Analysis Report

Bruker IVDr Quantification in URine B.I.Quant-UR b™

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno40.100000.10r

Measuring Date: 23-Dec-2014 13:32:22
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Quantification Method Version: Quant-UR B.1.1.0

Disclaimer

RESEARCH USE ONLY: This is no clinical diagnostic analysis report. Must not be used for clinical (medical or IVD) diagnosis or for patient management! Additional concentration range information (95% range) provided numerically or graphically in this report must not be used for clinical diagnostic interpretation.

Application of B.I.Quant-UR B 1.1.0 requires use of Bruker's B.I.Methods SOP for urine.

Summary

The following metabolites were found with concentrations outside the 95% range of Bruker Quant-UR B.1.1.0 urine metabolite concentration database:

Amines and derivatives: Trimethylamine (54 mmol/mol Crea),
Amino acids and derivatives: 2-Furoylglycine (65 mmol/mol Crea), N,N-Dimethylglycine (16 mmol/mol Crea),
Benzene and substituted derivatives: Benzoic acid (25 mmol/mol Crea),
Carboxylic acids: Acetic acid (220 mmol/mol Crea), Succinic acid (54 mmol/mol Crea), Trigonelline (110 mmol/mol Crea),
Keto acids and derivatives: Acetone (11 mmol/mol Crea), Pyruvic acid (100 mmol/mol Crea),
Purine, Pyridine and Pyrimidine derivatives: Allantoin (67 mmol/mol Crea), Caffeine (160 mmol/mol Crea).

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Further detailed information is provided on the following pages.

Contents

1 Creatinine

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/L
Creatinine	1.5	0.3	1.485	100 ●	0.033	1 - 19

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

2 Amines and derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
Dimethylamine	0.05	36	31	0.053	100 ●	0.001	≤ 54
Trimethylamine	0.08	54	2	0.080	99 ●	0.006	≤ 3

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

3 Amino acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
1-Methylhistidine	< 0.02	< 15	15	0.000	0 ○	0.011	≤ 15
2-Furoylglycine	0.10	65	39	0.097	99 ●	0.006	≤ 40
4-Aminobutyric acid	< 0.03	< 20	20	0.000	0 ○	0.146	≤ 20
Alanine	0.04	30	10	0.045	100 ●	0.003	11 - 72
Arginine	< 1.1	< 750	750	0.162	33 ○	0.343	≤ 750
Betaine	0.05	31	7	0.046	100 ●	0.005	9 - 78
Creatine	0.07	51	50	0.075	100 ●	0.033	≤ 280
Glycine	0.65	440	34	0.648	100 ●	0.018	38 - 440
Guanidinoacetic acid	< 0.15	< 100	100	0.103	96 ●	0.035	≤ 140
Methionine	< 0.03	< 18	18	0.000	0 ○	1.304	≤ 18
N,N-Dimethylglycine	0.02	16	5	0.024	91 ●	0.005	≤ 15
Sarcosine	0.00	3	2	0.005	78 ○	0.002	≤ 7
Taurine	< 0.21	< 140	140	0.028	17 ○	0.142	≤ 170
Valine	0.00	2	2	0.003	8 ○	0.005	≤ 7

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

4 Benzene and substituted derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
Benzoic acid	0.04	25	10	0.038	99 ●	0.004	≤ 10
D-Mandelic acid	< 0.01	< 2	2	0.000	0 ○	6.489	2 - 17
Hippuric acid	0.73	490	170	0.735	100 ●	0.035	≤ 660

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

5 Carboxylic acids

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
Acetic acid	0.33	220	5	0.334	100 ●	0.011	≤ 51
Citric acid	0.64	430	40	0.636	100 ●	0.059	≤ 700
Formic acid	0.05	31	10	0.047	100 ●	0.002	≤ 43
Fumaric acid	0.00	2	2	0.003	100 ●	0.000	≤ 3
Imidazole	< 0.07	< 48	48	0.016	0 ○	0.018	≤ 48
Lactic acid	< 0.07	< 49	49	0.031	99 ●	0.038	≤ 110
Proline betaine	0.04	29	25	0.043	63 ○	0.032	≤ 280
Succinic acid	0.08	54	5	0.080	98 ●	0.008	≤ 39
Tartaric acid	0.04	23	5	0.035	100 ●	0.001	≤ 110
Trigonelline	0.16	110	35	0.158	100 ●	0.006	≤ 67

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

6 Fatty acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
2-Methylsuccinic acid	< 0.07	< 48	48	0.000	0 ○	0.080	≤ 48

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

7 Keto acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
2-Oxoglutaric acid	< 0.14	< 92	92	0.020	38 ○	0.056	≤ 92
3-Hydroxybutyric acid	< 0.15	< 100	100	0.047	79 ○	1.016	≤ 100
Acetoacetic acid	< 0.02	< 14	14	0.012	61 ○	0.010	≤ 30
Acetone	0.02	11	2	0.016	99 ●	0.001	≤ 7
Oxaloacetic acid	< 0.03	< 17	17	0.012	12 ○	0.020	≤ 66
Pyruvic acid	0.15	100	9	0.154	100 ●	0.010	≤ 13

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

8 Purine, Pyridine and Pyrimidine derivatives

Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
1-Methyladenosine	< 0.01	< 5	5	0.000	0 ○	0.121	≤ 5
1-Methylnicotinamide	< 0.05	< 32	32	0.022	80 ○	0.014	≤ 32
Adenosine	< 0.58	< 390	390	0.000	0 ○	0.698	≤ 390
Allantoin	0.10	67	17	0.099	58 ○	0.062	≤ 47
Allopurinol	< 0.01	< 10	10	0.009	98 ●	0.009	≤ 11
Caffeine	0.24	160	45	0.238	99 ●	0.084	≤ 61
Inosine	< 0.03	< 19	19	0.012	67 ○	0.019	≤ 19

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

9 Sugars and derivatives

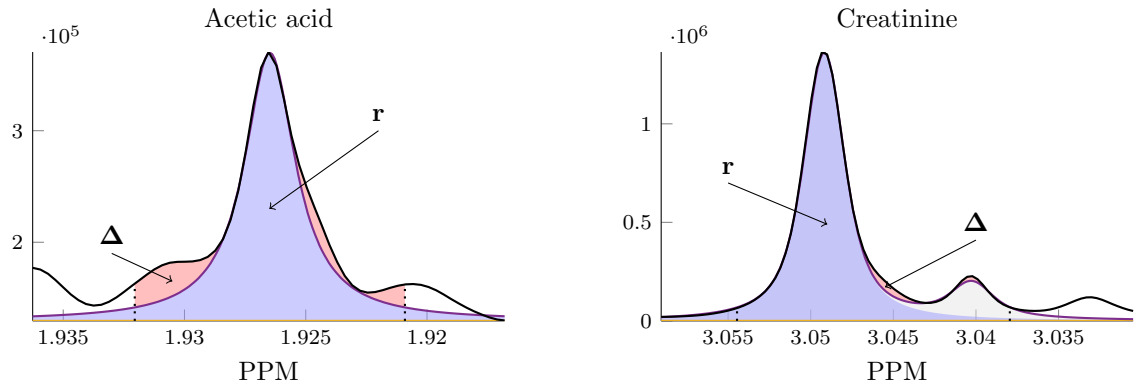
Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
D-Galactose	< 0.06	< 43	43	0.000	0 ○	0.879	≤ 44
D-Glucose	0.09	57	34	0.085	98 ●	0.008	≤ 140
D-Lactose	< 0.14	< 96	96	0.063	1 ○	0.080	≤ 96
D-Mannitol	< 0.27	< 180	180	0.000	0 ○	0.642	≤ 180
D-Mannose	< 0.01	< 6	6	0.000	0 ○	2.993	≤ 8
Myo-Inositol	< 6.6	< 4400	4400	0.000	0 ○	0.778	≤ 4400

(*) Gray horizontal boxes represent 95% concentration range, black vertical lines represent sample value.

10 Explanations

This section contains the definition of the parameters used above. In the section 10.1 a short manual, how to interpret the results, is presented. The section 10.3 contains the exact definitions of the parameters $\mathbf{r}$, ρ and $\mathbf{\Delta}$.

10.1 How to read the result



(a) Single signal fitting.

(b) Simultaneous fitting of two signals.

Figure 1: Examples of fitting.

In the figure 1(a), the black line, the blue line and the yellow line represent the original spectrum, the calculated signal fit and its baseline, respectively.

The blue area relates to the metabolite concentration to be determined and the red area represents a residue.

In case of the signal overlap a different approach is used: two or more overlapping signals are being fitted simultaneously. The most iconic example of such signals are the ones generated by $\mathrm{CH_3}$ groups of Creatinine and Creatine. In such a case, the blue line and the grey area relate the sum of all fitted signals. The blue area corresponds to the concentration of the metabolite of interest (cf. figure 1(b)).

10.2 Result parameters

a) **Conc.** is the final result concentration of the metabolite,

b) **LOD** is the *limit of detection* of the given metabolite,

c) $\mathbf{r}$ is the *raw concentration* i.e. the concentration equivalent of the resulting signal fit prior to comparing to **LOD** (relates to the blue area, cf. α)),

d) ρ is the correlation of lineshape metabolite signal with calculated fit characterizing the match between metabolite signal and fit (cf. β)). Depending on the value of ρ, the following *flag* is displayed:

- ●, if the correlation is 95%,
- ●, if the correlation is in between 85% and 95%,
- ○, if the correlation is less than 85%,

e) **Δ** is the concentration equivalent of the difference between metabolite signal and calculated fit (residue corresponding to the the red area, cf. γ)).

10.3 Detailed definitions

Let s, f and b denote the functions describing the *raw spectra*, *fitted curve* and *(fitted) baseline* respectively. These functions are chosen such that $s \approx f + b$. Moreover, let I be a relevant PPM interval and P_N be the proton number for given metabolite/signal.

α) $\mathbf{r}$ (*raw concentration*) is defined as

$$\mathbf{r} = \frac{1}{P_N} \int_{\mathbb{R}} f(\xi)\, \mathrm{d}\xi.$$

β) ρ is the *correlation* of the functions s and $f + b$, i.e.

$$\rho = \max\left(0, \operatorname{corr}\left(\overline{s}, \overline{f + b}\right)\right),$$

where $\overline{s}$, $\overline{f + b}$ are numerical representations of the functions s and $f + b$ on sufficiently fine mesh of the interval I.

γ) **Δ** is the the area between the raw signal s and the fitted data $f + b$ on the interval I expressed in the terms of the concentration, i.e.

$$\mathbf{\Delta} = \frac{1}{P_N} \int_I |s(\xi) - f(\xi) - b(\xi)|\, \mathrm{d}\xi.$$