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Supplementary material to

Glyphosate-based herbicide metabolic profiles in human urine samples through proton nuclear magnetic resonance analysis

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Abbrevations used in Tables S1 to S9:
AMPA - aminomethylphosphonic acid
AP-3 - - 2-amino-3-phosphonopropionic acid
GLY - glyphosate
$T_{1/2}$ - elimination half-life
T_{max} - peak time of GLY and its metabolites concentration in urine
C_{max} - maximum concentration in urine
AUC_{0-t} - area under the curve from 0 to the final time point *t*
R^2 - correlation coefficient

Table S1. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 1.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	17.0	35.8	12.0	5.2	20.2	26.8	29.2
T_{max} / h	12.0	12.0	18.0	18.0	18.0	18.0	18.0
C_{max} / μg g^{-1} creatinine	60.5	10.4	9.2	0.2	0.4	0.2	26.4
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	815.3	364.6	305.6	1.8	12.2	2.7	410.5
R^2	1.0	0.8	0.9	1.0	0.9	0.5	0.9

Table S2. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 2.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	4.2	14.7	19.8	7.7	34.0	8.4	501.6
T_{max} / h	12.0	6.0	24.0	42.0	6.0	42.0	30.0
C_{max} / μg g^{-1} creatinine	28.4	4.3	2.6	0.4	0.3	1.1	2.3
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	414.5	122.5	85.7	7.7	6.3	19.1	94.7
R^2	0.9	0.9	0.9	1.0	0.8	0.6	0.6

Table S3. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 3.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	29.5	53.6	12.6	13.7	27.2	7.1	35.3
T_{max} / h	12.0	24.0	18.0	48.0	6.0	6.0	12.0
C_{max} / μg g^{-1} creatinine	16.1	9.1	9.5	0.2	1.3	0.7	9.5
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	302.3	282.9	174.3	5.8	22.6	21.4	234.3
R^2	0.5	0.4	0.9	0.6	0.6	0.8	0.6

Table S4. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 4.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	5.5	2.4	6.8	9.3	4.4	8.2	5.6
T_{max} / h	24.0	12.0	18.0	6.0	24.0	12.0	24.0
C_{max} / μg g^{-1} creatinine	11.3	9.3	5.4	0.2	0.3	1.7	8.5
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	181.6	247.8	126.0	3.9	9.1	32.6	190.3
R^2	0.9	1.0	0.8	0.8	1.0	0.6	1.0

Table S5. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 5.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	51.8	53.3	24.2	26.8	8.8	12.5	14.3
T_{max} / h	48.0	30.0	24.0	18.0	36.0	48.0	48.0
C_{max} / μg g^{-1} creatinine	15.5	4.5	2.8	0.1	1.9	0.6	5.8
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	478.4	146.1	72.8	1.4	20.0	11.7	159.3
R^2	1.0	0.7	0.8	0.9	0.7	0.8	1.0

Table S6. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 6.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	111.1	22.9	14.9	5.2	3.1	6.6	8.8
T_{max} / h	36.0	36.0	48.0	24.0	54.0	12.0	42.0
C_{max} / μg g^{-1} creatinine	15.4	20.9	9.0	0.5	2.0	0.3	21.2
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	474.2	767.6	283.8	18.6	33.5	6.3	368.1
R^2	0.5	0.8	1.0	1.0	1.0	1.0	0.9

Table S7. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 7.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	31.5	24.8	14.9	31.8	62.3	10.7	8.6
T_{max} / h	18.0	48.0	48.0	24.0	6.0	30.0	42.0
C_{max} / μg g^{-1} creatinine	12.0	9.5	9.0	3.6	1.5	0.2	30.7
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	462.6	438.4	283.8	45.6	19.2	3.4	392.8
R^2	0.9	0.9	1.0	0.3	0.3	0.6	0.7

Table S8. Toxicokinetic parameters of urinary GLY and its metabolites in Subject 8.

Kinetic parameters	Formal-dehyde	Sarcosine	AMPA	Glyoxylic acid	Methyl-amine	GLY	AP-3
$T_{1/2}$ / h	26.9	23.2	28.0	12.2	16.3	27.0	13.3
T_{max} / h	24.0	12.0	12.0	18.0	6.0	24.0	18.0
C_{max} / μg g^{-1} creatinine	11.3	11.3	9.3	0.7	1.1	0.5	10.8
AUC_{0-t}, μg g^{-1} creatinine h^{-1}	299.9	313.9	226.7	18.0	18.8	10.5	261.7
R^2	0.6	1.0	1.0	0.9	0.8	0.4	1.0

Table S9. The Spearman rank correlation coefficients manifested the subsequent associations between GYL and other metabolites, with GLY as the reference for comparative analysis.

	Subject number								
	1	2	3	4	5	6	7	8	Average
Glyphosate	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
AP-3	0.84	0.24	0.68	0.78	0.69	0.52	0.48	0.29	0.50
Sarcosine	0.37	-0.31	-0.07	0.99	0.83	-0.07	0.15	0.05	0.62
Methylamine	0.98	-0.22	0.56	0.84	0.55	0.35	-0.27	0.07	0.48
AMPA	0.98	0.03	0.26	0.90	0.86	0.00	-0.03	0.07	0.44
Glyoxylic acid	0.76	0.92	0.66	0.95	0.08	0.67	0.14	0.83	0.38
Formaldehyde	0.48	-0.32	0.55	0.89	0.54	0.31	0.37	0.61	0.32

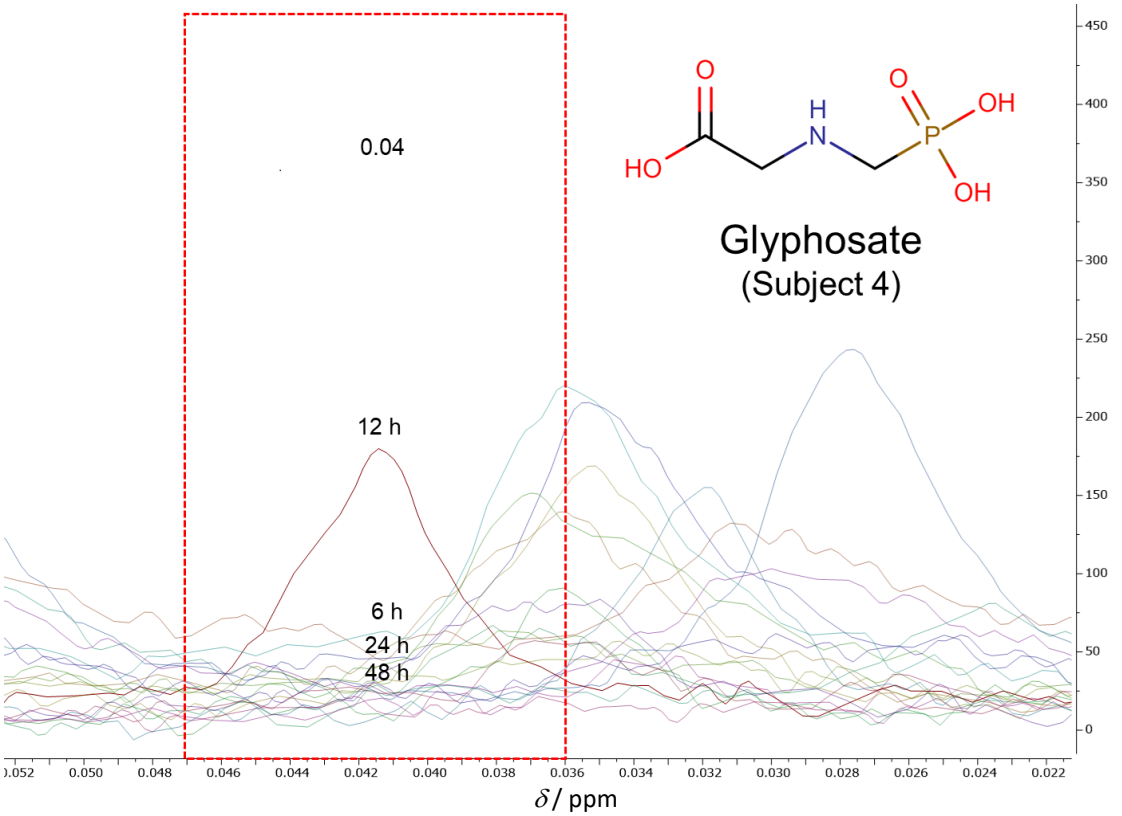

Figure S1. Results of NMR-Based Metabolomics Analysis. The 500 MHz ^{1}H-NMR spectra of glyphosate in urine samples from subject number 4 are presented. The chromatogram overlay highlights distinctions between samples collected at different time points, demonstrating changes in the metabolite profile over time. The structure of glyphosate was obtained from the Human Metabolome Database (https://hmdb.ca/).

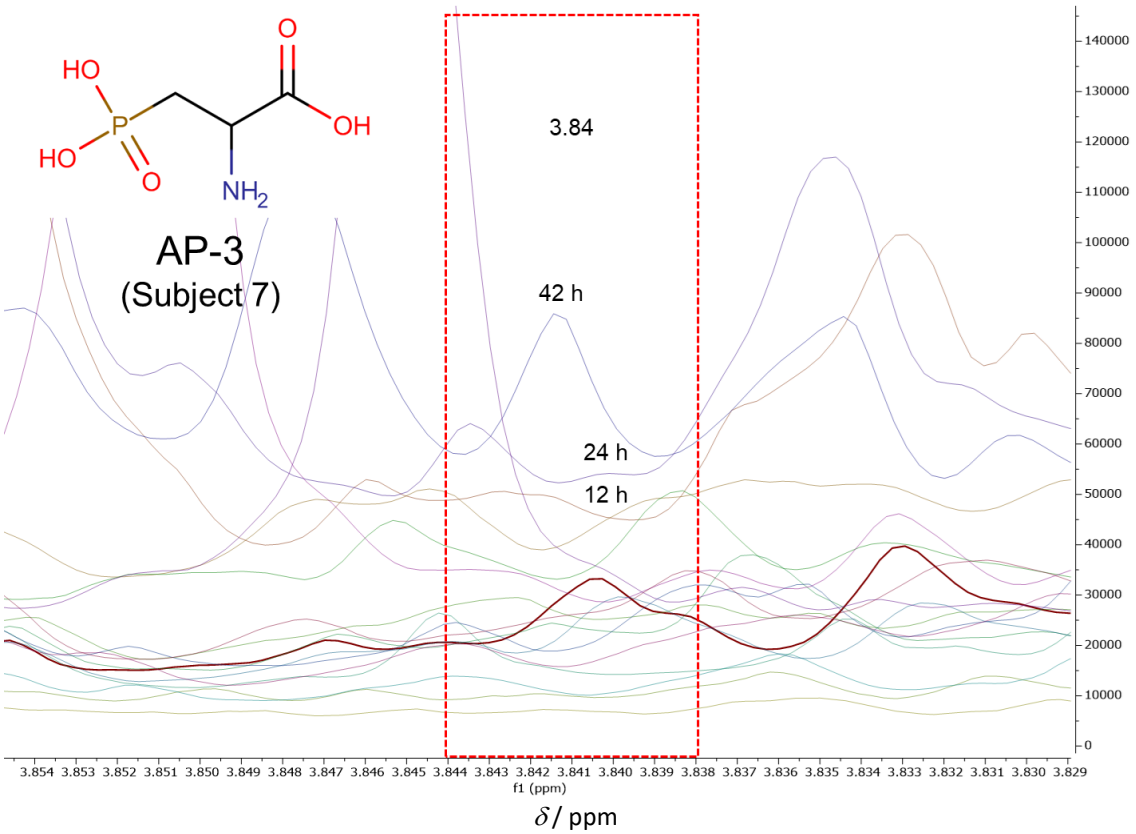

Figure S2. Results of NMR-based metabolomics analysis. The 500 MHz ^{1}H-NMR spectra of 2-amino-3-phosphonopropionic acid (AP-3) in urine samples from subject number 7 are presented. The chromatogram overlay highlights distinctions between samples collected at different time points, demonstrating changes in the metabolite profile over time. The structure of AP-3 was obtained from the Human Metabolome Database (https://hmdb.ca/).

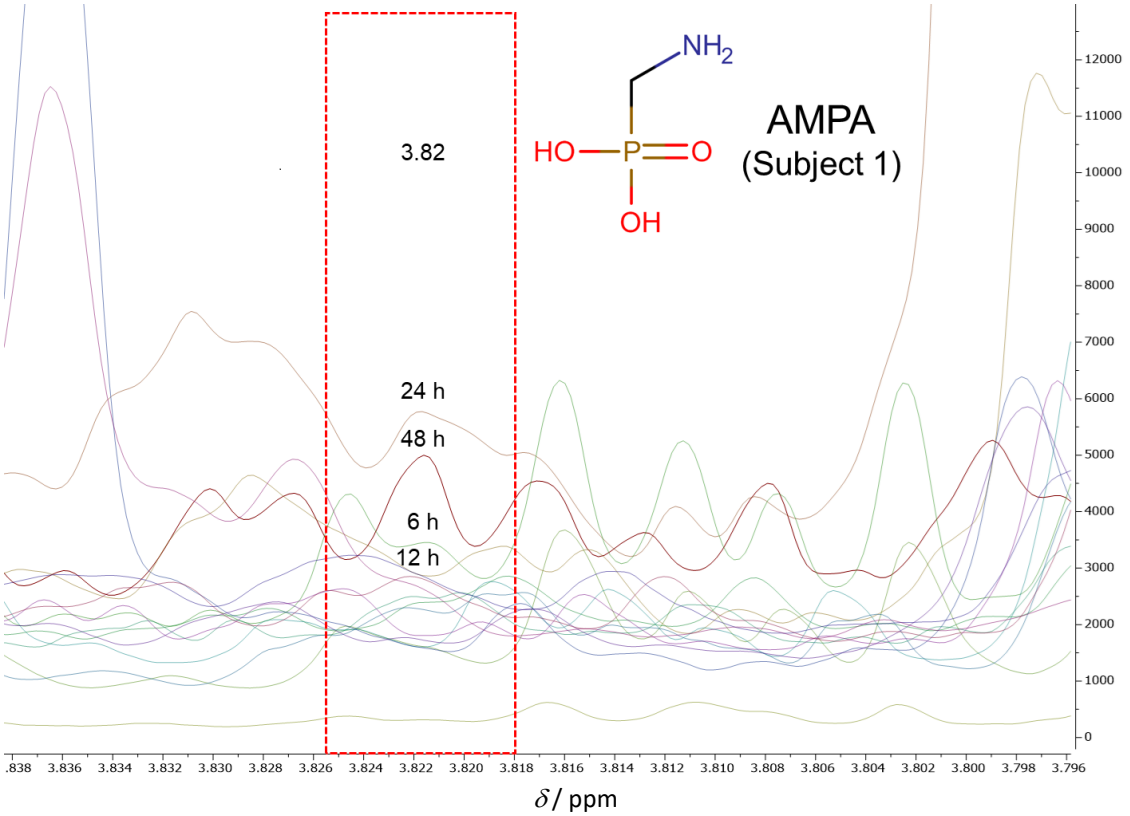

Figure S3. Results of NMR-Based Metabolomics Analysis. The 500 MHz ^{1}H-NMR spectra of aminomethylphosphonic acid (AMPA) in urine samples from subject number 1 are presented. The chromatogram overlay highlights distinctions between samples collected at different time points, demonstrating changes in the metabolite profile over time. The structure of AMPA was obtained from the Human Metabolome Database (https://hmdb.ca/).

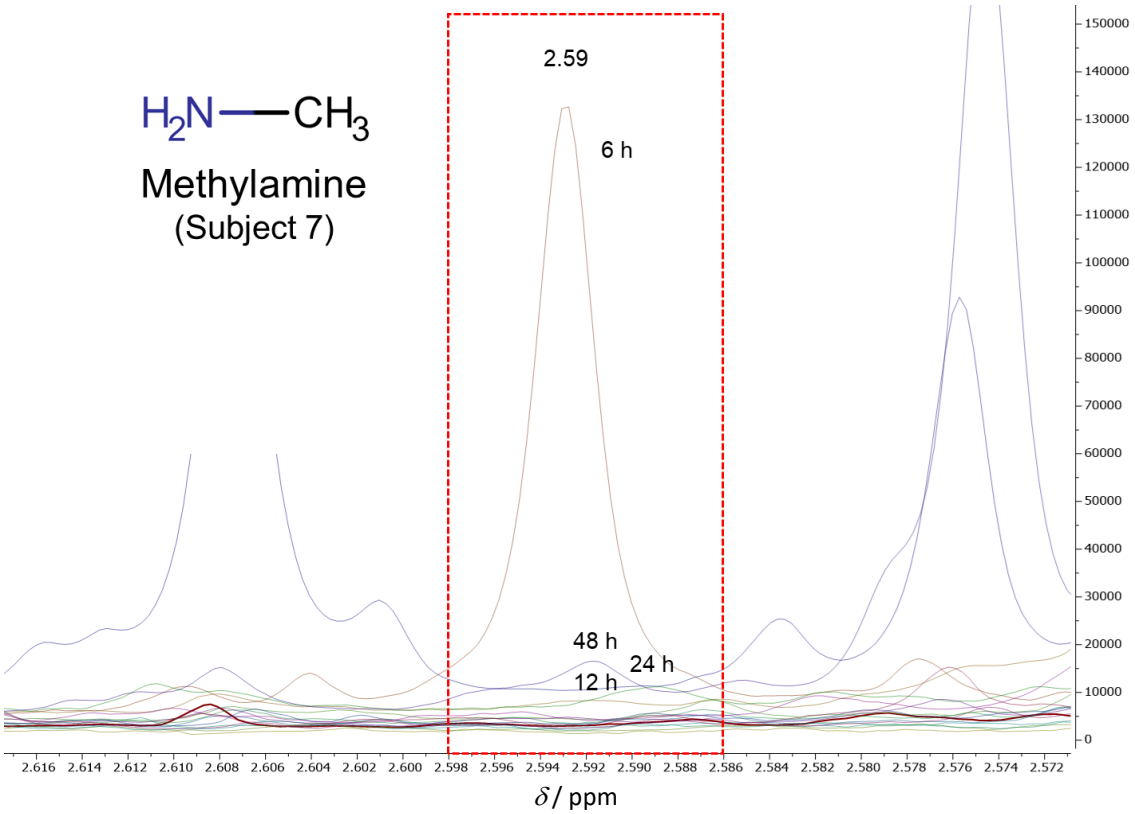

Figure S4. Results of NMR-Based Metabolomics Analysis. The 500 MHz ^{1}H-NMR spectra of methylamine in urine samples from subject number 7 are presented. The chromatogram overlay highlights distinctions between samples collected at different time points, demonstrating changes in the metabolite profile over time. The structure of methylamine was obtained from the Human Metabolome Database (https://hmdb.ca/).

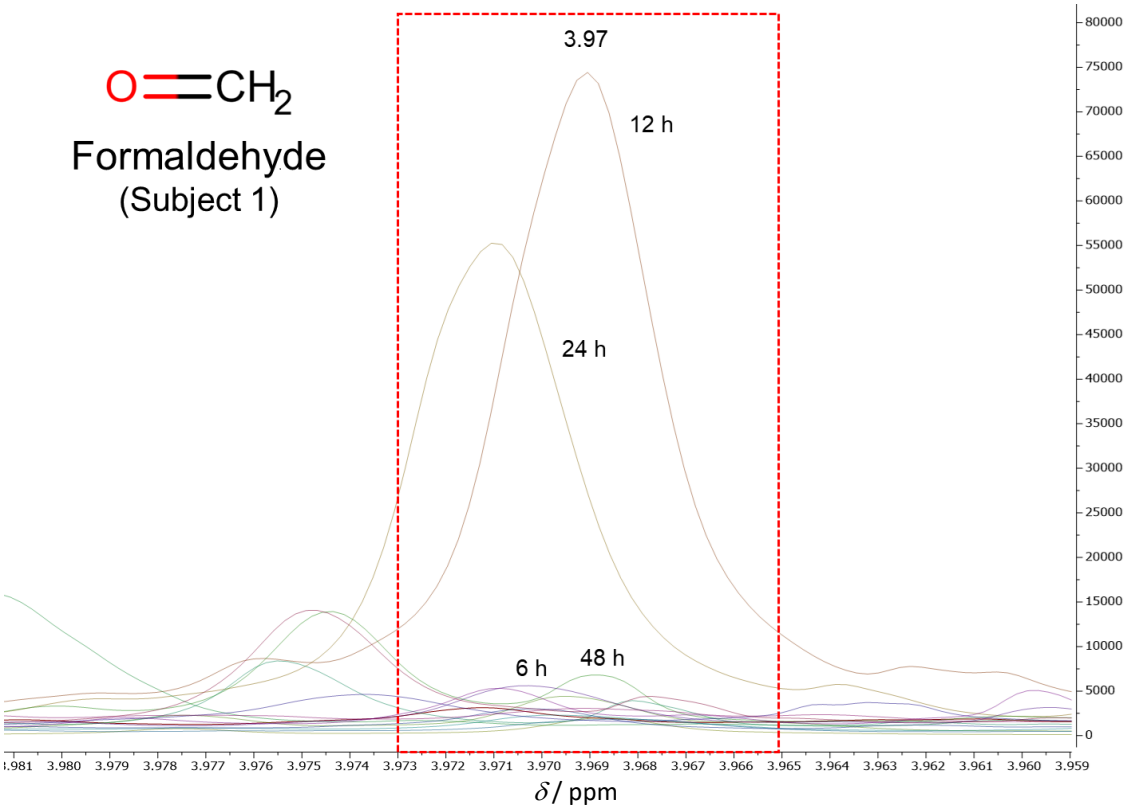

Figure S5. Results of NMR-Based Metabolomics Analysis. The 500 MHz ^{1}H-NMR spectra of formaldehyde in urine samples from subject number 1 are presented. The chromatogram overlay highlights distinctions between samples collected at different time points, demonstrating changes in the metabolite profile over time. The structure of formaldehyde was obtained from the Human Metabolome Database (https://hmdb.ca/).

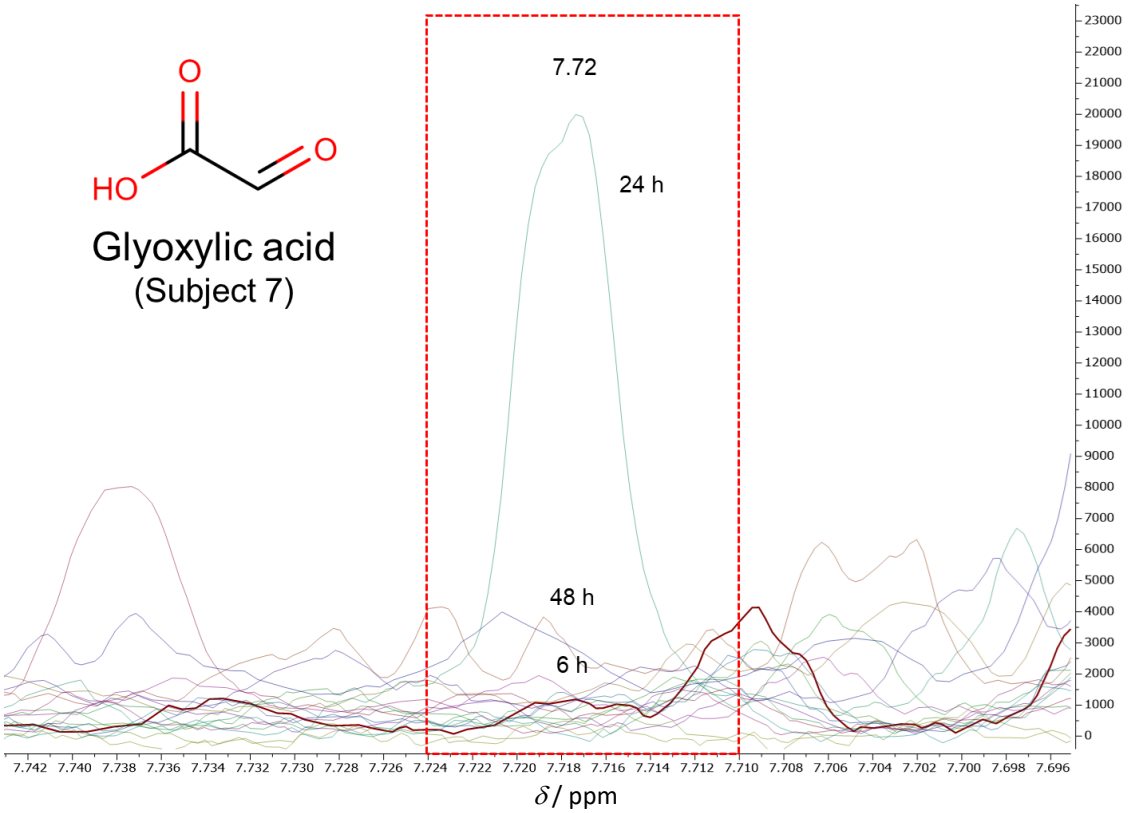

Figure S6. Results of NMR-Based Metabolomics Analysis. The 500 MHz ^{1}H-NMR spectra of glyoxylic acid in urine samples from subject number 7 are presented. The chromatogram overlay highlights distinctions between samples collected at different time points, demonstrating changes in the metabolite profile over time. The structure of glyoxylic acid was obtained from the Human Metabolome Database (https://hmdb.ca/).

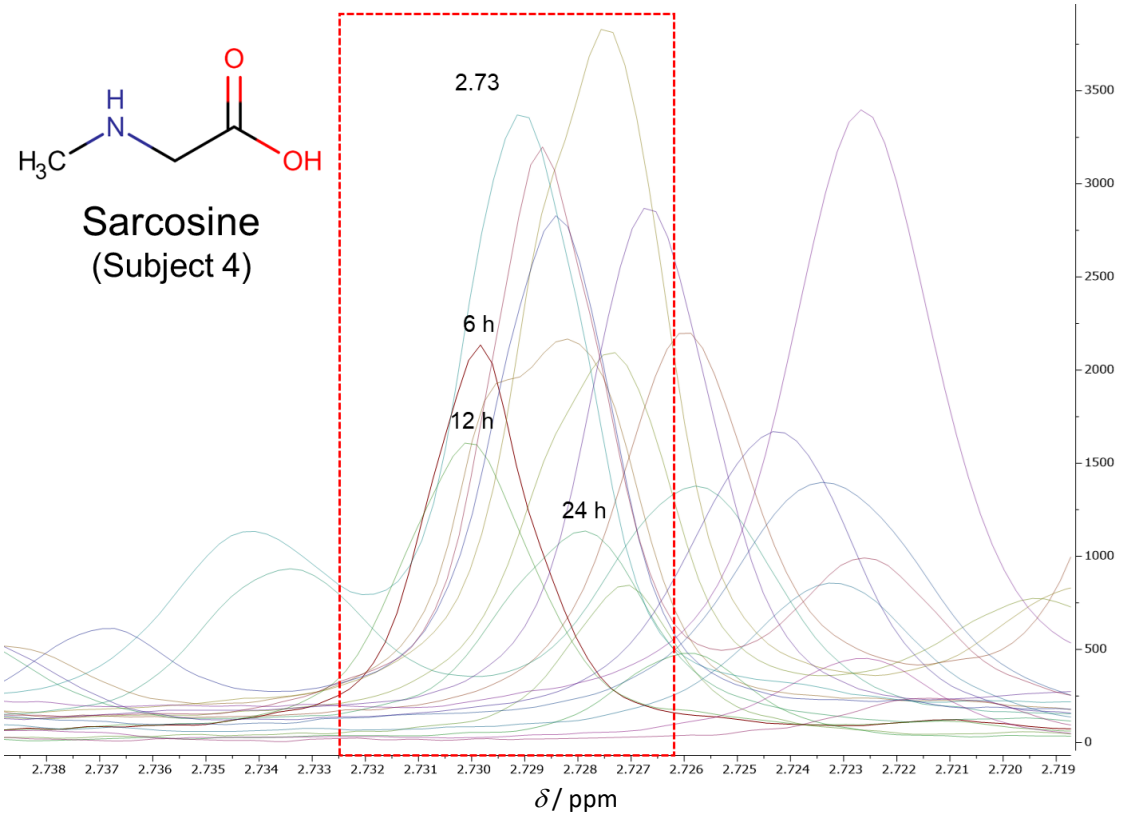

Figure S7. Results of NMR-Based Metabolomics Analysis. The 500 MHz ^{1}H-NMR spectra of sarcosine in urine samples from subject number 4 are presented. The chromatogram overlay highlights distinctions between samples collected at different time points, demonstrating changes in the metabolite profile over time. The structure of sarcosine was obtained from the Human Metabolome Database (https://hmdb.ca/).