Electronic Supplementary Material (ESI) for Analyst.

Supplementary files

Quantitative profiling of carbonyl metabolites directly in crude biological extracts using Chemoselective Tagging and nanoESI-FTMS

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Table S-1. Fitted rate constants for the reaction between carbonyl standards and QDA.

The reaction of QDA with standards (Figure 3) was fitted using the equation $P = a(1\text{-}e^{-kt})$, where P is the FTMS signal for QDA product, k is the apparent rate constant and t is the reaction time (min).

	a	k /min	SSE[a]	R^2	Half-life (min)
ADP ribose	0.07202 (0.06598, 0.07806)[#]	0.01127 (0.00786, 0.01469)	0.0001086	0.9637	61.5037
Acetoacetate	0.1793 (0.1668, 0.1918)	0.0158 (0.01116, 0.02045)	0.000606	0.9329	43.8701
Deoxyribose	0.1778 (0.1564, 0.1993)	0.01409 (0.00726, 0.02092)	0.001643	0.9508	49.1943
GAP	0.1039 (0.09362, 0.1143)	0.01208 (0.00759, 0.01656)	0.0003358	0.9464	57.3797
Galacturonic acid	0.1568 (0.1095, 0.2041)	0.008087 (0.00059, 0.01559)	0.005193	0.8191	85.7113
Glc-6P	0.05354 (0.05031, 0.05678)	0.01581 (0.01177, 0.01985)	0.00004085	0.9684	43.8423
Glucose	0.06544 (0.06112, 0.06975)	0.01185 (0.00896, 0.01475)	0.00005765	0.9817	58.4934
MDA	0.1847 (0.09812, 0.2712)	0.007837 (-0.00330, 0.01897)	0.01703	0.5661	88.4455
PLP	0.08576 (0.0835, 0.08803)	0.05388 (0.04256, 0.0652)	0.00003228	0.8847	12.8646
Pyruvate	0.1753 (0.1575, 0.193)	0.009307 (0.00621, 0.01241)	0.0008093	0.9574	74.4759
Ribose	0.1091 (0.08986, 0.1283)	0.009714 (0.00396, 0.01547)	0.0009814	0.9377	71.3555
Ribose-5P	0.07011 (0.05645, 0.08377)	0.008524 (0.00329, 0.01376)	0.0004495	0.8904	81.3171
4-HNE	0.1734 (0.1713, 0.1755)	0.02261 (0.02127, 0.02394)	0.00002155	0.9969	30.6567
alpha-KG	0.2019 (0.1789, 0.2249)	0.01187 (0.00686, 0.01689)	0.001644	0.9369	58.3949

[#]: 95% confidence interval
a sum squared error

Table S-2. Detected QDA/*QDA ion pairs in patient-derived mouse tumor xenograft by nanoESI-FTMS.

Measured m/z of QDA adduct	Mass Error (mDa)	Intensity	Molecular Formula of carbonyl	Adduct	Comment
284.2825	0.24	3.25E+04	C2H2O2	di-QDA	present in blank
291.2899	-0.11	1.27E+05	C3H4O2	di-QDA	
299.3057	0.01	7.42E+06	C2H4O1	QDA	present in blank
311.3057	-0.01	2.03E+04	C3H4O1	QDA	present in blank
313.3213	0.00	2.59E+06	C3H6O1	QDA	present in blank
314.3166	0.03	1.90E+03	C2H5N1O1	QDA	
315.3006	0.02	5.57E+05	C2H4O2	QDA	present in blank
327.3370	-0.04	5.52E+05	C4H8O1	QDA	present in blank
328.3323	0.02	5.26E+03	C3H7N1O1	QDA	
329.2798	-0.03	8.33E+04	C2H2O3	QDA	
329.3162	-0.02	1.11E+06	C3H6O2	QDA	present in blank
341.3162	-0.05	3.25E+04	C4H6O2	QDA	
341.3526	-0.03	3.89E+05	C5H10O1	QDA	present in blank
342.3479	-0.03	8.87E+03	C4H9N1O1	QDA	
343.2955	-0.02	3.80E+06	C3H4O3	QDA	
343.3319	-0.03	3.37E+05	C4H8O2	QDA	present in blank
345.3111	-0.05	3.10E+06	C3H6O3	QDA	
351.3005	-0.07	1.90E+05	C5H4O2	QDA	present in blank
355.3318	-0.06	3.71E+05	C5H8O2	QDA	present in blank
355.3682	-0.06	1.25E+06	C6H12O1	QDA	present in blank
357.3111	-0.11	7.76E+05	C4H6O3	QDA	
359.2903	-0.14	2.43E+03	C3H4O4	QDA	
361.3213	-0.09	1.77E+05	C7H6O1	QDA	present in blank
369.3475	-0.09	3.78E+05	C6H10O2	QDA	
369.3839	-0.08	9.83E+05	C7H14O1	QDA	present in blank
371.3267	-0.09	2.59E+05	C5H8O3	QDA	present in blank
371.3631	-0.08	1.39E+06	C6H12O2	QDA	present in blank
372.3219	-0.18	4.75E+03	C4H7N1O3	QDA	
375.3216	-0.09	2.83E+05	C4H8O4	QDA	
377.3161	-0.12	3.38E+04	C7H6O2	QDA	present in blank
383.3995	-0.11	1.01E+06	C8H16O1	QDA	present in blank
385.3424	-0.11	2.69E+05	C6H10O3	QDA	present in blank
386.3376	-0.11	5.65E+04	C5H9N1O3	QDA	
387.3216	-0.13	1.11E+04	C5H8O4	QDA	present in blank
389.3373	-0.12	2.64E+05	C5H10O4	QDA	
389.3525	-0.12	1.20E+06	C9H10O1	QDA	present in blank
393.3838	-0.15	3.11E+04	C9H14O1	QDA	present in blank

395.3631	-0.07	1.92E+04	C8H12O2	QDA	present in blank
399.3580	-0.14	1.96E+05	C7H12O3	QDA	present in blank
400.3169	-0.12	3.00E+04	C5H7N1O4	QDA	
401.3009	-0.12	3.15E+05	C5H6O5	QDA	
401.3373	-0.11	5.74E+04	C6H10O4	QDA	present in blank
402.3114	-0.13	2.80E+05	C8H5N1O2	QDA	present in blank
402.3325	-0.11	1.76E+04	C5H9N1O4	QDA	
405.3322	-0.14	1.20E+06	C5H10O5	QDA	
405.3474	-0.13	1.48E+04	C9H10O2	QDA	present in blank
406.3063	-0.16	2.44E+04	C7H5N1O3	QDA	
407.3267	-0.15	7.19E+04	C8H8O3	QDA	present in blank
409.3787	-0.17	8.60E+04	C9H14O2	QDA	
411.3943	-0.16	2.90E+05	C9H16O2	QDA	
411.4307	-0.18	5.30E+04	C10H20O1	QDA	present in blank
413.3372	-0.19	3.08E+04	C7H10O4	QDA	present in blank
417.3474	-0.17	1.57E+04	C10H10O2	QDA	
419.3267	-0.17	1.61E+05	C9H8O3	QDA	
419.3478	-0.16	2.05E+05	C6H12O5	QDA	
421.3059	-0.16	4.19E+06	C8H6O4	QDA	present in blank
421.3423	-0.21	7.10E+03	C9H10O3	QDA	present in blank
422.3376	-0.15	7.60E+04	C8H9N1O3	QDA	
425.2773	-0.18	6.10E+05	C3H7O6P1	QDA	
429.3321	-0.21	2.71E+03	C7H10O5	QDA	present in blank
433.3270	-0.18	2.27E+04	C6H10O6	QDA	
435.3216	-0.15	4.01E+05	C9H8O4	QDA	
435.3427	-0.12	1.60E+07	C6H12O6	QDA	
437.3736	-0.22	4.29E+04	C10H14O3	QDA	
439.3892	-0.23	3.53E+05	C10H16O3	QDA	
439.4621	-0.08	4.69E+03	C12H24O1	QDA	present in blank
443.3477	-0.24	1.17E+04	C8H12O5	QDA	
445.3787	-0.16	4.01E+04	C12H14O2	QDA	present in blank
447.3063	-0.21	2.80E+06	C6H8O7	QDA	
447.3579	-0.23	1.51E+05	C11H12O3	QDA	present in blank
449.3219	-0.24	1.14E+05	C6H10O7	QDA	
449.3372	-0.23	2.01E+05	C10H10O4	QDA	present in blank
453.3684	-0.26	3.03E+04	C10H14O4	QDA	present in blank
453.4413	-0.14	2.81E+03	C12H22O2	QDA	present in blank
455.2878	-0.31	6.90E+03	C4H9O7P1	QDA	
461.3219	-0.25	1.75E+05	C7H10O7	QDA	
461.3735	-0.28	4.62E+04	C12H14O3	QDA	present in blank
465.3168	-0.22	7.65E+05	C6H10O8	QDA	
469.3034	-0.29	7.38E+03	C5H11O7P1	QDA	
475.3892	-0.25	1.15E+04	C13H16O3	QDA	
476.3692	-0.23	4.90E+05	C8H15N1O6	QDA	

479.3268	-0.07	2.60E+03	C14H8O3	QDA	
479.3324	-0.25	1.57E+06	C7H12O8	QDA	
479.3590	-0.14	4.59E+03	C10H12N2O4	QDA	
479.4204	-0.31	2.64E+04	C13H20O3	QDA	present in blank
490.3151	-0.04	7.52E+04	C5H11O8P1[b]	QDA	
492.3640	-0.32	9.47E+04	C8H15N1O7	QDA	
495.5245	-0.31	1.36E+03	C16H32O1	QDA	
497.4673	-0.37	4.49E+03	C14H26O3	QDA	
502.3038	-0.25	1.26E+03	C8H10N1O6P1	QDA	
507.4517	-0.32	1.40E+04	C15H24O3	QDA	present in blank
515.3089	-0.29	3.78E+05	C6H13O9P1	QDA	
520.3602	-0.41	3.85E+03	C10H11N5O4	QDA	
523.3585	-0.37	4.54E+04	C9H16O9	QDA	
525.4986	-0.40	3.03E+04	C16H30O3	QDA	present in blank
529.3243	-0.50	2.14E+03	C7H15O9P1	QDA	
553.5299	-0.37	4.07E+03	C18H34O3	QDA	
556.3353	-0.43	4.06E+04	C8H16O9N1P1	QDA	
564.3851	-0.41	1.21E+05	C11H19N1O9	QDA	
577.4933	-0.63	5.75E+03	C19H30O4	QDA	
580.3799	-0.49	3.50E+04	C11H19N1O10	QDA	
597.3953	-0.44	3.91E+06	C12H22O11	QDA	
613.4576	0.12	2.84E+05	C21H26O5	QDA	
622.4278	0.44	2.81E+03	C14H25N1O10	QDA	
638.4217	-0.56	1.56E+04	C14H25N1O11	QDA	
759.4478	-0.72	2.45E+06	C18H32O16	QDA	
800.4743	-0.72	4.15E+03	C20H35N1O16	QDA	
814.3504	-0.76	1.95E+05	C15H23N5O14P2	QDA	
921.5005	-0.80	5.72E+05	C24H42O21	QDA	

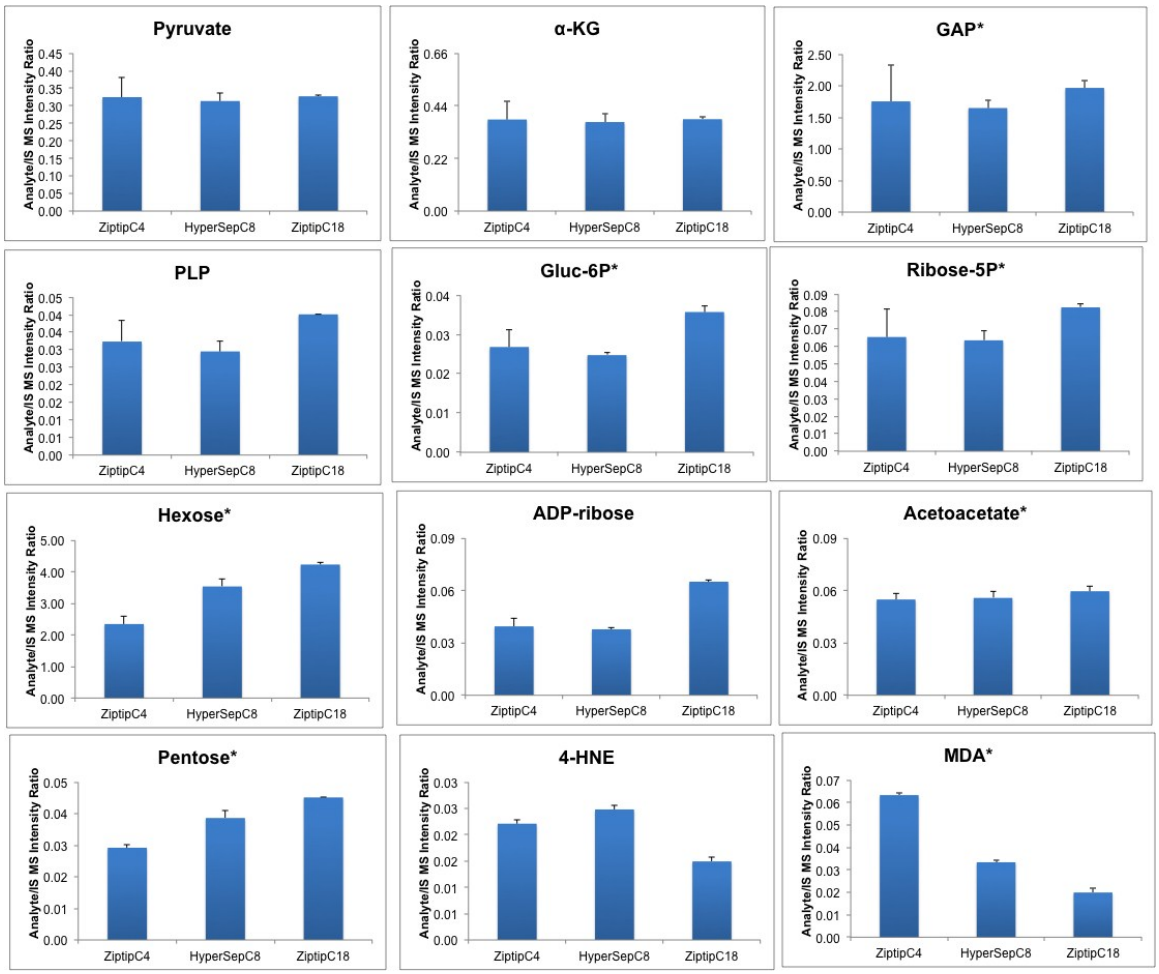


Figure S-1. Extraction of carbonyl-QDA derivatives with different reversed-phase micro-extraction tips. *: metabolites that may have mass isomers, which could not be resolved from each other under the current conditions.

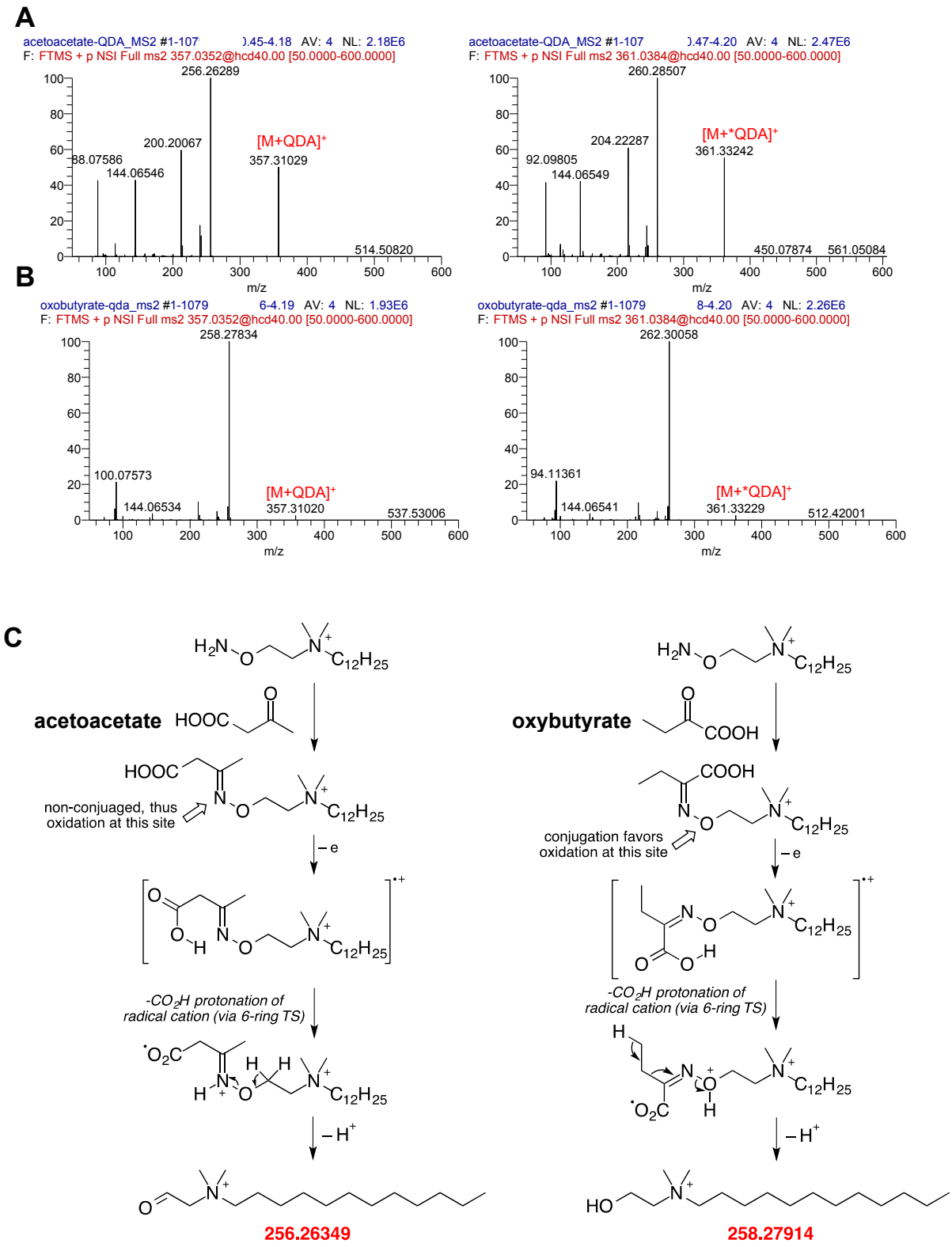
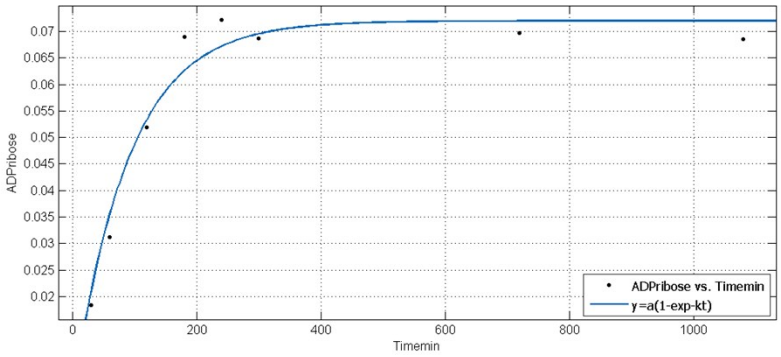


Figure S-2. Product ion spectra for derivatized acetoacetate (A) and oxybutyrate (B), and proposed fragment pathways (C).

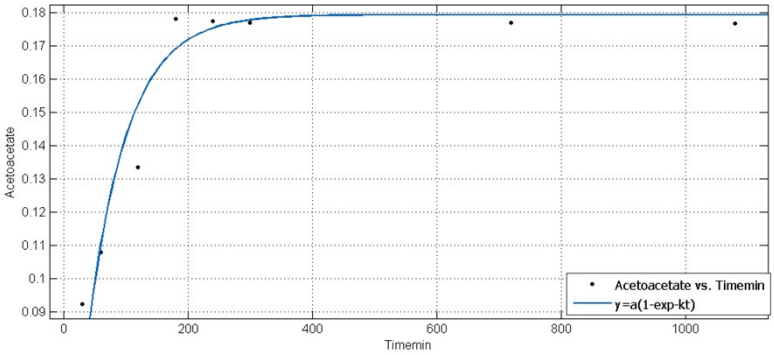
Figure S-3. The regression curves for the reaction between carbonyl metabolites and QDA.

Data were collected as described in the Methods, and fit according to Eq. (1) in the text. The continuous blue line is the non-liner regression line to the data, using the optimized parameters a and k. The values on parentheses are the 95% confidence limits. SSE is the residual sum squared deviations (observed – calculated), and R-square is coefficient of determination for the fit.

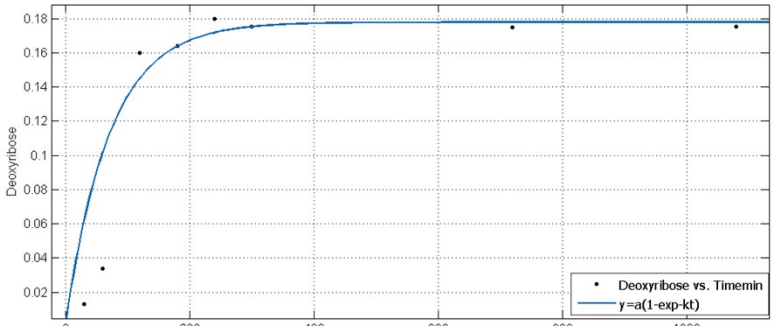
ADP ribose
a = 0.07202
(0.06598, 0.07806)
k = 0.01127
(0.007858, 0.01469)
Goodness of fit:
SSE: 0.0001086
R-square: 0.9637



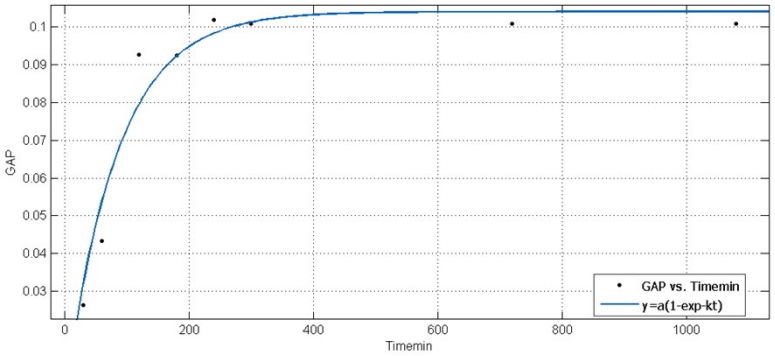
Acetoacetate
a = 0.1793 (0.1668, 0.1918)
k = 0.0158 (0.01116, 0.02045)
Goodness of fit:
SSE: 0.000606
R-square: 0.9329



Deoxyribose
a = 0.1778 (0.1564, 0.1993)
k = 0.01409 (0.007257, 0.02092)
Goodness of fit:
SSE: 0.001643
R-square: 0.9508

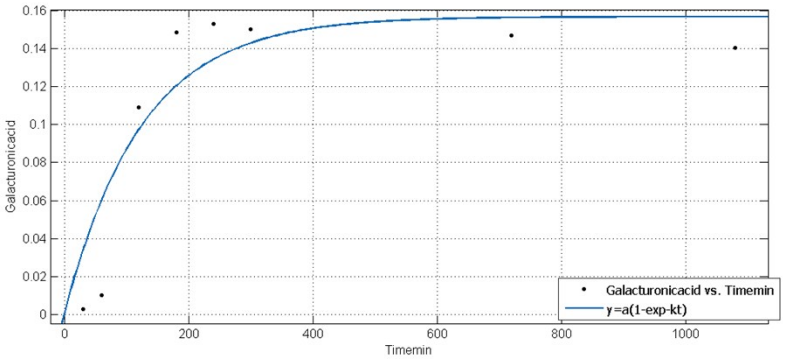


GAP
a = 0.1039
(0.09362, 0.1143)
k = 0.01208
(0.007593, 0.01656)
Goodness of fit:
SSE: 0.0003358
R-square: 0.9464



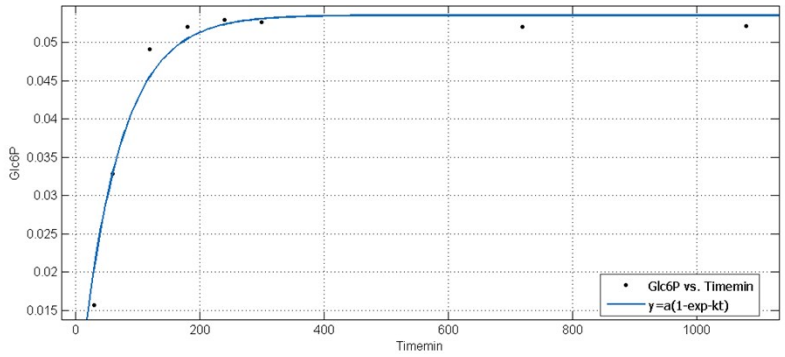
Galacturonic acid

a = 0.1568 (0.1095, 0.2041)
k = 0.008087 (0.000588, 0.01559)
Goodness of fit:
SSE: 0.005193
R-square: 0.8191



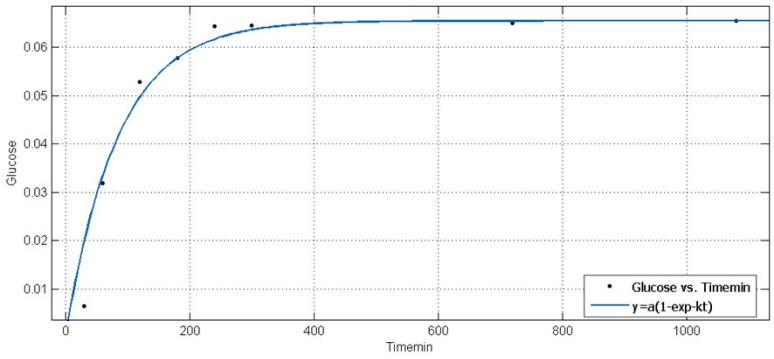
Glc-6P

a = 0.05354 (0.05031, 0.05678)
k = 0.01581 (0.01177, 0.01985)
Goodness of fit:
SSE: 4.085e-05
R-square: 0.9684



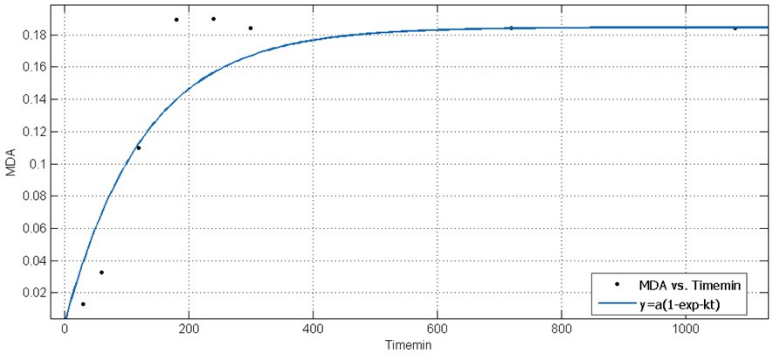
Glucose

a = 0.06544 (0.06112, 0.06975)
k = 0.01185 (0.008961, 0.01475)
Goodness of fit:
SSE: 5.765e-05
R-square: 0.9817



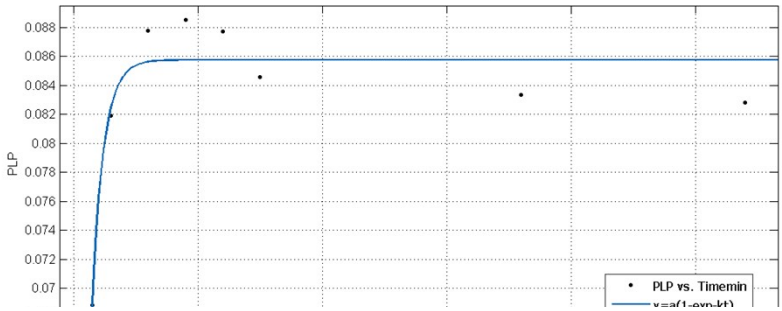
MDA

a = 0.1847 (0.09812, 0.2712)
k = 0.007837 (-0.003296, 0.01897)
Goodness of fit:
SSE: 0.01703
R-square: 0.5661



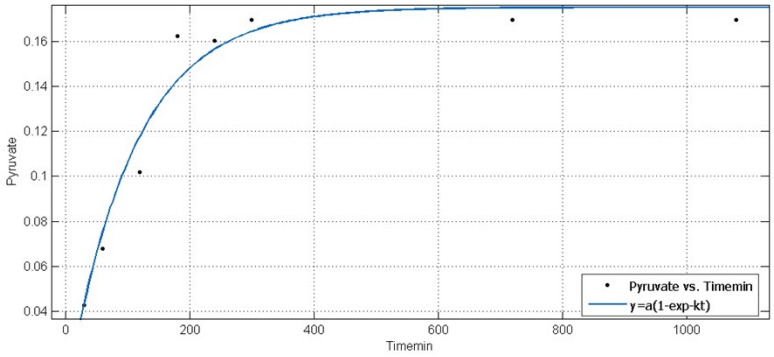
PLP

a = 0.08576 (0.0835, 0.08803)
k = 0.05388 (0.04256, 0.0652)
Goodness of fit:
SSE: 3.228e-05
R-square: 0.8847



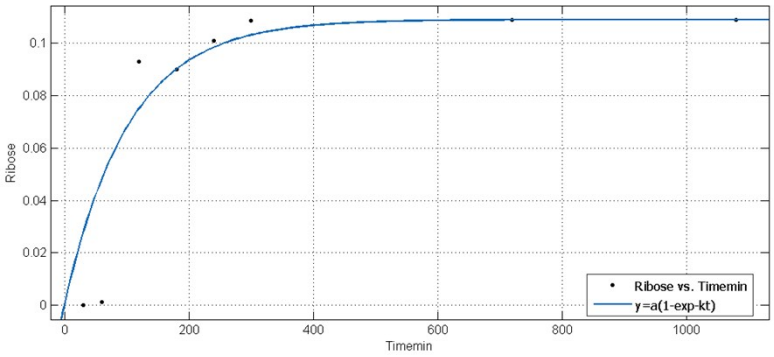
Pyruvate

a = 0.1753 (0.1575, 0.193)
k = 0.009307 (0.006207, 0.01241)
Goodness of fit:
SSE: 0.0008093
R-square: 0.9574



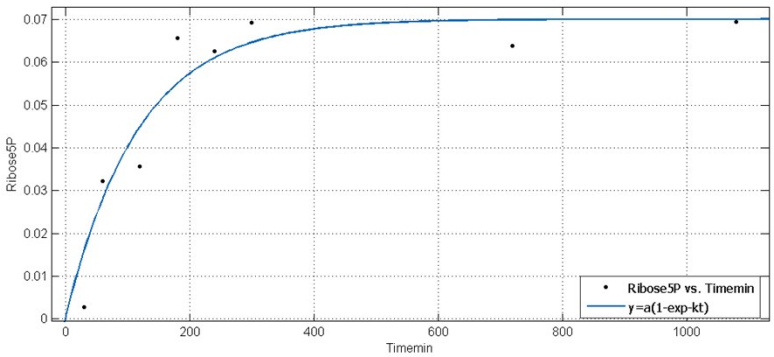
Ribose

a = 0.1091 (0.08986, 0.1283)
k = 0.009714 (0.003961, 0.01547)
Goodness of fit:
SSE: 0.0009814
R-square: 0.9377



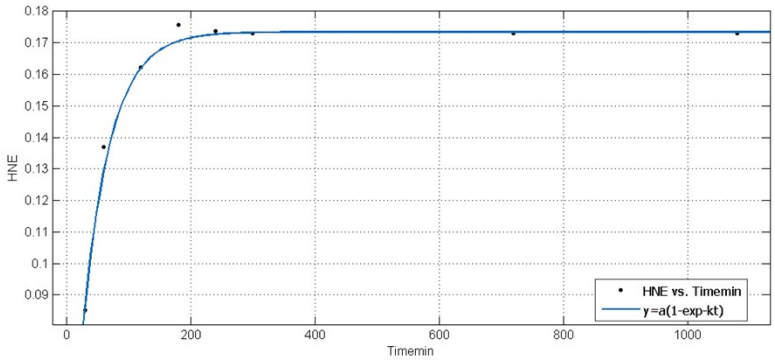
Ribose-5P

a = 0.07011 (0.05645, 0.08377)
k = 0.008524 (0.00329, 0.01376)
Goodness of fit:
SSE: 0.0004495
R-square: 0.8904



4-HNE

a = 0.1734 (0.1713, 0.1755)
k = 0.02261 (0.02127, 0.02394)
Goodness of fit:
SSE: 2.155e-05
R-square: 0.9969



α-KG

a = 0.2019 (0.1789, 0.2249)
k = 0.01187 (0.006856, 0.01689)
Goodness of fit:
SSE: 0.001644
R-square: 0.9369