	-80.99	-5.35	-13.38	-14.58	1.67	-5.933	-3.521
MET025	-13.18	-12.63	-12.92	-2.37	-1.88	-2.52	-0.57	-0.55	-0.56	19.85	-106.5	-148.72	0.48	-2.93	-0.66	0.86	-4.63	-6.466
MET026	-11.33	-11.80	-8.91	-1.15	-0.48	-0.96	-0.47	-0.48	-0.37	-91.32	-105.17	-85.32	-6.24	-3.68	-2.19	-3.81	-4.382	-3.555
MET027	-7.86	-8.90	-7.15	-0.70	-0.21	0.00	-0.33	-0.37	-0.30	-14.82	43.5	-135.84	1.09	2.58	-12.36	-0.62	1.812	-5.66

MET028	-10.34	-11.12	-8.69	-0.47	0.00	0.00	-0.43	-0.46	-0.36	-53.48	-172.27	-222.89	3.36	-23.24	-10.53	-2.23	-7.178	-9.287
MET029	-8.89	-9.69	-6.65	-0.57	-0.96	-1.29	-0.37	-0.40	-0.28	20.35	-58.37	56.46	-0.57	6.51	4.31	0.85	-2.432	2.353
MET030	-7.81	-9.09	-8.65	-1.03	-0.48	-0.95	-0.33	-0.38	-0.36	-35.49	86.87	-80.53	-2.74	12.62	-5.36	-1.48	3.62	-3.355
MET031	-10.92	-12.27	-9.14	-1.06	-0.72	-0.96	-0.45	-0.51	-0.38	-58.19	-62.47	-147.05	-3.16	3.35	-0.71	-2.43	-2.603	-6.127
MET032	-8.65	-9.14	-7.30	-0.79	-0.48	-0.48	-0.36	-0.38	-0.30	9.61	-179.12	-103.93	3.38	-7.69	1.12	0.40	-7.463	-4.33
MET033	-8.31	-9.30	-7.91	-1.67	-0.48	-0.86	-0.35	-0.39	-0.33	64.72	-87.53	-132.86	1.37	1.75	-6.44	2.70	-3.647	-5.536
MET034	-11.60	-12.77	-8.85	-2.24	-1.00	-1.44	-0.43	-0.53	-0.36	-85.80	32.85	-164.69	-3.32	8.93	-8.79	-3.58	1.369	-6.862
MET035	-11.63	-12.27	-11.16	-1.94	-0.81	-0.96	-0.48	-0.51	-0.47	-46.08	98.46	-146.3	0.29	11.36	-9.27	-1.92	4.103	-6.096
MET036	-13.07	-13.08	-10.76	-2.88	-2.40	-1.92	-0.53	-0.51	-0.45	-17.64	-170.39	-233.51	-0.74	-8.72	-5.94	-0.74	-7.1	-9.73
MET037	-11.42	-13.40	-9.95	-1.72	-1.36	-1.44	-0.47	-0.56	-0.41	-18.98	-153.75	-115.38	5.23	-2.66	-4.52	-0.79	-6.406	-4.807
MET038	-8.99	-9.67	-7.79	-1.96	-1.37	-1.44	-0.38	-0.40	-0.32	-10.30	-123.42	-71.93	-1.27	-2.04	-3.93	-0.43	-5.143	-2.997
MET039	-9.48	-9.46	-8.12	-1.59	-1.51	-1.52	-0.40	-0.39	-0.34	69.81	-29.38	-193.81	3.67	1.6	-25.15	2.91	-1.224	-8.076
MET040	-10.03	-9.86	-9.67	-2.25	-1.44	-2.40	-0.42	-0.41	-0.40	-13.98	-94.27	-268.98	1.64	1.55	-21.96	-0.58	-3.928	-11.208
MET041	-9.08	-9.94	-8.65	-1.09	-0.99	-1.02	-0.38	-0.41	-0.36	-24.68	28.83	-186.72	0.35	8.34	-11.38	-1.03	1.201	-7.78
MET042	-10.74	ND	-9.77	-0.60		-1.16	-0.34		-0.30	-28.92		-130.03	0.24		-8.7	-1.21		-5.418
MET043	-4.37	-2.37	-9.60	-0.37	0.00	0.00	-0.18	-0.10	-0.40	41.77	-94.77	-191.73	2.24	-2.86	-10.19	1.74	-3.949	-7.989
MET044	-13.49	-11.76	-10.59	-0.59	-0.10	-1.20	-0.56	-0.49	-0.44	0.47	5.69	-188.44	6.35	1.79	-6.39	0.02	0.237	-7.852
MET045	-8.74	-12.80	-11.25	-1.92	-1.92	-1.44	-0.34	-0.51	-0.45	27.49	-160.14	56.09	3.52	-10.29	0.93	1.15	-6.673	2.337
MET046	-12.41	-10.62	-10.07	-1.11	-0.75	-0.48	-0.52	-0.44	-0.42	-73.51	160.31	-215.92	-5.19	9.52	-7.18	-3.06	6.68	-8.997
MET047	-10.35	-11.89	-10.91	-2.40	-1.92	-2.25	-0.41	-0.48	-0.43	-61.58	-37.41	36.66	-1.73	-0.23	3.44	-2.57	-1.559	1.527
MET048	-10.40	-11.72	-9.73	-1.02	-0.48	-1.81	-0.43	-0.49	-0.40	49.80	45.72	-237.28	0.42	-0.59	-9.91	2.08	1.905	-9.887
MET049	-7.48	-4.80	-5.93	-0.35	-0.58	-0.02	-0.31	-0.20	-0.25	25.68	-32.36	-1.06	-5.30	-0.79	-8.57	1.07	-1.349	-0.044
MET050	-12.40	-12.07	-9.99	-2.04	-1.68	-1.51	-0.52	-0.50	-0.42	-67.98	-79.63	-98.07	-5.23	-2.17	-8.45	-2.83	-3.318	-4.086
MET051	-12.32	-11.63	-13.20	-1.63	-1.44	-1.72	-0.51	-0.48	-0.49	-15.38	-53.99	-196.14	1.41	-0.16	-14.05	-0.64	-2.25	-8.173
MET052	-8.52	-4.72	-7.32	-0.71	-0.96	-0.96	-0.36	-0.20	-0.31	65.89	94.38	-31.92	-2.17	6.53	1.6	2.75	3.932	-1.33
MET053	-6.14	-4.03	-9.45	-0.55	-0.83	-0.57	-0.20	-0.17	-0.39	-17.71	16.41	-60.2	0.87	-7.77	-5.42	-0.74	0.684	-2.508
MET054	-10.07	-12.38	-9.00	-1.58	-1.19	-1.87	-0.42	-0.52	-0.38	-11.47	-80.02	-171.7	-2.03	-2.47	-9.89	-0.48	-3.334	-7.154
MET055	-12.40	-12.59	-9.67	-0.92	-1.18	-1.31	-0.52	-0.52	-0.40	-10.32	-189.68	-25.15	-2.62	-9.86	0.73	-0.43	-7.903	-1.048
MET056	-10.55	-12.19	-6.93	-1.15	-0.50	-0.78	-0.42	-0.47	-0.27	10.58	-32.81	-121.34	2.12	-0.35	2.14	0.42	-1.313	-4.854
MET057	-8.30	-9.29	-7.34	-0.40	-0.10	0.00	-0.33	-0.37	-0.29	-31.75	107.28	-12.81	-2.97	10.25	-4.99	-1.27	4.291	-0.512
MET058	-8.05	-12.52	-6.86	-0.63	-0.48	-0.48	-0.32	-0.50	-0.27	-54.83	-103.16	-137.84	3.91	-5.81	-3.33	-2.19	-4.126	-5.514
MET059	-8.81	-11.91	-7.86	-0.79	-0.46	-0.96	-0.35	-0.47	-0.26	-83.06	28.62	-164.55	-5.28	5.24	-12.75	-3.32	1.145	-6.582
MET060	-6.35	-12.52	-9.61	-0.62	-0.48	-0.87	-0.25	-0.50	-0.38	-32.75	-84.58	-145.86	1.45	5.4	-1.97	-1.31	-3.383	-5.834
MET061	-8.02	-8.66	-6.96	-0.35	-0.60	0.00	-0.32	-0.35	-0.28	19.23	113.49	-128.46	5.10	7.3	-7.23	0.77	4.54	-5.138
MET062	-11.15	-13.25	-9.28	-1.77	-1.36	-1.15	-0.44	-0.53	-0.37	-15.07	-29.78	-148.15	-2.05	2.24	-9.93	-0.60	-1.191	-5.926
MET063	-8.60	-9.21	-8.15	-1.22	-0.74	-0.56	-0.34	-0.37	-0.33	-14.61	-105.89	-161.45	1.65	-1.67	2.35	-0.58	-4.236	-6.458
MET064	-11.85	-13.81	-9.32	-2.05	-1.40	-1.92	-0.47	-0.55	-0.37	-36.18	-129.93	-148.82	3.97	-9.17	-8.65	-1.45	-5.197	-5.953
MET065	-8.70	-13.44	-9.19	-1.45	-1.66	-1.44	-0.28	-0.54	-0.37	72.17	19.35	-211.01	9.77	6.62	-18.22	2.89	0.774	-8.44
MET066	-8.27	-9.25	-7.66	-0.87	-0.78	-0.36	-0.33	-0.37	-0.31	-33.72	11.9	-126.43	-0.38	-0.33	-4.01	-1.35	0.476	-5.057
MET067	-7.98	-9.72	-8.25	-0.94	-1.16	-0.58	-0.32	-0.39	-0.33	-80.59	-118.15	-200.81	-2.37	-6.63	-5.76	-3.22	-4.726	-8.033

MET068	-8.62	-12.36	-11.45	-1.55	-1.78	-1.55	-0.34	-0.49	-0.46	-76.04	-36.02	-82.22	-3.35	2.79	0.43	-3.04	-1.441	-3.289
MET069	-10.48	-10.15	-9.01	-1.37	-1.04	-1.41	-0.42	-0.41	-0.36	-110.20	-235.78	-160.39	-4.73	-6.83	-8.59	-4.41	-9.431	-6.416
MET070	-9.09	-6.72	-8.38	-1.44	-0.49	-0.96	-0.36	-0.27	-0.34	-66.08	13.28	-212.77	0.58	-2.44	-14.79	-2.64	0.531	-8.511
MET071	-10.73	-11.57	-8.57	-1.08	-0.87	-0.51	-0.41	-0.45	-0.33	-45.21	-12.58	-206.9	-10.02	-2.76	-14.72	-1.81	-0.503	-8.276
MET072	-6.85	-5.30	-6.47	-0.46	0.00	-0.27	-0.27	-0.21	-0.26	14.90	51.95	-252.35	-6.61	1.02	-19.78	0.60	2.078	-10.094
MET073	-7.73	ND	-7.84	-0.77		-0.70	-0.31		-0.30	52.27		-138.41	1.90		-1.61	2.09		-5.536
MET074	-9.34	-8.24	-7.22	-0.50	0.00	0.00	-0.37	-0.33	-0.29	-12.25	-105.74	-214.01	-4.75	-6.65	-5.67	-0.49	-4.229	-8.561
MET075	-9.84	-8.18	-7.19	-1.52	-1.06	-2.26	-0.39	-0.32	-0.26	-40.77	77.81	-178.79	-8.06	-1.66	-16.84	-1.63	3.112	-7.152
MET076	-7.93	-4.15	-6.92	-1.16	-0.48	-1.23	-0.32	-0.17	-0.28	-16.13	-15.7	-55.5	-8.05	0.58	-7.63	-0.65	-0.628	-2.22
MET077	-5.40	-8.81	-7.06	-0.48	-0.49	-0.48	-0.22	-0.35	-0.28	-41.80	38.01	-131.74	-6.43	-2.38	-13.13	-1.67	1.52	-5.27
MET078	-5.42	-8.18	-7.35	-0.79	-0.75	-0.49	-0.22	-0.33	-0.29	65.31	128.12	-138.21	-0.44	10.94	-13.53	2.61	5.125	-5.528
MET079	-12.88	-6.51	-7.58	-1.06	-0.83	-0.71	-0.52	-0.26	-0.30	-1.42	-66.95	-128.37	-7.49	-2.81	-9.79	-0.06	-2.678	-5.135
MET080	-8.87	-10.92	-7.32	-0.70	0.00	-0.35	-0.34	-0.42	-0.28	87.67	-95.59	-183.63	6.15	3.29	-11.66	3.37	-3.677	-7.063
MET081	-9.01	-10.94	-9.17	-1.96	-1.42	-1.95	-0.36	-0.44	-0.37	68.79	-43.01	-37.3	1.14	-10.06	-1.69	2.75	-1.72	-1.492
MET082	-6.61	-8.71	-8.65	-1.23	-0.39	-0.96	-0.25	-0.34	-0.33	-104.21	-106.35	-189.16	-0.76	-1.14	-10.85	-4.01	-4.09	-7.275
MET083	-12.33	-13.69	-7.99	-1.61	-1.44	-0.96	-0.47	-0.53	-0.31	-66.01	-18.72	-180.22	-2.65	3.22	-4.25	-2.54	-0.72	-6.931
MET084	-8.73	-12.04	-9.18	-1.19	-0.75	-0.96	-0.29	-0.41	-0.35	-3.08	100.46	-62.66	2.56	9.94	-1.51	-0.12	3.864	-2.41
MET085	-6.04	-13.36	-9.67	-1.31	-0.90	-0.86	-0.23	-0.51	-0.37	-119.01	-67.28	-253.97	-3.64	2.13	-12.65	-4.58	-2.588	-9.768
MET086	-8.05	-9.10	-6.72	-1.24	-0.34	-0.35	-0.31	-0.35	-0.26	-6.49	19.47	-204.26	3.30	5.27	-18.81	-0.25	0.749	-7.856
MET087	-10.06	-9.09	-6.85	-0.90	-0.48	-0.73	-0.39	-0.35	-0.26	-53.63	76.83	-174.67	-5.03	2	-10.34	-2.06	2.955	-6.718
MET088	-8.17	ND	-8.22	-0.96		-0.63	-0.31		-0.32	35.19		-55.43	1.75		-5.63	1.35		-2.132
MET089	-7.62	ND	-8.26	-0.48		-0.48	-0.29		-0.32	16.68		-203.24	1.97		-10.92	0.64		-7.817
MET090	-8.10	-12.29	-8.38	-0.96	-1.29	-0.96	-0.30	-0.45	-0.31	24.61	-70.25	157.5	-1.51	-5.38	2.4	0.95	-2.702	6.058
MET091	-11.31	-12.56	-8.61	-1.81	-1.04	-2.08	-0.43	-0.48	-0.32	11.46	-120.82	-77.24	2.39	-3.05	-0.92	0.44	-4.647	-2.971
MET092	-9.71	-12.55	-7.55	-1.31	-1.57	-1.44	-0.35	-0.46	-0.27	16.70	-128.28	-62.67	3.05	-9.37	-0.08	0.64	-4.934	-2.41
MET093	-11.50	-10.19	-10.22	-1.79	-1.08	-2.10	-0.44	-0.39	-0.39	94.58	48.3	-75.69	2.40	-2.97	-11.66	3.64	1.858	-2.911
MET094	-11.20	-11.94	-7.95	-0.50	-0.48	-1.32	-0.43	-0.46	-0.30	39.39	-107.63	-127.23	-3.04	-5.81	-8.48	1.52	-4.14	-4.894
MET095	-6.69	-8.97	-6.95	-1.13	-1.10	-1.32	-0.26	-0.35	-0.27	51.81	-8.53	-134.47	2.79	-4.08	-12	1.99	-0.328	-5.172
MET096	-5.75	-8.86	-6.30	-1.74	-0.85	-0.48	-0.22	-0.34	-0.24	-11.35	40.85	-222.64	2.24	-1.6	-17.65	-0.44	1.571	-8.563
MET097	-7.25	ND	-6.80	-0.83		-0.26	-0.28		-0.26	3.90		-160	-0.78		-14.72	0.15		-6.154
MET098	-7.05	-2.37	-6.75	-0.48	-0.55	-0.62	-0.27	-0.09	-0.26	52.62	5.88	69.88	1.06	3.61	5.13	2.02	0.226	2.688
MET099	-6.39	-7.09	-6.03	-1.10	-0.88	-0.07	-0.25	-0.27	-0.23	21.38	137.12	-202.8	-1.68	2.36	-13.2	0.82	5.274	-7.8
MET100	-10.43	ND	-7.74	-2.40		-0.96	-0.38		-0.27	-40.94		-75.25	0.15		-6.9	-1.58		-2.894
MET101	-10.25	-10.54	-10.87	-1.21	-1.98	-0.96	-0.30	-0.38	-0.40	-4.60	-129.87	-98.53	0.76	2.92	-4.77	-0.18	-4.995	-3.79
MET102	-8.45	-10.23	-9.76	-1.68	-1.44	-1.43	-0.29	-0.35	-0.34	-101.37	182.89	-86.89	-3.25	12.95	-1.01	-3.90	7.034	-3.342
MET103	-6.81	-8.42	-8.10	-0.24	-0.71	-0.76	-0.26	-0.32	-0.31	-74.43	85.46	-138.47	-4.22	9.51	-13.4	-2.86	3.287	-5.326
MET104	-9.16	-7.44	-6.50	-1.10	-0.57	-0.51	-0.35	-0.29	-0.25	30.60	171.11	-124.31	1.02	11.73	-8.41	1.18	6.581	-4.781
MET105	-6.93	-12.54	-9.55	-1.31	-1.42	-0.96	-0.27	-0.48	-0.37	75.90	-49.58	-109.28	1.56	-3.6	-0.33	2.92	-1.907	-4.203
MET106	-10.19	-7.20	-9.58	-0.83	-0.48	-0.81	-0.39	-0.27	-0.36	-1.42	-4.45	-74.88	1.63	0.48	-1.35	-0.06	-0.171	-2.88
MET107	-8.82	-7.12	-10.68	-0.96	-0.85	-1.86	-0.24	-0.27	-0.41	-27.99	156.39	-84.81	-11.45	10.21	-3.7	-1.08	6.015	-3.262

MET108	-7.73	ND	-9.19	-0.69		-0.48	-0.30		-0.35	45.57		53.82	7.68		6.68	1.75		2.07
MET109	-6.66	ND	-9.33	-0.48		-0.48	-0.25		-0.36	186.60		-279.41	15.07		-15.46	7.18		-10.747
MET110	-12.66	-12.49	-11.02	-1.55	-1.15	-2.01	-0.49	-0.48	-0.42	2.02	-17.72	-176.37	-0.92	5.32	-5.51	0.08	-0.682	-6.783
MET111	-12.97	-8.02	-10.26	-1.92	-1.41	-0.96	-0.50	-0.31	-0.39	-48.27	5.83	-143.74	-1.59	3.59	-15.28	-1.86	0.224	-5.528
MET112	-12.66	-11.36	-10.30	-1.26	-1.13	-1.18	-0.49	-0.44	-0.40	-35.39	-100.6	-131.47	4.40	1.8	-7.22	-1.36	-3.869	-5.057
MET113	-13.86	-11.53	-11.68	-1.65	-1.22	-2.40	-0.53	-0.44	-0.45	26.27	83.14	-91.42	-0.23	4.06	-1.41	1.01	3.198	-3.516
MET114	-12.33	-12.19	-10.81	-2.10	-1.61	-1.70	-0.47	-0.44	-0.42	-47.52	28.75	-211.24	-5.61	2.87	-9.21	-1.83	1.106	-8.125
MET115	-6.53	-9.38	-8.06	-0.90	-1.31	-0.50	-0.25	-0.36	-0.31	45.96	-15	-68.62	-0.93	-4.18	-12.66	1.77	-0.577	-2.639
MET116	-7.22	-3.62	-7.39	-1.31	-1.16	-1.18	-0.28	-0.14	-0.28	-9.21	-26.05	-75.78	-2.00	2.31	-2.34	-0.35	-1.002	-2.915
MET117	-9.83	-1.62	-6.40	-1.51	-1.08	-0.96	-0.38	-0.06	-0.25	-66.01	1.09	-138.51	-1.49	0.78	-11.31	-2.54	0.042	-5.327
MET118	-11.40	-11.76	-9.76	-1.25	-1.51	-0.96	-0.44	-0.45	-0.38	46.49	-83.85	-211.52	2.52	-4.85	-9.92	1.79	-3.225	-8.135
MET119	-4.20	-10.45	-8.56	-0.75	-0.41	-1.00	-0.16	-0.39	-0.32	-18.76	-169.01	-174.85	6.10	-6.16	1.92	-0.70	-6.259	-6.476
MET120	-8.70	-8.71	-7.91	-0.66	-0.37	0.00	-0.32	-0.32	-0.29	10.22	-4.66	-71.36	2.60	3.26	-0.88	0.38	-0.173	-2.643
MET121	-6.38	-6.57	-6.54	-1.37	-1.21	-0.50	-0.24	-0.24	-0.24	-34.38	19.91	-177.86	3.99	3.38	-6.35	-1.27	0.737	-6.588
MET122	-8.04	-9.42	-6.24	-0.96	-0.94	-0.48	-0.30	-0.35	-0.23	33.20	-213.4	-128.27	4.36	-12.91	-3.4	1.23	-7.904	-4.751
MET123	-8.34	ND	-5.15	-0.96		-1.05	-0.31		-0.19	16.41		-152.74	3.42		-8.26	0.61		-5.657
MET124	-8.61	-5.47	-6.84	-0.75	-0.80	-0.64	-0.32	-0.20	-0.25	-48.90	-61.84	-26.53	-5.61	-10.76	-1.51	-1.81	-2.29	-0.983
MET125	-9.75	-9.42	-8.47	-0.14	0.00	-0.93	-0.36	-0.35	-0.31	18.41	46.09	-134.28	-0.59	-6.36	-3.4	0.68	1.707	-4.973
MET126	-9.30	-12.07	-9.53	-1.18	-1.79	-1.72	-0.34	-0.45	-0.30	0.93	-121.84	-131.59	-2.03	-14.29	-13.81	0.04	-4.512	-4.874
MET127	-10.22	-8.04	-7.54	-1.31	-0.59	-1.29	-0.38	-0.25	-0.28	-70.38	-175.38	-114.11	-7.61	-18.67	-5.77	-2.61	-6.495	-4.226
MET128	-5.00	-5.97	-7.10	-1.18	-1.03	-1.74	-0.19	-0.22	-0.26	-20.60	-25.48	-113.42	-9.04	-7.14	-0.74	-0.76	-0.944	-4.201
MET129	-4.46	-4.79	-7.09	-1.13	-0.56	-0.83	-0.17	-0.18	-0.26	9.16	-97.75	3.29	-3.24	-9.49	-5.13	0.34	-3.62	0.122
MET130	-5.99	-13.22	-9.71	-2.42	-1.80	-1.07	-0.22	-0.49	-0.35	-31.32	21.19	-192.39	0.87	2.7	-16.43	-1.16	0.785	-7.126
MET131	-7.17	-9.64	-6.55	-0.88	-0.83	-0.82	-0.27	-0.36	-0.24	85.36	-82.63	-214.92	2.74	-9.17	-15.67	3.16	-3.06	-7.96
MET132	-8.80	ND	-6.67	-1.07		-0.96	-0.33		-0.25	-20.97		-116.04	-3.52		-4.95	-0.78		-4.298
MET133	-6.42	-2.59	-10.07	-0.48	-0.48	-0.95	-0.24	-0.10	-0.37	135.81	-67.48	-104.89	6.70	-5.33	-13.67	5.03	-2.499	-3.885
MET134	-8.24	-12.81	-9.00	-0.80	-1.27	-1.62	-0.30	-0.47	-0.33	14.58	-6.68	-163	-0.94	2.97	-8.18	0.54	-0.247	-6.037
MET135	-8.93	-7.49	-6.83	-1.08	-0.96	-1.44	-0.33	-0.28	-0.25	10.82	-54.63	-186.45	-1.33	-3.23	-22.02	0.40	-2.023	-6.905
MET136	-9.12	-7.02	-6.98	-0.73	-0.48	-1.01	-0.34	-0.26	-0.26	47.23	11.09	15.56	1.39	-5.28	-0.94	1.75	0.411	0.576
MET137	-10.86	ND	-8.94	-0.96		-0.96	-0.40		-0.33	4.96		-0.91	-4.34		-5.91	0.18		-0.034
MET138	-12.31	-10.87	-6.15	-0.54	-0.48	-0.48	-0.46	-0.40	-0.23	10.07	-82.66	-116.75	-2.52	-5.61	-9.12	0.37	-3.062	-4.324
MET139	-5.48	ND	-6.67	-1.79		-1.58	-0.20		-0.24	-28.39		-129.66	-4.63		-13.47	-1.01		-4.631
MET140	-9.22	-5.32	-7.05	-0.83	-1.17	-1.30	-0.33	-0.19	-0.25	-9.59	-195.94	-179.86	-0.25	-6.06	-5.14	-0.34	-6.998	-6.424
MET141	-6.86	-11.97	-7.51	-0.79	-0.83	-0.55	-0.25	-0.43	-0.27	61.68	-104.96	-223.14	-0.40	-10.17	-8.65	2.20	-3.748	-7.969

Table S5 — Key molecular docking parameters for metformin (control) and selected phytocomponents (Berberine, Piperin, Palmatine, Magnoflorine Iodide and Rotundine) against OCTs

Complex	Interaction/Bond	Distance	Category	Types	From Chemistry	To Chemistry
OCT1-Metformin (T01)	T01:N3 - GLU386:OE1	4.83	Electrostatic	Attractive Charge	Positive	Negative
	T01:H8 - GLN241:OE1	1.74	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H10 - GLU386:OE1	2.16	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H11 - GLN241:O	2.57	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
OCT2-Metformin (T01)	T01:H8 - GLU387:OE1	2.45	Hydrogen Bond;Electrostatic	Salt Bridge;Attractive Charge	H-Donor;Positive	H-Acceptor;Negative
	T01:N2 - GLU387:OE2	5.37	Electrostatic	Attractive Charge	Positive	Negative
	T01:N4 - GLU448:OE2	4.68	Electrostatic	Attractive Charge	Positive	Negative
	T01:H9 - THR444:OG1	2.91	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H12 - GLN242:O	2.52	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H1 - GLN242:OE1	2.48	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	T01:N2 - TYR362	3.32	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	T01:H11 - PHE447	2.64	Hydrogen Bond;Electrostatic	Pi-Cation;Pi-Donor Hydrogen Bond	Positive;H-Donor	Pi-Orbitals;Pi-Orbitals
OCT3-Metformin (T01)	T01:H8 - GLU451:OE2	2.08	Hydrogen Bond;Electrostatic	Salt Bridge;Attractive Charge	H-Donor;Positive	H-Acceptor;Negative
	T01:N3 - GLU390:OE1	4.88	Electrostatic	Attractive Charge	Positive	Negative
	GLN247:HE22 - T01:N2	1.84	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H8 - THR447:O	2.45	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H9 - GLU390:OE1	2.12	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H10 - GLU390:OE1	2.32	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H11 - THR447:O	2.78	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H11 - GLU451:OE2	2.24	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	T01:H5 - T01:N4	2.66	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
OCT2-Piperin (M30)	GLN242:HA - M30:O1	2.49	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M30:H10 - GLN242:O	2.50	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M30:H18 - ASN157:OD1	2.68	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M30:H19 - CYS474:O	2.42	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	TYR37 - M30	3.79	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE447 - M30	4.90	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	M30:C17 - CYS474	4.40	Hydrophobic	Alkyl	Alkyl	Alkyl
	TYR37 - M30	5.17	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TYR37 - M30:C17	4.96	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TRP218 - M30	4.37	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	PHE245 - M30	5.48	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	PHE245 - M30	4.21	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TYR362 - M30	4.63	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TYR362 - M30	5.41	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	PHE447 - M30	4.44	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl

	M30 - CYS474	4.70	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
OCT2-Berberine (M37)	SER359:HA - M37:O3	2.76	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H1 - SER246:OG	2.84	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H3 - GLN242:O	2.71	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H7 - GLN242:O	2.68	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H17 - CYS474:O	2.88	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:N1 - TRP218	4.81	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	M37:N1 - PHE447	3.97	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	CYS474:SG - M37	3.69	Other	Pi-Sulfur	Sulfur	Pi-Orbitals
	TYR37 - M37	3.96	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE245 - M37	5.22	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE245 - M37	5.05	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE447 - M37	4.46	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE447 - M37	3.57	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE447 - M37	4.88	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	M37:C20 - CYS474	4.98	Hydrophobic	Alkyl	Alkyl	Alkyl
	TYR37 - M37:C20	5.27	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TRP218 - M37:C6	5.35	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TRP218 - M37:C6	4.70	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	PHE245 - M37:C6	3.55	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
OCT2-Palmatine (M43)	M43:H2 - ASN157:OD1	2.92	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H3 - CYS474:O	2.62	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H3 - M43:O2	2.42	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H5 - SER359:O	2.95	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H7 - SER359:O	3.06	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H17 - SER246:OG	2.96	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H18 - GLU387:OE1	2.96	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H19 - GLN242:O	3.04	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H20 - GLN242:OE1	2.79	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:H21 - GLN242:O	2.74	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M43:N1 - TRP218	4.84	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	PHE245 - M43	5.07	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE245 - M43	5.30	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE447 - M43	3.60	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE447 - M43	4.00	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	TYR37 - M43:C5	5.29	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TRP218 - M43:C21	4.80	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	PHE245 - M43:C21	3.54	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	M43 - CYS474	4.59	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl

OCT3-Berberine (M37)	LYS220:HZ3 - M37:O4	2.49	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	CYS477:HG - M37:O3	2.68	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	M37:H1 - SER386:O	2.68	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H13 - GLN247:OE1	2.51	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H14 - PHE450:O	2.52	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H17 - SER474:OG	3.04	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:H18 - ASP478:OD1	2.51	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M37:N1 - PHE250	3.60	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	M37:N1 - PHE450	3.93	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	PHE250 - M37	4.16	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE250 - M37	3.52	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE450 - M37	4.57	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE450 - M37	3.63	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE450 - M37	5.20	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE32 - M37	5.56	Hydrophobic	Pi-Pi T-shaped	Pi-Orbitals	Pi-Orbitals
	PHE36 - M37	4.96	Hydrophobic	Pi-Pi T-shaped	Pi-Orbitals	Pi-Orbitals
	TYR365 - M37	4.81	Hydrophobic	Pi-Pi T-shaped	Pi-Orbitals	Pi-Orbitals
	M37:C1 - ILE254	4.39	Hydrophobic	Alkyl	Alkyl	Alkyl
	M37:C20 - CYS477	3.56	Hydrophobic	Alkyl	Alkyl	Alkyl
	PHE250 - M37:C6	4.69	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TRP358 - M37:C20	5.27	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TYR365 - M37:C1	4.62	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
OCT3-Magnoflorine Iodide (M41)	M41:N1 - ASP478:OD1	4.29	Electrostatic	Attractive Charge	Positive	Negative
	GLN247:HE22 - M41:O4	2.39	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	M41:H6 - M41:O3	1.59	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	M41:H8 - GLN247:OE1	1.76	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	M41:H1 - SER386:O	2.75	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M41:H2 - SER386:O	2.95	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M41:H15 - ASP478:OD1	2.63	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M41:N1 - PHE36	4.48	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	PHE250 - M41	4.75	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE250 - M41	3.82	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE450 - M41	4.25	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	TYR454 - M41	4.78	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	TYR365 - M41	4.96	Hydrophobic	Pi-Pi T-shaped	Pi-Orbitals	Pi-Orbitals
	TRP223 - M41:C14	4.95	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TRP223 - M41:C14	4.07	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	PHE250 - M41:C14	4.14	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TYR365 - M41:C1	5.41	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
OCT3-Rotundine	GLN366:HE21 - M44:O1	2.11	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor

(M44)	GLN366:HE21 - M44:O2	2.25	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
	M44:H20 - THR447:O	2.91	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:H20 - GLU451:OE2	2.79	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:H21 - GLN247:O	2.63	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:H21 - GLU451:OE2	3.08	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:H21 - M44:O4	2.49	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:H22 - THR447:O	2.68	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:H23 - GLN247:OE1	2.60	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:H24 - GLN247:OE1	2.80	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
	M44:N1 - PHE250	4.73	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
	M44:H26 - PHE450	2.48	Hydrogen Bond;Electrostatic	Pi-Cation;Pi-Donor Hydrogen Bond	Positive;H-Donor	Pi-Orbitals;Pi-Orbitals
	PHE250 - M44	4.08	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE450 - M44	5.45	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	PHE450 - M44	5.13	Hydrophobic	Pi-Pi Stacked	Pi-Orbitals	Pi-Orbitals
	ALA362 - M44:C1	3.95	Hydrophobic	Alkyl	Alkyl	Alkyl
	ALA484 - M44:C1	3.99	Hydrophobic	Alkyl	Alkyl	Alkyl
	M44:C5 - VAL369	4.80	Hydrophobic	Alkyl	Alkyl	Alkyl
	PHE36 - M44:C5	4.99	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	PHE250 - M44:C21	4.26	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	TYR365 - M44:C5	4.86	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
	M44 - ALA362	5.18	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl