Supporting information

The role of secondary metabolites in the production of CuO nanoparticles by fungi: A physiological and metabolic approach

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Supplementary Methods

X-ray photoelectron spectroscopy (XPS) Testing for biosynthesized CuONPs: XPS measurement was performed using PHI 5700, which was equipped with an Electronic Supplementary Material (ESI) for Chemical Communications monochromatic Al Kα X-ray source (hν = 1486.7 eV) incident at 90^{o} relative to the axis of a hemispherical energy analyzer. Spectrometer measurement was performed in both high and low resolutions with pass energies of 23.5 and 187.85 eV, respectively. A photoelectron take-off angle of 45^{o} from the surface, and analyzer spot diameter of 1.1 mm was used. The survey spectra were carried out at the energies from 1 to 1400 eV, and a high solution spectrum was collected for photoelectron emitted for Cu1s and O1s. All spectra were collected at room temperature with a base pressure of 1 x 10^{-8} torr. Electron binding energies were calibrated with respect to the C1s line at 284.8 eV. Data processing was performed using PHI Multipak software (version 7.0A). The high-resolution data was first analyzed by background subtraction using the Shirley routine and a subsequent nonlinear fitting to mixed Gaussian-Lorentzian functions. Atomic compositions were derived from the high-resolution scans. Peak areas were obtained after subtraction of the integrated baseline and corrected for sensitivity factors.

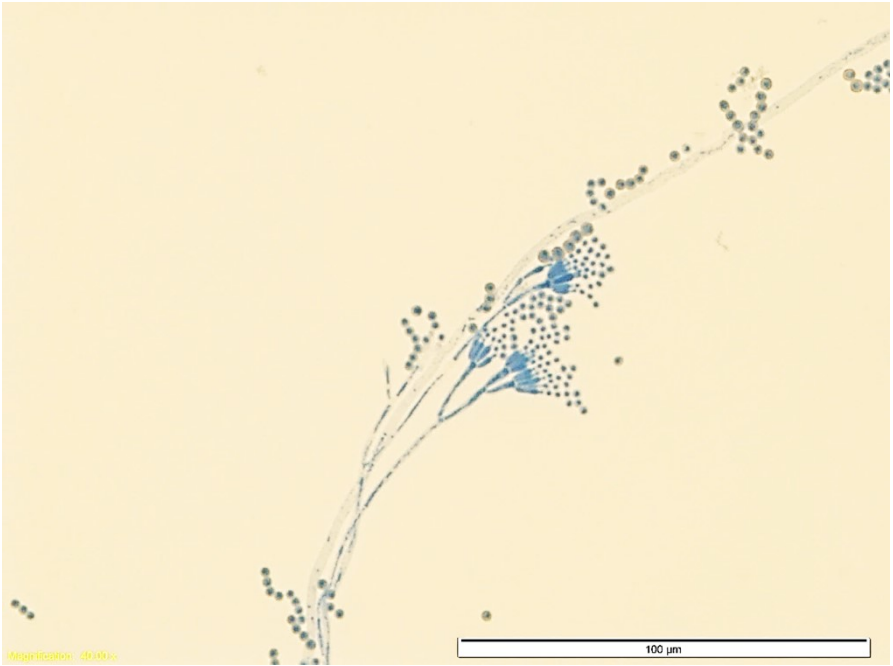


Figure S1. The morphologic characteristic of *Penicillium* spp.

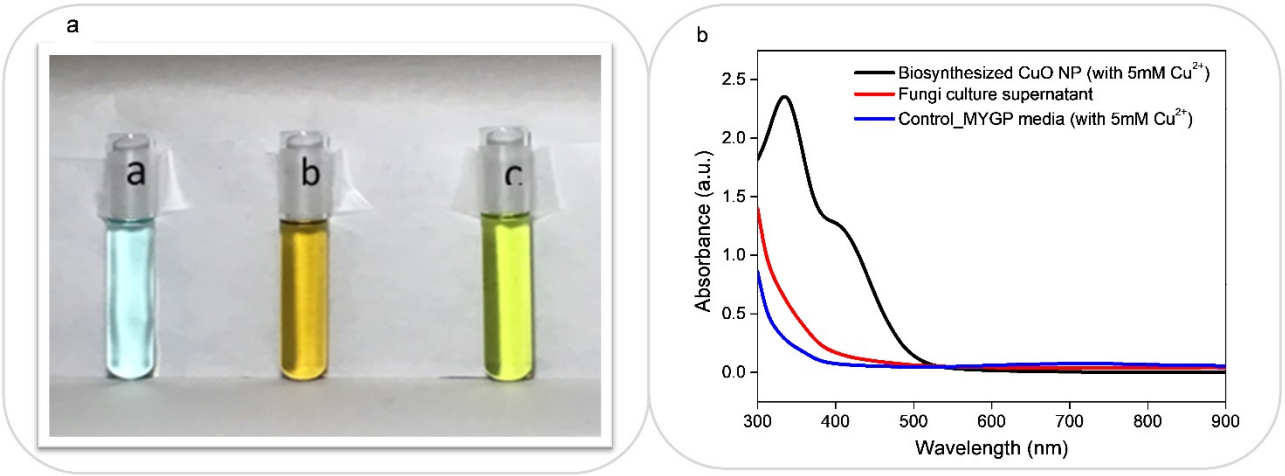


Figure S2. (a) Tube a, b, c represents Fungal growth supernatant (control), MYGP media with 5 mM Cu^{2+} (control) and biosynthesized CuONPs respectively. **(b)** UV vis measurement of CuONPs sample and controls.

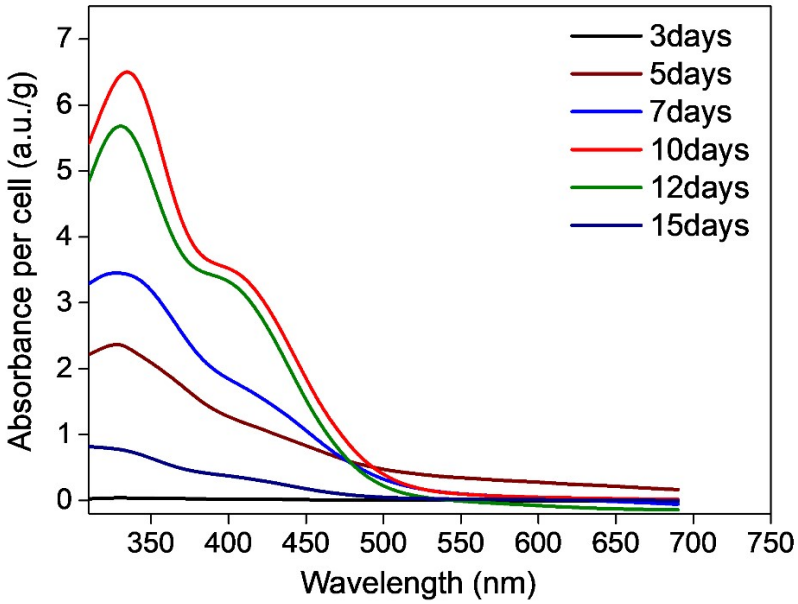


Figure S3. Effects of fungal age on CuONPs synthesis. The absorbance at 330nm was normalized to fungal dried biomass.

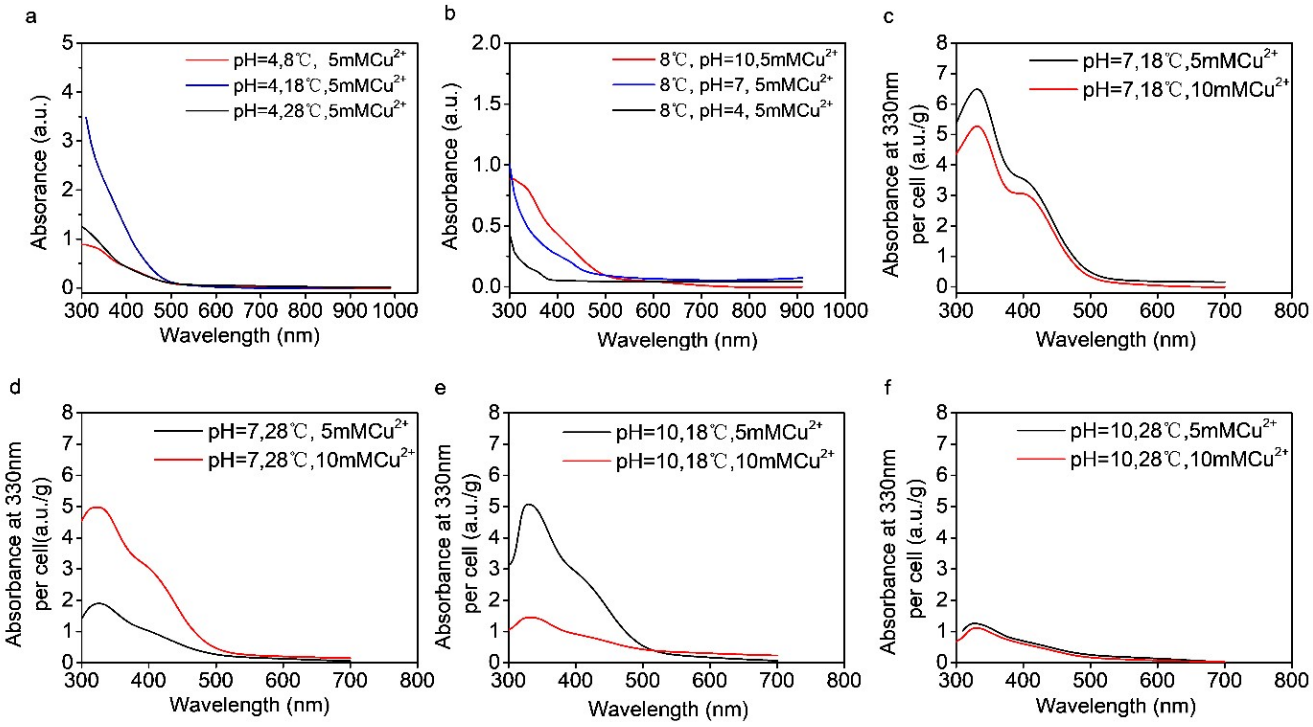


Figure S4. UV-vis measurement of CuONPs samples: Average UV absorption peak (at 330nm) in the cell-free supernatant of fungi with different testing pH, temperatures and copper dosage. **(a)** No UV absorption peak for the CuONPs synthesized at pH=4, $C_{Cu^{2+}}$ = 5 mM, T = 8℃,18℃,28℃. **(b)** No UV absorption peak for the CuONPs synthesized at 8℃ under different testing pH and copper concentration. **(c)** The CuONP samples synthesized at pH=7, T=18℃, $C_{Cu^{2+}}$ = 5 mM,10 mM. **(d)** The CuO samples synthesized at pH=7, T=28℃, $C_{Cu^{2+}}$ = 5 mM,10 mM. **(e)** The CuO samples synthesized at pH=10, T=28℃, $C_{Cu^{2+}}$ = 5 mM,10 mM. **(f)** The CuO samples synthesized

at pH=10, T=28℃, $C_{Cu^{2+}}$ = 5 mM, 10 mM. The absorbance peaks（Fig. S5. e - f） were normalized to the fungal dried mass.

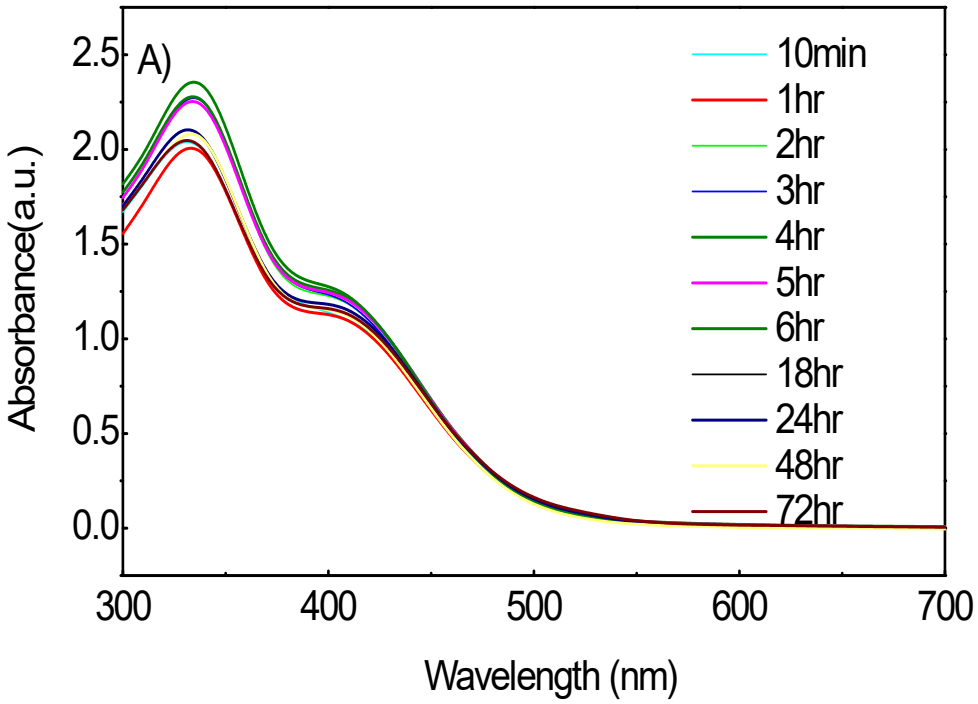


Figure S5. Effects of synthesis time on CuONPs synthesis. (a) Spectra with the 330 nm peak, characteristic peak of CuONPs at 18℃, pH = 7 and 5 mM Cu^{2+}. The absorbance was normalized to the dried fungal mass.

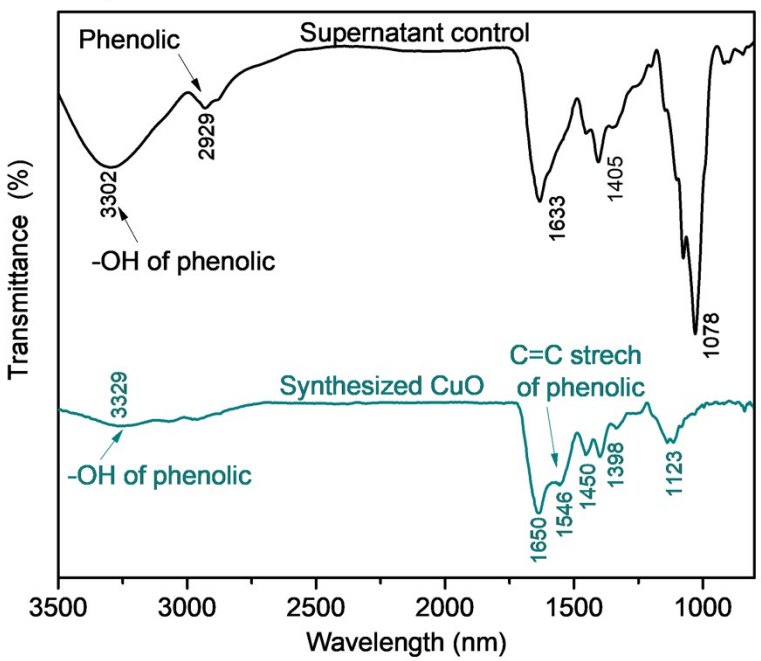


Figure S6. FT-IR spectrum of the biosynthesized CuO nanoparticles (before and after bio-reduction)

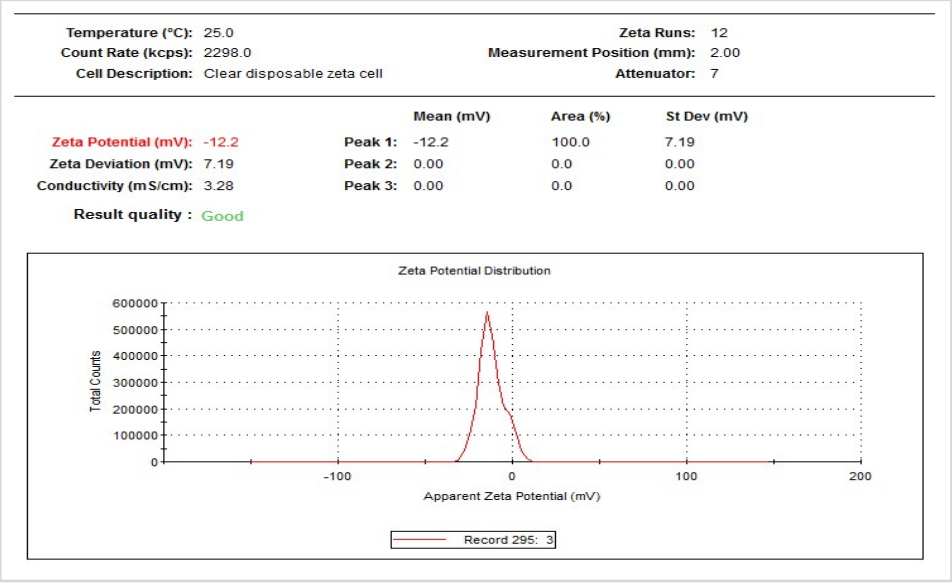


Figure S7. Zeta potential analysis of biosynthesized CuO nanoparticles

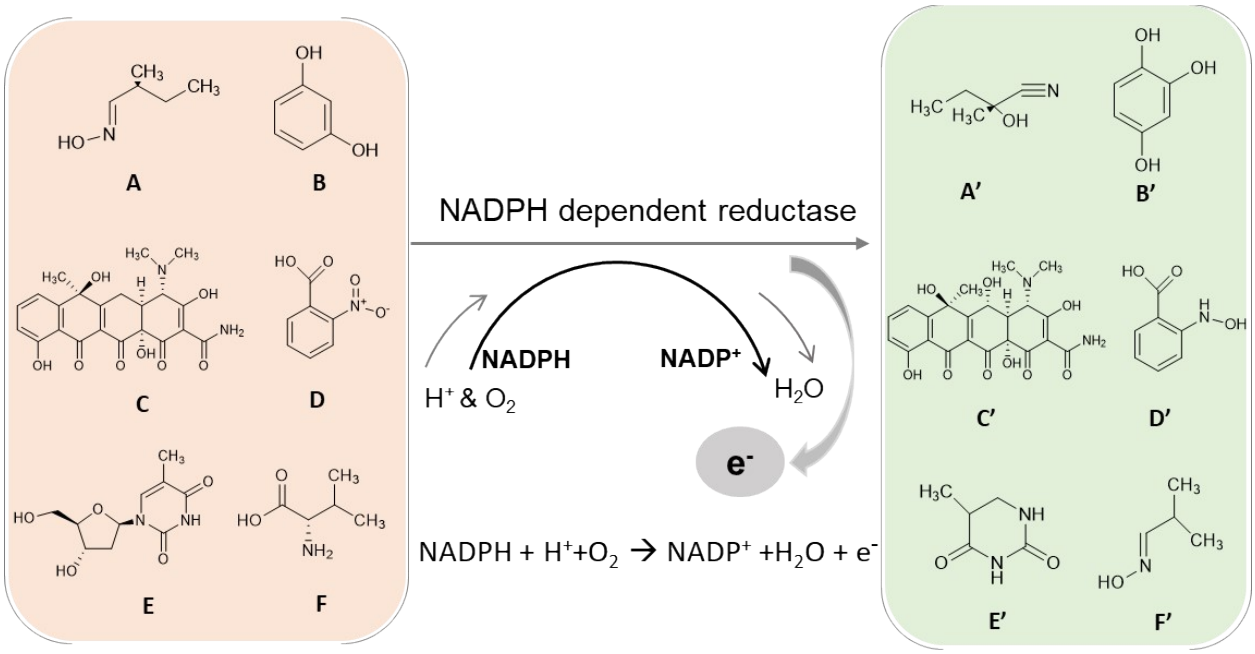


Figure S8. NADPH-dependent oxidoreductase enzymatic reactions involve donating electrons to copper ions: detailed electron transfer reactions

Supplementary Tables

Table. S1. Profiling metabolites data based on Thermo LC-MS/MS based profiling analysis (including total 257 metabolic components（169 ESI(+) and 88ESI(-) components）from MYGP supernatant and 33 of 257 compounds (23 ESI(+) and 11ESI(-) components) from PDB supernatant, in negative mode (ESI (-), Table S.1 A) and in positive mode (ESI (+), Table S.1B) respectively).

Table S1 a. Negative ion mode ESI (-) compounds: 88 components in MYGP and 11compounds in PDB supernatant，P-value <0.005 and Fold change >2.

	Name	Formula	Molecular Weight	RT [min]	Area (Max.)
88 of 105 components in MYGP media identified based on P-value <0.005 and Fold change > 2					
1	2,2'-Iminobis (4-hydroxybenzoic acid)	$C_{14}H_{11}NO_6$	289.0591	5.703	1.13E+08
2	3-(3-formyl-4-hydroxy-5-nitrophenyl)benzoic acid	$C_{14}H_9NO_6$	287.0434	3.555	57753498
3	Gluconic acid	$C_6H_{12}O_7$	196.0584	0.857	54183351
4	Diethyl nitromalonate/Cyanoglucoside	$C_7H_{11}NO_6$	205.0587	0.876	20997863
5	YWA1	$C_{14}H_{12}O_6$	276.0638	5.979	11711000
6	3-Methyl-2-buten-1-yl (2E)-3-(3,4-dihydroxyphenyl)acrylate	C14 H16 O4	248.1052	8.973	10564821
7	N-Acetyl-DL-norvaline?	C7 H13 N O3	159.0897	2.72	8117219
8	Thymidine	$C_{10}H_{14}N_2O_5$	242.0906	2.555	7805096
9	NA	$C_{14}H_9NO_6$	287.0434	2.333	7783231
10	leucodelphinidin	$C_{15}H_{14}O_8$	322.0692	4.642	7657316
11	Propanoicacid, 2,2-dimethyl-,4-(chlorosulfonyl)-2-[2-(2-pyridinyl)diazenyl]-1-naphthalenyl ester	$C_{20}H_{18}ClN_3O_4$	399.1063	0.85	7430631
12	Benzeneaceticacid, a-[(4-nitrobenzoyl)oxy]-	$C_{15}H_{11}NO_6$	301.0591	1.918	7008825
13	1-Butanone,4-[(3,5-dinitrobenzoyl)oxy]-2-methyl-1-phenyl-	$C_{18}H_{16}N_2O_7$	372.0961	2.061	5591425
14	NA	$C_{14}H_{22}N_4O_6$	342.1543	1.303	5470632
15	Digallic acid	$C_{14}H_{10}O_9$	322.0328	4.442	4336288
16	Medronic Acid	$CH_6O_6\ P_2$	175.9635	0.677	3686323
17	ophthalmic acid	$C_{11}H_{19}N_3O_6$	289.1279	2.242	3575528
18	NA	$C_{23}H_{23}N_8O_5P$	522.1533	7.147	3525633
19	Uracil	$C_4H_4N_2O_2$	112.0274	1.174	3315725
20	Exifone	$C_{13}H_{10}O_7$	278.043	2.62	3123835
21	3-(4-Chlorobenzoyl)propionic acid/Ethyl 4-chlorobenzoylformate	$C_{10}H_9ClO_3$	212.0243	6.876	3043124
22	1,4-Naphthalenedione,2,3,5,6,8-pentahydroxy	$C_{10}H_6O_7$	238.0117	4.467	2660346
23	nicotianamine	$C_{12}H_{21}N_3O_6$	303.1434	3.321	2611136
24	Baicalin	$C_{21}H_{18}O_{11}$	446.0855	4.958	2077304
25	APM	$C_7H_{13}NO_4$	175.0846	1.797	2057495
26	Methyl alpha-D-mannopyranoside	$C_7H_{14}O_6$	194.0791	1.09	1981482
27	NA	$C_{29}H_{22}N_4O_8$	554.1434	7.051	1962932
28	L-Alanine,N-(3,5-dimethyl-4-isoxazolyl)-N-(methoxymethyl)-	$C_{11}H_{18}N_2O_4$	242.127	4.315	1937528
29	Hydroxyhydroquinone	$C_6H_6O_3$	126.0318	3.261	1900930
30	Salicylic acid, 5-nitro-	$C_7H_5NO_5$	183.017	2.482	1816275
31	propionylcarnitine	$C_{10}H_{19}NO_4$	217.1315	5.807	1804273
32	Pseudouridine	$C_9H_{12}N_2O_6$	244.0698	1.115	1795235
33	(3S,4R)-3,4,5-Trihydroxy-4'-oxo-3',4,4',5-tetrahydro-2'H,3H-spiro[furan-2,1'-naphthalene]-6'-carboxylic acid	$C_{14}H_{14}O_7$	294.0745	3.944	1762356

34	Pantothenic acid	$C_9H_{17}NO_5$	219.1109	2.841	1642913
35	NA	$C_{10}H_{15}N_3O_6$	273.0965	1.276	1637613
36	NA	$C_{20}H_{41}N_4O_{11}P$	544.2501	3.991	1634531
37	NA	$C_{27}H_{43}N_3O_{14}$	633.2765	3.742	1611164
38	(Z)-3-butylidenephthalide	$C_{12}H_{12}O_2$	188.0838	5.979	1564355
39	Oxagrelate	$C_{14}H_{16}N_2O_4$	276.1116	4.843	1465053
40	Naphtho[2,3-c] furan-4,9-dione,5,6,8-trihydroxy-3-methoxy-1-methyl-	$C_{14}H_{10}O_7$	290.0432	4.319	1457814
41	2-Naphthalenebutanoicacid	$C_{14}H_{16}O_4$	248.1052	7.09	1428814
42	NA	$C_{15}H_{20}N_8O_3$	360.1652	2.304	1405539
43	Benserazide	$C_{10}H_{15}N_3O_5$	257.1016	1.339	1389387
44	N-Acetyl-L-phenylalanine	$C_{11}H_{13}NO_3$	207.0897	4.992	1388527
45	YWA1	$C_{14}H_{12}O_6$	276.0638	6.615	1359808
46	1-(4-Acetoxy-3-methoxyphenyl)-2-propen-1-yl acetate	$C_{14}H_{16}O_5$	264.1001	6.068	1358584
47	NA	$C_5H_5N_6P_3S_2$	305.9217	0.697	1316302
48	Trolox	$C_{14}H_{18}O_4$	250.1208	7.106	1291172
49	1-Pentofuranosyl-2,4(1H,3H)-pyrimidinedione	$C_9H_{12}N_2O_6$	244.0697	1.355	1287893
50	3-Allyl-2-hydroxybenzoic acid	$C_{10}H_{10}O_3$	178.0631	6.908	1217670
51	3-{[(2E)-4-Methoxy-4-oxo-2-butenoyl]amino}-L-alanine	$C_8H_{12}N_2O_5$	216.0749	1.203	1155935
52	Dimethyl chloroterephthalate	$C_{10}H_9ClO_4$	228.0193	4.854	1111701
53	2-Furanpropanoic acid,5-(2-nitrophenyl)-b-oxo-	$C_{15}H_{13}NO_6$	303.0747	6.074	1105503
54	Furo[3,4-e]-1,3-benzodioxole-6-carboxylicacid, 6,8-dihydro-8-oxo-	$C_{10}H_6O_6$	222.0166	3.914	1058333
55	1-[(2'-Methoxyethyl)amino]-2-nitro-4-[di-(2'-hydroxyethyl)amino]benzene	$C_{13}H_{21}N_3O_5$	299.1485	4.419	978503
56	(1R)-1,5-Anhydro-6-deoxy-1-(1-hydroxy-10,12-dimethoxy-6-oxo-8-vinyl-6H-dibenzo[c,h]chromen-4-yl)-D-galactitol	$C_{27}H_{26}O_9$	494.1584	7.17	920786.4
57	YWA1	$C_{14}H_{12}O_6$	276.0638	4.866	891412.9
58	Butanedioic acid,1-[2-(3-carboxy-1-oxopropyl)hydrazide	$C_8H_{12}N_2O_6$	232.0698	1.203	865566.7
59	NA	$C_{22}H_{39}O_7P_3S$	540.164	7.203	829216.4
60	Maraniol	$C_{12}H_{12}O_3$	204.0788	5.979	827914.9
61	Piracetam	$C_6H_{10}N_2O_2$	142.0744	1.172	824855.9
62	1-Allyl-2,3,4,5-tetramethoxybenzene	$C_{13}H_{18}O_4$	238.1208	6.861	761110.3
63	1,1'-(2,4,6-Trihydroxy-1,3-phenylene)diethanone	$C_{10}H_{10}O_5$	210.053	4.531	751655
64	NA	$C_9H_{20}N_7O_9P$	401.1059	0.849	740350.6
65	Itaconic acid	$C_5H_6O_4$	130.0268	0.855	714730.5
66	Aminolevulinic acid	$C_5H_9NO_3$	131.0584	1.486	661808.1
67	cytarabine	$C_9H_{13}N_3O_5$	243.0858	1.313	651414
68	NA	$C_{12}H_{17}N_3O_7$	315.1072	1.905	642143.6

69	alpha-Glutamyl-4-hydroxyproline	$C_{10}H_{16}N_2O_6$	260.1011	0.918	627082.2
70	NA	$C_{28}H_{25}N_4O_4P_3$	574.1093	5.98	620349.8
71	UNII:PP1L5D6A0Y	$C_{12}H_{16}O_4$	224.1052	6.651	606378.2
72	Maclurin monohydrate	$C_{13}H_{12}O_7$	280.0587	6.31	540689.3
73	Methyl-2-acetamido-3 (3,4 diacetoxy- phenyl)-2-propenoate	$C_{16}H_{17}NO_7$	335.101	5.578	540064.3
74	1-[N-(g-L-Glutamyl)amino]-D-proline	$C_{10}H_{17}N_3O_5$	259.1171	0.928	535979.9
75	Ferulic acid?	$C_{10}H_{10}O_4$	194.058	4.697	534153.1
76	6-Methoxy-2-oxo-2H-chromen-7-yl acetate	$C_{12}H_{10}O_5$	234.0531	4.951	523244.3
77	4-hydroxy-4-(indol-3-ylmethyl)glutamic acid	$C_{14}H_{16}N_2O_5$	292.1064	3.339	519229.4
78	[(2S)-2-acetyloxy-3-[2-(6-aminohexanoy lamino) ethoxyhydroxyphosphoryl] oxypropyl] acetate	$C_{15}H_{29}N_2O_9P$	412.1599	2.746	512602.8
79	5-Aminovaleric acid	$C_5H_{11}NO_2$	117.0791	2.72	483035.5
80	N-{2-[(2-Amino-2-carboxyethyl)amino]-2-carboxyethyl}aspartic acid	$C_{10}H_{17}N_3O_8$	307.1019	0.816	469497.3
81	Urea,N-nitroso-N,N'-bis(tetrahydro-2H-pyran-4-yl)-	$C_{11}H_{19}N_3O_4$	257.1379	1.024	465906.9
82	Dihydrouridine	$C_9H_{14}N_2O_6$	246.0854	1.138	433532.5
83	DL-Glutamic acid	$C_5H_9NO_4$	147.0533	1.059	410163.7
84	NA	$C_{12}H_{23}N_4O_8PS$	414.0988	0.854	399529
85	1,1'-Thiobis(2-acetoacetoxyethane), TBEA.	$C_{12}H_{18}O_6S$	290.0829	6.986	379089.3
86	1H-1,4,7-Triazonine-1,4,7-triaceticaci	$C_{12}H_{19}N_3O_6$	301.1277	0.93	368171.5
87	Nicotianamine	$C_{12}H_{21}N_3O_6$	303.1434	2.211	354792.4
88	Diosmetin	$C_{16}H_{12}O_6$	300.0638	6.986	333816.4

11 of 105 components identified in PDB media based on P-value < 0.005 and Fold change >5

1	(2S)-3-Methyl-2-({[(3S,4S,5R)-2,3,4-trihydroxy-5-(hydroxymethyl)tetrahydro-2 furanyl]methyl}amino)butanoic acid (non-preferred name)	$C_{11}H_{21}NO_7$	279.132	1.224	4103317
2	DL-Tyrosine	$C_9H_{11}NO_3$	181.074	1.632	1871530
3	NA	C_6H_7NO	109.0529	2.746	1514189
4	N-Tigloylglycine	$C_7H_{11}NO_3$	157.0741	2.768	1062470
5	Phenyl D-glucopyranosiduronic acid	$C_{12}H_{14}O_7$	270.0743	2.459	677165.4
6	(2R,3S,4S,5R,8R,10R,11S,12S)-2,10-Bis(hydroxymethyl)-1,6,9,13-tetraoxadispiro[4.2.4.2]tetradecane-3,4,11,12-tetrol	$C_{12}H_{20}O_{10}$	324.106	1.831	632431.4
7	NA	$C_{17}H_{14}N_6$	302.1271	3.819	558412.4
8	N-ethylmaleimide	$C_6H_7NO_2$	125.0478	2.72	553834.9
9	Butanamide, N-(1,2-dihydro-8-methoxy-1,4-dimethyl-2-oxo-7-quinolinyl)-3-oxo-	$C_{16}H_{18}N_2O_4$	302.1271	3.961	427655.8
10	3-Hydroxypyridine?	C_5H_5NO	95.0372	3.529	403433.1
11	1-Pyrrolidineaceticacid/1H-Imidazole	$C_{12}H_{18}N_4O_4$	282.1331	2.25	377713.7

Table. S1 b. Positive ion mode ESI (+) compounds:169 components from MYGP and 22 components from PDB supernatant, P-value <0.005 and Fold change >2

	Name	Formula	Molecular Weight	RT [min]	Area (Max.)
169 ESI (+) components in MYGP media identified based on P-value <0.005 and Fold change > 2					
1	Acetic acid,2-[(2-nitronaphtho[2,1-b]furan-7-yl)oxy]-	$C_{14}H_9NO_6$	287.04293	3.943	1.63E+08
2	2,2'-Iminobis (4-hydroxybenzoic acid)	$C_{14}H_{11}NO_6$	289.05856	6.114	62054389
3	thr-asp	$C_8H_{14}N_2O_6$	234.08528	1.056	61741960
4	Aceglutamide	$C_7H_{12}N_2O_4$	188.07984	1.06	59365303
5	NA	$C_{12}H_{27}N_2O_7P$	342.154	1.532	52084518
6	NA	$C_{20}H_{20}N_2O_8$	416.12206	2.102	33532141
7	Diethyl nitromalonate	$C_7H_{11}NO_6$	205.05879	1.083	20885306
8	1,3-Dioxolane-4,4-diaceticacid, 5-oxo-, 4-(phenylmethyl) ester	$C_{14}H_{14}O_7$	294.07393	5.971	20775534
9	NA	$C_{22}H_{14}N_6O_5$	442.10144	2.918	18449849
10	Nicotinic acid	$C_6H_5NO_2$	123.03214	1.5	18200968
11	3-[(4-cyano-2-pyrimidin-2-ylpyrazol-3-yl)diazenyl]-2,6-dihydroxy-N-phenylbenzamide	$C_{21}H_{14}N_8O_3$	426.11789	2.226	17450904
12	2-(3,4-dihydroxy-2-nitrosophenyl)-4-(2,3,4-trihydroxyphenyl) cyclobutane-1,3-dione	$C_{16}H_{11}NO_8$	345.04856	2.188	15794519
13	NA	$C_{26}H_{33}N_2O_{13}P$	612.17071	2.808	15773536
14	1-(4-Acetoxy-3-methoxyphenyl)-2-propen-1-yl acetate	$C_{14}H_{16}O_5$	264.09968	6.769	15437440
15		$C_{25}H_{18}N_{10}O_4$	522.15262	7.49	14877961
16	(2Z)-3-[4,5-Dihydroxy-2-(2-hydroxy-2-propanyl)-2,3-dihydro-1-benzofuran-7-yl] acrylic acid	$C_{14}H_{16}O_6$	280.0946	5.863	14265172
17	(4aS,5aS,6S,12aR)-1,6,10,11,12a-pentahydroxy-6-methyl-3,12-dioxo-4,4a,5,5a-tetrahydro tetracene-2-carboxamide	$C_{20}H_{19}NO_8$	401.11107	4.742	13639537
18		$C_{19}H_{18}N_2O_5$	354.12201	1.867	12391190
19	Uracil?	$C_4H_4N_2O_2$	112.02734	1.406	12217773
20	N-Methylpyrrolidone	C_5H_9NO	99.06846	3.064	11887808
21	2,6-bis-(4,6-dimethoxy-pyrimidin-2-yl-oxy) benzoate	$C_{20}H_{20}N_4O_8$	444.12845	2.191	11519041
22	5-(acridin-9-ylamino)-4,6-dinitro-1,3-dihydrobenzimidazol-2-one	$C_{20}H_{12}N_6O_5$	416.08564	2.335	11383728
23	6-nitro-2,3-bis(3-nitrophenyl)quinoxaline	$C_{20}H_{11}N_5O_6$	417.06973	2.625	10660514
24	3-[(4-cyano-2-pyrimidin-2-ylpyrazol-3-yl)diazenyl]-2,6-dihydroxy-N-phenylbenzamide	$C_{21}H_{14}N_8O_3$	426.11771	2.425	10464478

25	2-amino-1-naphthalen-2-yl-6,7-dinitropyrrolo[3,2-b]quinoxaline-3-carbonitrile	$C_{21}H_{11}N_7O_4$	425.08599	1.628	10434899
26	NA	$C_{25}H_{35}N_4O_{11}P$	598.20248	2.493	10166246
27	NA	$C_{22}H_{14}N_6O_7$	474.09124	2.865	9456515
28	N,2-bis(3-nitrophenyl)quinazolin-4-amine	$C_{20}H_{13}N_5O_4$	387.09524	3.944	8701355
29	4-Hydroxy-6-methyl-2-pyrone	$C_6H_6O_3$	126.03185	3.655	8190673
30	ophthalmic acid	$C_{11}H_{19}N_3O_6$	289.12746	2.567	7842053
31	NA	$C_{29}H_{43}N_3O_9P_2S$	671.21863	2.473	7832949
32	4-Methylene-L-glutamic acid	$C_6H_9NO_4$	159.05333	1.083	7452647
33	na	$C_{17}H_7N_5O_4$	345.04866	2.273	6734179
34	2-[3-(benzotriazol-2-yl)-2-hydroxyphenyl]-6-nitrobenzo[de]isoquinoline-1,3-dione	$C_{24}H_{13}N_5O_5$	451.09068	3.596	6602125
35	NA	$C_{20}H_{20}N_2O_9$	432.11675	1.505	6420085
36	5-azido-4-(1,2-oxazol-3-yl)-3-[4-(1,2-oxazol-3-yl)-1,3-oxazol-2-yl]-1,2-oxazole	$C_{12}H_5N_7O_4$	311.04043	6.154	6411940
37	1,2-Benzenedicarboxylic acid/3a,4,5,7a-Tetrahydro-7-methyl-5-(tetrahydro-2,5-dioxofuran-3-yl)isobenzofuran-1,3-dione	$C_{13}H_{12}O_6$	264.06342	6.108	6024058
38	4-hydroxy-7-[3-(4-methyl-2-nitrophenoxy)propoxy]-3-nitrochromen-2-one	$C_{19}H_{16}N_2O_9$	416.08561	2.839	5975077
39	L-Arginine,N2-(5-oxo-L-prolyl)-; Pyroglutamyl-L-arginine	$C_{11}H_{19}N_5O_4$	285.14361	1.463	5650426
40	5a,11a-Dehydrooxytetracycline	$C_{22}H_{22}N_2O_9$	458.13247	4.939	5562417
41	2-[7-(carboxymethyl)-4-[2-hydroxy-3-(2-phenylmethoxyethoxycarbonylamino)propyl]-10-(phosphonomethyl)-1,4,7,10-tetrazacyclododec-1-yl]acetic acid	$C_{26}H_{44}N_5O_{11}P$	633.27593	4.066	4898857
42	NA	$C_{21}H_{14}N_6O_3$	398.11193	1.867	4732346
43	L-Alanine/Glycine/Butanoic acid	$C_{11}H_{18}N_2O_4$	242.1267	4.964	4585870
44	Butabarbital	$C_{10}H_{16}N_2O_3$	212.1162	2.103	4334662
45	Laguncurin	$C_{13}H_{10}O_6$	262.04785	7.089	4298820
46	gamma-Glutamylleucine	$C_{11}H_{20}N_2O_5$	260.13733	3.887	4084744
47	5-[[6-(3-nitrophenyl)-[1,2,4]triazolo[4,3-b]pyridazin-3-yl]methyl]-2H-isoquinolin-1-one	$C_{19}H_{11}N_5O_4$	373.07988	2.794	3971158
48	NA	$C_{19}H_{20}N_4O_6$	400.13852	2.201	3715474
49	2-Methyl-5-acetonyl-7-hydroxychromone	$C_{13}H_{12}O_4$	232.07358	6.042	3597246
50	pantothenic acid	$C_9H_{17}NO_5$	219.1109	3.192	3590202

51	Benzoic acid/2H-1-Benzopyran-3-aceticacid	$C_{16}H_{13}NO_7$	331.06925	2.262	3537893
52	(2S)-3-(1H-Imidazol-4-yl)-2-({[(3S,4S,5R)-2,3,4-trihydroxy-5-(hydroxymethyl)tetrahydro-2-furanyl]methyl}amino)propanoic acid (non-preferred name)	$C_{12}H_{19}N_3O_7$	317.12234	1.215	3310321
53	[Similar to: Rottlerin; ΔMass: 250.0993 Da]		266.07911	6.69	3289805
54	DL-Proline	$C_5H_9NO_2$	115.06342	2.884	3287841
55	(2R,3S,4S,5S,6R)-2-(hydroxymethyl)-6-[4-[4-(2H-tetrazol-5-yl)phenyl]phenoxy]oxane-3,4,5-triol	$C_{18}H_{15}NO_9$	389.07473	2.867	3266584
56	methyl 2,6-bis[(4,6-dimethoxypyrimidin-2-yl)oxy]benzoate	$C_{20}H_{20}N_4O_8$	444.12839	2.285	3238538
57	propionylcarnitine	$C_{10}H_{19}NO_4$	217.13143	6.308	3222692
58	Valyl-4-hydroxyproline	$C_{10}H_{18}N_2O_4$	230.1268	1.813	3187264
59	Tetraacetylethylenediamine	$C_{10}H_{16}N_2O_4$	228.11119	3.706	3117527
60	Laguncurin	$C_{13}H_{10}O_6$	262.0478	6.19	3006762
61	NA	$C_{20}H_{41}N_4O_{11}P$	544.24964	4.364	2877736
62	(E)-4-Methoxycinnamic acid	$C_{10}H_{10}O_3$	178.06301	7.279	2871230
63	Hydroxy-D-proline isomer	$C_5H_9NO_3$	131.05837	1.761	2839043
64	Purpurin	$C_{14}H_8O_5$	256.03694	7.274	2801205
65	Ethyl 4-chlorobenzoylformate/3-Acetoxy-2-methylbenzoyl chloride	$C_{10}H_9ClO_3$	212.02399	7.262	2789234
66	[Similar to: Methyl N-[5-(4-oxo-3,4-dihydrophthalazin-1-yl)-1H-benzo[d]imidazol-2-yl]carbamate; ΔMass: 0.0015 Da]	$C_{17}H_{13}N_5O_3$	335.10029	5.984	2709883
67	[similar to :Butanoic acid/Carbamic acid,2-propynyl-/Glycine/L-Alanine	$C_{11}H_{18}N_2O_4$	242.1267	4.743	2595028
68	2-Phenylethyl octanoate	$C_{16}H_{24}O_2$	248.17753	7.281	2441243
69	[(2S,3R,5S)-5-(4-amino-2-oxopyrimidin-1-yl)-2-(hydroxymethyl)oxolan-3-yl] (2S)-2-amino-3-methylbutanoate	$C_{14}H_{22}N_4O_5$	326.15896	2.327	2345549
70	[(2S,3R,5S)-5-(4-amino-2-oxopyrimidin-1-yl)-2-(hydroxymethyl)oxolan-3-yl] (2S)-2-amino-3-methylbutanoate	$C_{13}H_{30}N_3O_8P$	387.17531	1.467	2204712
71	1,3-Benzenedimethanol	$C_{14}H_{15}ClO_6$	314.05571	5.801	2192994
72	NA	$C_{12}H_{18}N_4O_2$	250.14307	2.558	2098321
73	4-Hydroxyprolylleucine	$C_{11}H_{20}N_2O_4$	244.14248	2.692	2084640

74	3-Methyl-2-buten-1-yl (2E)-3-(3,4-dihydroxyphenyl)acrylate	$C_{14}H_{16}O_4$	248.10475	7.351	2074661
75	N-(1-Hydroxycyclopropyl)glutamine	$C_8H_{14}N_2O_4$	202.09547	1.088	1962414
76	8-methyl-1,3-dipropyl-7H-purine-2,6-dione	$C_{14}H_{24}N_4O_7$	360.16453	2.623	1802190
77	N-(4-Heptanyl)-1,3-benzodioxole-5-carboxamide	$C_{15}H_{21}NO_3$	263.15217	6.885	1800054
78	Oxagrelate	$C_{14}H_{16}N_2O_4$	276.11109	5.275	1763495
79	trimethadione	$C_6H_9NO_3$	143.05837	6.308	1703829
80	NA	$C_{26}H_{31}N_4O_2P_3$	524.16861	7.449	1700329
81	NA	$C_{15}H_{22}N_6O$	302.18558	7.648	1661645
82	NA	$CH_3N_2O_6P_3$	231.92095	0.866	1623103
83	Cytosine?	$C_4H_5N_3O$	111.04334	2.085	1615302
84	NA	$C_{56}H_{80}N_{10}O_{16}P_2$	1608.74021	3.581	1597398
85	D-Glucono-delta-lactone	$C_6H_{10}O_6$	178.04784	1.062	1556026
86	NA	$C_{12}H_9ClN_6O_4$	336.03765	5.802	1545185
87	DL-Stachydrine	$C_7H_{13}NO_2$	143.09474	1.303	1531368
88	NA	$C_{11}H_8N_6O_3S$	304.03819	5.561	1521821
89	NA	$C_{13}H_{19}N_9O_3$	349.16143	5.173	1493127
90	Benzeneaceticacid	$C_{15}H_{11}NO_6$	301.0588	4.634	1491449
91	[simiar to 2'-O-Methyluridine	$C_{10}H_{14}N_2O_6$	258.08528	2.079	1487783
92	NA	$C_{16}H_{26}N_6$	302.22209	8.105	1433292
93	NA	$C_8H_{16}N_2O_2$	172.12146	2.956	1406436
94	NA	$C_{24}H_{45}N_3O_{15}$	615.28659	4.067	1390608
95	NA	$C_8H_{15}N_7O_3$	257.12389	1.378	1360745
96	NA	$C_{30}H_{39}N_7O_5P_2S$	671.22247	4.071	1300815
97	Citrinin?	$C_{13}H_{14}O_5$	250.08409	6.234	1284442
98	N-(tert-Butoxycarbonyl)-L-leucine	$C_{11}H_{21}NO_4$	231.1472	3.003	1268033
99	NA	$C_4H_6N_6O_5$	218.04031	1.065	1263770
100	NA	$C_{16}H_{24}N_6O_4$	364.18594	7.393	1248896
101	NA	$C_{56}H_{80}N_{10}O_{16}P_2$	1210.5224	2.695	1247446
102	NA	$C_{12}H_9ClN_6O_3$	320.04264	7.085	1229503
103	NA	$C_9H_7N_7O$	229.07153	5.454	1136685
104	(2Z)-3-(3,4,5-Trimethoxyphenyl)-2-propen-1-yl acetate	$C_{14}H_{18}O_5$	266.11529	7.232	1094125
105	tolcapone?	$C_{14}H_{11}NO_5$	273.06369	5.702	1053435
106	[Similar to: N1,N5-Bis(3-pyridinyl)pentanediamide; ΔMass: -0.0001 Da]	$C_{15}H_{16}N_4O_2$	284.1274	3.356	1034386
107	YWA1	$C_{14}H_{12}O_6$	276.06335	5.249	1034155
108	NA	$C_{55}H_{72}N_3O_{15}P$	1045.46982	5.327	1026571
109	Oxolinic acid	$C_{13}H_{11}NO_5$	261.06385	2.78	1025209
110	4-Amino-3-hydroxybenzoic acid	$C_7H_7NO_3$	153.04278	2.945	1002378

111	1-Hydroxy-1-[(6R)-4-hydroxy-2-imino-1,2,5,6,7,8-hexahydro-6-pteridinyl]-2-propanyl beta-D-glucopyranoside	$C_{15}H_{25}N_5O_8$	403.17038	1.185	993739.4
112	NA	$C_{23}H_{27}N_9O_4$	493.21765	3.792	993300.4
113	4,4-Dimethyl-5-(methylcarbamoyloxyimino)valeronitrile	$C_9H_{15}N_3O_2$	197.11649	1.019	990684.1
114	1-[N-(g-L-Glutamyl)amino]-D-proline	$C_{10}H_{17}N_3O_5$	259.11688	1.283	984747.3
115	Benserazide	$C_{10}H_{15}N_3O_5$	257.10126	1.587	967057.5
116	Benzo[b]thiophene-2-carboxylicacid, 5,6-diethoxy-;5,6-Diethoxybenzo[b]thiophene-2-carboxylicacid	$C_{13}H_{14}O_4S$	266.06115	7.295	966580.3
117	NA	$C_{34}H_{71}N_5O_{17}P_2S$	915.40475	2.12	925686.1
118	NA	$C_{35}H_{71}N_2O_{13}P_3S$	852.38987	3.932	904742.3
119	dinotefuran	$C_7H_{14}N_4O_3$	202.10677	1.191	903018.9
120	(1R)-1,5-Anhydro-6-deoxy-1-(1-hydroxy-10,12-dimethoxy-6-oxo-8-vinyl-6H-dibenzo[c,h]chromen-4-yl)-D-galactitol		494.15769	7.519	882781.7
121	UNII:Z5JO63XGNK	$C_{17}H_{26}O_2$	262.19309	7.626	862319.6
122	(+)-Riboflavin	$C_{17}H_{20}N_4O_6$	376.13814	4.939	822614.4
123	2-Pyrrolidone	C_4H_7NO	85.0528	1.048	814093.5
124	[similar to 1H-Benzimidazole-2-acetonitrile]	$C_{14}H_8N_4O_3$	280.05831	6.781	805500.1
125	NA	$C_{26}H_{33}N_8O_2P_3$	582.19628	4.364	805044.3
126	Thymine?	$C_5H_6N_2O_2$	126.04301	2.269	801481.7
127	NA	$C_{21}H_{16}N_6O_3$	400.12715	2.147	794418.7
128	NA	$C_{11}H_{15}N_9O_3$	321.13014	4.844	788852.8
129	NA	$C_{27}H_{51}N_6O_{14}P$	714.31843	4.055	781780.7
130	1-[{2-hydroxyethyl)amino] cyclobutene-1-carbonitrile	C_8H_9N	119.07365	5.454	780792.4
131	6-Hydroxy-8-methoxy-3-methyl-3,4-dihydro-1H-isochromen-1-one	$C_{11}H_{12}O_4$	208.07367	5.671	779119.1
132	NA	$C_{22}H_{25}N_{10}O_9P$	604.1555	6.416	763159.8
133	NA	$C_8H_{17}O_8P$	272.06606	6.233	758759.5
134	NA	$C_{14}H_{11}ClN_6O_4$	362.05331	7.015	747512.4
135	Argininosuccinic acid	$C_{10}H_{18}N_4O_6$	290.12259	1.021	744688.8
136	N, N-Dimethyladenosine	$C_{12}H_{17}N_5O_4$	295.12813	3.838	724680.1
137	capuride	$C_9H_{18}N_2O_2$	186.13709	3.604	713597.7
138	Aspartyl-L-proline	$C_9H_{14}N_2O_5$	230.0904	2.101	702758.2
139	NA	$C_{13}H_{15}O_2P_3$	296.02955	7.275	699556
140	Paramethadione	$C_7H_{11}NO_3$	157.0741	2.386	698043.2

141	NA	$C_{13}H_{20}N_8O_6S$	416.12229	1.543	690981.4
142	Benserazide	$C_{10}H_{15}N_3O_5$	257.10135	2.085	688806.1
143	Triazine-3,5(C175,C181)-dione,2-(2-deoxy-b-D-arabino-hexopyranosyl)-6-methyl-(8CI)	$C_{10}H_{15}N_3O_6$	273.09607	1.506	688461.9
144	epsilon-(gamma-Glutamyl)-lysine	$C_{11}H_{21}N_3O_5$	275.14832	3.301	654256.5
145	NA	$C_{12}H_{17}N_9O_3$	335.1456	4.279	640720
146	n-Ribosylhistidine	$C_{11}H_{17}N_3O_6$	287.11169	1.149	635073.5
147	9H-Purin-6-amine	$C_{10}H_{11}N_5O_3$	249.08621	2.891	618739
148	NA	$C_{11}H_{10}N_8O_2$	286.093	5.014	617247.8
149	NA	$C_{12}H_8N_6O_4$	300.06108	5.683	609763
150	3-(5-Fluoro-2-hydroxy-4-oxo-3,4-dihydro-1(2H)-pyrimidinyl)-L-alanine	$C_7H_{10}FN_3O_4$	219.06585	5.561	595129.5
151	1-Pentofuranosyl-2,4(1H,3H)-pyrimidinedione	$C_9H_{12}N_2O_6$	244.06964	1.607	594542.6
152	NA	$C_{19}H_{27}N_7O_3$	401.21758	7.624	592980.4
153	Dyphylline	$C_{10}H_{14}N_4O_4$	254.10156	1.217	586828.9
154	NA	$C_{12}H_{24}N_2P_2$	258.14092	1.23	573900.6
155	NA	$C_{10}H_{11}N_4O_5P$	298.04549	5.248	566875.6
156	NA	$C_{14}H_{20}N_6O$	288.17	7.579	529502.3
157	NA	$C_{17}H_{26}N_2O_2S_2$	354.14412	7.445	519300.9
158	NA	$C_{15}H_{27}N_5O_9P_2$	483.12802	1.424	509096.2
159	a-D-Glucopyranoside	$C_7H_{15}NO_5$	193.0953	1.133	480503.1
160	NA	$C_4H_6N_7O_2P$	215.03183	1.071	471430.3
161	NA	$C_{13}H_{25}N_2O_6P_3S$	430.06379	1.072	467191.4
162	6-Methoxy-2-oxo-2H-chromen-7-yl acetate	$C_{12}H_{10}O_5$	234.05295	5.341	441297.5
163	2-Pyrimidinamine	$C_{10}H_{10}N_6O_2$	246.08688	7.112	435236
164	NA	$C_{29}H_{43}N_3O_8P_2S$	655.22379	2.496	431165
165	2-chyclohexyl-N-(piperidin-4-yl) acetamide hydrochloride	$C_{16}H_{11}NO_7$	329.05358	2.411	416763.1
166	NA	$C_5H_6N_8O_2$	210.0617	1.405	413744.1
167	2-2’ -sulfonyldiethanol	$C_5H_5N_7O_2$	195.05097	2.163	407806.3
168	NA	$C_{30}H_{34}S$	426.23817	7.476	380587.3
169	NA	$C_{15}H_{21}N_4O_4P$	352.12856	7.358	342381.6

22 ESI (+) Components in PDB media identified based on based on P-value < 0.005 and Fold change >2

1	D-Fructose,1-[[1-carboxy-2-(1H-indol-3-yl)ethyl]amino]-1-deoxy-	$C_{17}H_{22}N_2O_7$	366.14256	3.445	32663739
2	1-{[(3S,4S,5R)-2,3,4-Trihydroxy-5-(hydroxymethyl)tetrahydro-2-furanyl]methyl}-2-pyrrolidinecarboxylic acid (non-preferred name)	$C_{11}H_{19}NO_7$	277.11617	1.252	26335099
3	(2S)-3-Methyl-2-({[(3S,4S,5R)-2,3,4-trihydroxy-5-(hydroxymethyl)tetrahydro-2-	$C_{11}H_{21}NO_7$	279.13172	1.206	15815560

	furanyl]methyl}amino)butanoic acid (non-preferred name)				
4	Pyridoxine	$C_8H_{11}NO_3$	169.07401	1.622	12056005
5	3,5-Dimethyl-1h-Pyrrole-2,4-Dicarboxylic Acid	$C_8H_9NO_4$	183.05329	1.184	9504445
6	3-(4-Amino-2-methylpyrimidyl-5-methyl)-4-methyl-5,betahydroxyethylthiazolium nitrate	$C_{12}H_{17}N_5O_4S$	327.09869	1.109	8207362
7	4-Amino-3-[(1-carboxyvinyl)oxy]-1,5-cyclohexadiene-1-carboxylic acid	$C_{10}H_{11}NO_5$	225.06373	1.699	8065979
8	Phthalazino[2,3-b]phthalazine-5,12(7H,14H)-dione	$C_{16}H_{12}N_2O_2$	264.08981	5.956	6747292
9	4-Nitroacetophenone	$C_8H_7NO_3$	165.04277	3.091	6224828
10	(5R,6R)-3,3-dimethyl-7-oxo-6-(2-phenylethanoylamino)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid	$C_{16}H_{18}N_2O_4$	302.12667	4.166	2559272
11	(2S,5R,6R)-3,3-dimethyl-7-oxo-6-(2-phenylethanoylamino)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid	$C_{16}H_{18}N_2O_4$	302.12663	4.19	2452074
12	1-Pyrrolidineaceticacid/1H-Imidazole	$C_{12}H_{18}N_4O_4$	282.13282	2.096	2369748
13	Phenacetin?	$C_{10}H_{13}NO_2$	179.09471	5.284	1841262
14	[siimilar to 1-(oxiranylmethyl)-3,5-di-2-propenyl-1,3,5-Triazine-2,4,6(1H,3H,5H)-trione	$C_{12}H_{15}N_3O_4$	265.10614	3.441	1833240
15	[similar to L-Aspartic acid 4-tert-butyl este	$C_8H_{15}NO_4$	189.10025	2.4	1627202
16		$C_9H_{21}NO_{10}P_2$	365.06391	1.744	1363189
17	N-hydroxy-2-(6-oxo-4-phenyl-1,6-dihydropyrimidin-2-yl) acetamide	$C_{12}H_{11}N_3O_3$	245.08022	1.908	1126442
18	NA	$C_{13}H_{24}N_2O_8$	336.15315	1.162	1096218
19	NA	$C_{23}H_{16}N_6O$	392.13713	5.499	1074948
20	NA	$C_{13}H_7N_7O$	277.0714	7.29	700959.2
21	[similar to Alanine,N-[(4-methylphenyl)sulfonyl]-	$C_{10}H_{13}NO_4S$	243.05656	1.11	657213
22	Phenol,2-(4-nitrophenoxy)	$C_{12}H_9NO_4$	231.05338	2.177	551381.9

Table S2. Potentially relevant oxidases responsible for the formation of oxidants (hydrogen peroxide (H_2O_2))

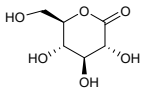
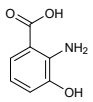
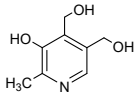
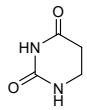
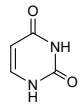
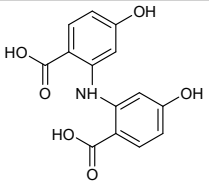
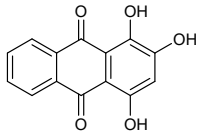
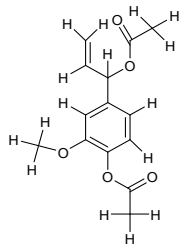
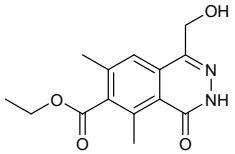
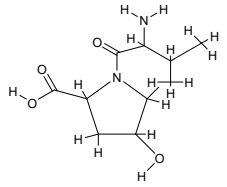
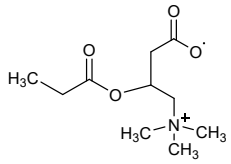
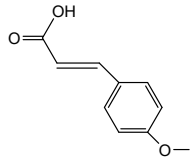
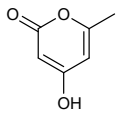
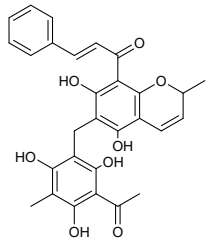
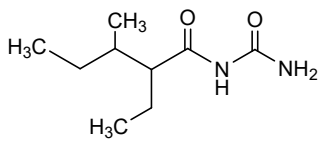
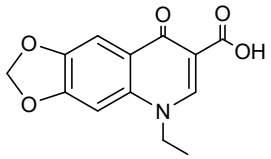
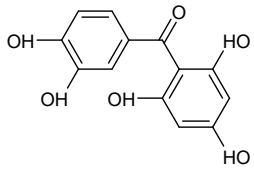
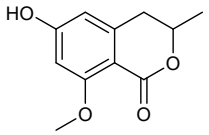
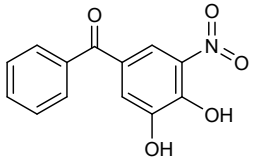
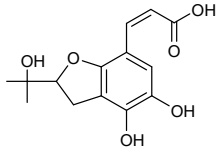
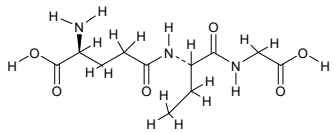
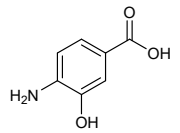
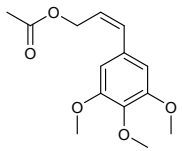
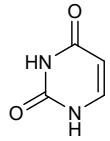
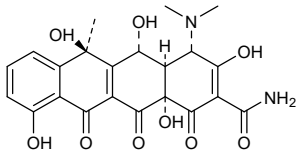
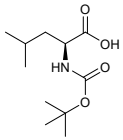
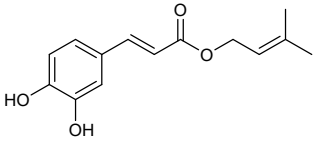
Metabolites	Formula	Structure	Pathway	Enzyme name
D-Glucono-1,5-lactone	$C_6H_{10}O_6$		-Pentose phosphate pathway; -Metabolic pathways; -Microbial metabolism in diverse environments;	Glucose oxyhydrase (EC 1.3.3.4); hexose oxidase (EC 1.3.3.5)
4-Amino-3-hydroxybenzoic acid	$C_7\ H_7\ N\ O_3$		-Tryptophan metabolism; -Aminobenzoate degradation; -Metabolic pathways; -Microbial metabolism in diverse environments;	3-Hydroxyanthranilate oxidase EC (1.10.3.5)
Pyridoxine	$C_8\ H_{11}N\ O_3$		-Vitamin B6 metabolism -Metabolic pathways -Microbial metabolism in diverse environments	Pyridoxine 4-oxidase(EC1.1.3.12) pyridoxamine phosphate oxidase (EC 1.4.3.5)
Hydrouracil	$C_4H_6N_2O_2$		-Pyrimidine metabolism; -beta-Alanine metabolism; -Pantothenate and CoA biosynthesis; -Metabolic pathways;	dihydrouracil oxidase (EC 1.3.3.7)
Uracil	$C_4H_4N_2O_2$		-Pyrimidine metabolism; -beta-Alanine metabolism; -Pantothenate and CoA biosynthesis; -Metabolic pathways;	dihydrouracil oxidase (EC 1.3.3.7)

Table S3a. Top 25 of total 169 ESI (+) compounds in MYGP culture media (ranking based on FC (fold change) number)

Ranking	Name	Formula	Structure	FC (Fold change) number	KEGG Pathways
1	2,2'-Iminobis (4-hydroxybenzoic acid)	$C_{14}H_{11}NO_6$		14.1301	NA
2	Purpurin	$C_{14}H_8O_5$		11.9657	NA
3	1-(4-Acetoxy-3-methoxyphenyl)-2-propen-1-yl acetate	$C_{14}H_{16}O_5$		11.3561	NA
4	N-(4-Heptanyl)-1,3-benzodioxole-5-carboxamide	$C_{15}H_{21}NO_3$		10.5023	NA

5	[Methyl N-[5-(4-oxo-3,4-dihydrophthalazin-1-yl)-1H-benzo[d]imidazol-2-yl]carbamate;	$C_{17}H_{13}N_5O_3$		10.381	NA
6	Propionylcarnitine	$C_{10}H_{19}NO_4$		9.9233	NA
7	(E)-4-Methoxycinnamic acid	$C_{10}H_{10}O_3$		9.9191	Metabolic pathways; Biosynthesis of secondary metabolites;2-Oxocarboxylic acid metabolism; Other
8	4-Hydroxy-6-methyl-2-pyrone or Hydroxyhydroquinone	$C_6H_6O_3$		9.5079	Metabolic pathways; Microbial metabolism in diverse environments; Biosynthesis of antibiotics; Aminobenzoate degradation; Other
9	Rottlerin	$C_{30}H_{28}O_8$		9.4200	Other

10	capuride	$C_9H_{18}N_2O_2$		9.3584	Metabolic pathways; Microbial metabolism in diverse environments; Biosynthesis of secondary metabolites;
11	Oxolinic acid	$C_{13}H_{11}NO_5$		9.3053	other
12	Laguncurin	$C_{13}H_{10}O_6$		9.2462	Metabolic pathways; Microbial metabolism in diverse environments; Other
13	6-Hydroxy-8-methoxy-3-methyl-3,4-dihydro-1H-isochromen-1-one	$C_{11}H_{12}O_4$		9.2035	Metabolic pathways; Microbial metabolism in diverse environments; Biosynthesis of secondary metabolites; Degradation of aromatic compounds; Other
14	tolcapone?	$C_{14}H_{11}NO_5$		8.9990	Metabolic pathways; Microbial metabolism in diverse environments; Biosynthesis of secondary metabolites;
15	(2Z)-3-[4,5-Dihydroxy-2-(2-hydroxy-2-propanyl)-2,3-dihydro-1-benzofuran-7-yl]acrylic acid	$C_{14}H_{16}O_6$		8.9382	Other

16	ophthalmic acid	$C_{11}H_{19}N_3O_6$		8.9119	Metabolic pathways; Other
17	4-Amino-3-hydroxybenzoic acid	$C_7H_7NO_3$		8.8332	Microbial metabolism in diverse environments /Aminobenzoate degradation
18	(2Z)-3-(3,4,5-Trimethoxyphenyl)-2-propen-1-yl acetate	$C_{14}H_{18}O_5$		8.8094	other
19	Uracil?	$C_4H_4N_2O_2$		8.16210	Metabolic pathways/ Pyrimidine metabolism; Other
20	5a,11a-Dehydrooxytetracycline	$C_{22}H_{22}N_2O_9$		8.0433	Tetracycline biosynthesis or Biosynthesis of type II polyketide products
21	N-(tert-Butoxycarbonyl)-L-leucine	$C_{11}H_{21}NO_4$		7.96167	Metabolic pathways/Biosynthesis of secondary metabolites;
22	3-Methyl-2-buten-1-yl (2E)-3-(3,4-dihydroxyphenyl) acrylate	$C_{14}H_{16}O_4$		7.5830	Biosynthesis of antibiotics; Other

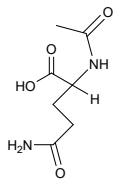
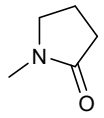
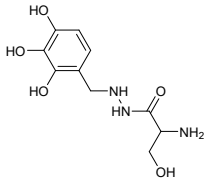
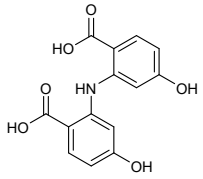
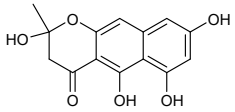
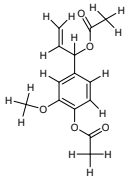
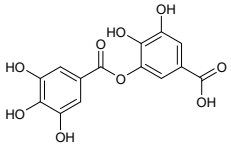
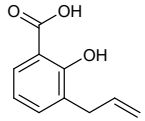
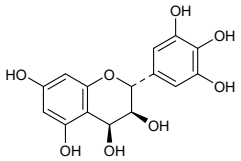
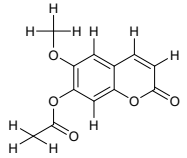
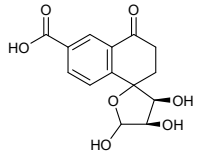
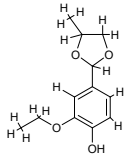
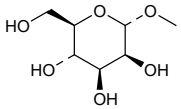
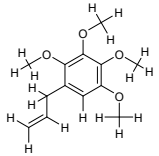
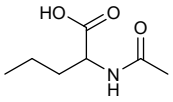
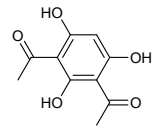
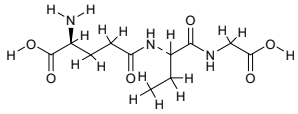
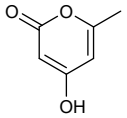
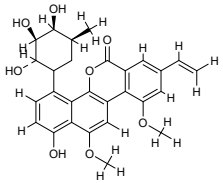
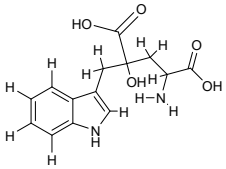
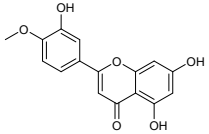
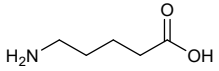
23	Aceglutamide	$C_7H_{12}N_2O_4$		7.4598	Biosynthesis of antibiotics; Other
24	N-Methylpyrrolidone	C_5H_9NO		7.3895	Biosynthesis of antibiotics; Other
25	Benserazide	$C_{10}H_{15}N_3O_5$		6.941	Metabolic pathways; Microbial metabolism in diverse environments; Biosynthesis of secondary metabolites;

Table S3b. TOP 25 of total 88 ESI (-) compounds in MYGP media (ranking based on FC number)

Ranking	Name	Formula	Structure	FC (Fold change) number	KEGG Pathways
1	2,2'-Iminobis (4-hydroxybenzoic acid)	$C_{14}H_{11}NO_6$		15.1975	NA
2	YWA1	$C_{14}H_{12}O_6$		11.5885	NA
3	1-(4-Acetoxy-3-methoxyphenyl)-2-propen-1-yl acetate	$C_{14}H_{16}O_5$		11.5607	Metabolic pathways/ Biosynthesis of secondary metabolites
4	Digallic acid	$C_{14}H_{10}O_9$		11.3164	NA
5	3-Allyl-2-hydroxybenzoic acid	$C_{10}H_{10}O_3$		10.6746	Metabolic pathways; Biosynthesis of secondary metabolites;2-Oxocarboxylic acid metabolism;

6	leucodelphinidin	$C_{15}H_{14}O_8$		10.5084	Biosynthesis of secondary metabolites;
7	6-Methoxy-2-oxo-2H-chromen-7-yl acetate	$C_{12}H_{10}O_5$		10.3994	Metabolic pathways; Microbial metabolism in diverse environments;
8	(3S,4R)-3,4,5-Trihydroxy-4'-oxo-3',4,4',5-tetrahydro-2'H,3H-spiro[furan-2,1'-naphthalene]-6'-carboxylic acid	$C_{14}H_{14}O_7$		10.3631	Biosynthesis of secondary metabolites;
9	UNII: PP1L5D6A0Y	$C_{12}H_{16}O_4$		10.0496	Other
10	Methyl alpha-D-mannopyranoside	$C_7H_{14}O_6$		9.8825	ABC transporters/Other
11	1-Allyl-2,3,4,5-tetramethoxybenzene	$C_{13}H_{18}O_4$		9.6714	Metabolic pathways; Microbial metabolism in diverse environments;
12	N-Acetyl-DL-norvaline?	$C_7H_{13}NO_3$		9.6049	Other

13	1,1'-(2,4,6-Trihydroxy-1,3-phenylene) diethanone	$C_{10}H_{10}O_5$		9.2201	Metabolic pathways; Biosynthesis of secondary metabolites;
14	ophthalmic acid	$C_{11}H_{19}N_3O_6$		9.1146	Metabolic pathways; Other
15	4-Hydroxy-6-methyl-2-pyrone	$C_6H_6O_3$		9.1075	Metabolic pathways; Microbial metabolism in diverse environments;
16	(1R)-1,5-Anhydro-6-deoxy-1-(1-hydroxy-10,12-dimethoxy-6-oxo-8-vinyl-6H-dibenzo[c,h]chromen-4-yl)-D-galactitol	$C_{27}H_{26}O_9$		8.9693	Metabolic pathways; Microbial metabolism in diverse environments;
17	4-hydroxy-4-(indol-3-ylmethyl)glutamic acid	$C_{14}H_{16}N_2O_5$		8.428	Biosynthesis of antibiotics;
18	Diosmetin	$C_{16}H_{12}O_6$		8.4212	Biosynthesis of secondary metabolites;
19	5-Aminovaleric acid	$C_5H_{11}NO_2$		8.4043	Metabolic pathways; Biosynthesis of secondary

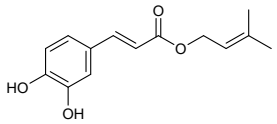
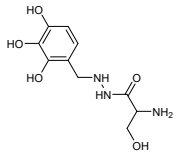
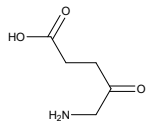
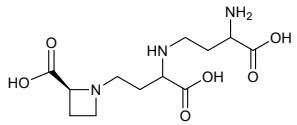
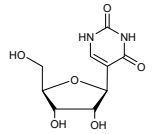
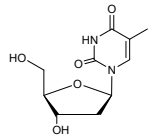
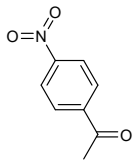
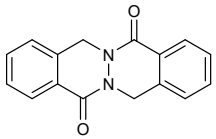
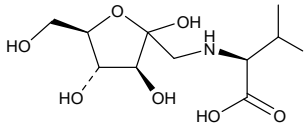
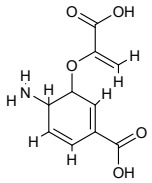
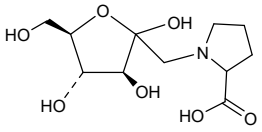
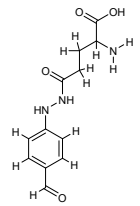
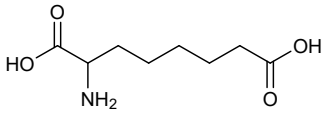
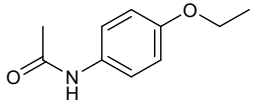
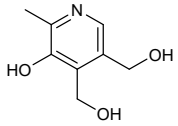
					metabolites;
20	3-Methyl-2-buten-1-yl (2E)-3-(3,4-dihydroxyphenyl) acrylate	$C_{14}H_{16}O_4$		7.844	Other
21	Benserazide	$C_{10}H_{15}N_3O_5$		7.8205	NA
22	Aminolevulinic acid	$C_5H_9NO_3$		7.8194	Metabolic pathways; Biosynthesis of secondary metabolites;Biosynthesis of amino acids;
23	Nicotianamine	$C_{12}H_{21}N_3O_6$		7.4543	NA
24	Pseudouridine	$C_9H_{12}N_2O_6$		7.3607	Metabolic pathways , Pyrimidine metabolism
25	Thymidine	$C_{10}H_{14}N_2O_5$		6.4196	Pyrimidine metabolism

Table S3 c. Key ESI (+) compounds in PDB media ((P-value < 0.005 and Fold change >2)

Ranking	Name	Formula	Structure	FC (fold change) number	KEGG Pathways
1	4-Nitroacetophenone	$C_8H_7NO_3$		8.1994	Microbial metabolism in diverse environments; Biosynthesis of secondary metabolites;
2	Phthalazino[2,3-b] phthala zine-5,12(7H,14H)-dione	$C_{16}H_{12}N_2O_2$		7.9908	Other
3	(2S)-3-Methyl-2-({[(3S,4S,5R)-2,3,4-trihydroxy-5-(hydroxymethyl) tetrahydro -2-furanyl]methyl}amino)butanoic acid (non-preferred name)	$C_{11}H_{21}NO_7$		7.8499	Metabolic pathways;
4	4-Amino-3-[(1-carboxyvinyl) oxy]-1,5-cyclohexadiene-1-carboxylic acid	$C_{10}H_{11}NO_5$		6.3481	Biosynthesis of antibiotics;
5	1-{[(3S,4S,5R)-2,3,4-Trihydroxy-5-(hydroxymethyl) tetrahydro-2-furanyl] methyl}-2-pyrrolidinecarboxylic acid (non-preferred name)	$C_{11}H_{19}NO_7$		5.6668	Metabolic pathways;

6	4-(Acetoxymethylnitrosamino)-1-(3-pyridyl)-1-butanone	$C_{12}H_{15}N_3O_4$		4.4366	
7	2-Aminooctanedioic acid	$C_8H_{15}NO_4$		3.7087	
8	Phenacetin	$C_{10}H_{13}NO_2$		2.479	Biosynthesis of secondary metabolites;2-Oxocarboxylic acid metabolism; Other
9	Pyridoxine	$C_8H_{11}NO_3$		2.0298	Metabolic pathways; Microbial metabolism in diverse environments; Other

Note: The key information for the compounds were presented in the above table based on Thermo Compound Discoverer analysis results.

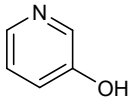
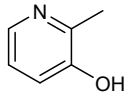
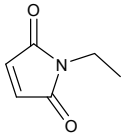
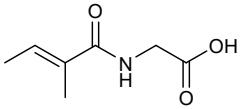
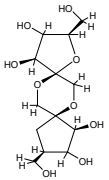
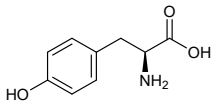
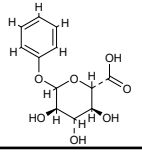
Ranking	Name	Formula	Structure	FC (fold change) number	KEGG Pathways
1	3-Hydroxypyridine	C_5H_5NO		8.00638	NA
2	4-Aminophenol	C_6H_7NO		7.5924	Microbial metabolism in diverse environments; Other
3	N-ethylmaleimide	$C_6H_7NO_2$		7.2775	Biosynthesis of secondary metabolites;Microbial metabolism in diverse environments;Other
4	N-Tigloylglycine	$C_7H_{11}NO_3$		7.0844	Biosynthesis of antibiotics
5	(2R,3S,4S,5R,8R,10R,11S,12S) -2,10-Bis(hydroxymethyl)- 1,6,9,13-tetraoxadispiro [4.2.4.2] tetradecane-3,4,11,12-tetrol	$C_{12}H_{20}O_{10}$		6.7645	NA
6	DL-Tyrosine	$C_9H_{11}NO_3$		6.0089	Metabolic pathways;Biosynthesis of antibiotics;Biosynthesis of secondary metabolites;Biosynthesis of amino acids; 2-Oxocarboxylic acid metabolism; etc.
7	Phenyl D-glucopyranosiduronic acid	$C_{12}H_{14}O_7$		4.68097	NA

Table S3 d. ESI (-) Compounds in PDB media (P-value < 0.005 and Fold change >2)

Note: The key metabolites were presented in the above table based on Thermo Compound Discoverer analysis.

Table S4. Functional groups presented in the metabolites of fungal supernatant growing in MYGP & in PDB media.

Functional groups	Proportion of the total functional groups (Top 25 ESI (+) components in MYGP media Vs. the components in PDB media.)		Proportion of the total functional groups (Top 25 ESI (-) components in MYGP media Vs. the components in PDB media.)	
	MYGP media	PDB media	MYGP media	PDB media
-COOH	24%	44%	28%	28%
Multi phenolic hydroxyl	40%	0	40%	0
Amide (-C=O-NH)	20%	44%	16%	14%
Amino (-NH2)	8%	22%	16%	14%
Carbonyl (C=O)	24%	22%	32%	28%