Analysis Report

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

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno50.100000.10r

Measuring Date: 23-Dec-2014 13:46:58
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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:

Amino acids and derivatives: Valine (8 mmol/mol Crea),
Carboxylic acids: Citric acid (980 mmol/mol Crea), Formic acid (64 mmol/mol Crea),
Keto acids and derivatives: Acetoacetic acid (77 mmol/mol Crea), Acetone (9 mmol/mol Crea).

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	2.0	0.3	2.036	100 ●	0.047	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	0.08	40	31	0.082	100 ●	0.002	$\leq$ 54
Trimethylamine	$<$ 0.01	$<$ 2	2	0.002	99 ●	0.000	$\leq$ 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	$<$ 0.03	$<$ 15	15	0.023	29 ○	0.027	$\leq$ 15
2-Furoylglycine	$<$ 0.08	$<$ 39	39	0.000	0 ○	0.033	$\leq$ 40
4-Aminobutyric acid	$<$ 0.04	$<$ 20	20	0.019	21 ○	0.250	$\leq$ 20
Alanine	0.10	49	10	0.101	100 ●	0.005	11 - 72
Arginine	$<$ 1.5	$<$ 750	750	0.153	81 ○	0.502	$\leq$ 750
Betaine	0.12	60	7	0.122	100 ●	0.005	9 - 78
Creatine	0.34	170	50	0.345	100 ●	0.047	$\leq$ 280
Glycine	0.56	280	34	0.563	100 ●	0.015	38 - 440
Guanidinoacetic acid	0.29	140	100	0.294	100 ●	0.039	$\leq$ 140
Methionine	$<$ 0.04	$<$ 18	18	0.000	0 ○	0.174	$\leq$ 18
N,N-Dimethylglycine	0.02	10	5	0.020	96 ●	0.017	$\leq$ 15
Sarcosine	0.00	2	2	0.004	7 ○	0.005	$\leq$ 7
Taurine	0.30	150	140	0.296	97 ●	0.099	$\leq$ 170
Valine	0.01	8	2	0.015	46 ○	0.015	$\leq$ 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	< 0.02	< 10	10	0.000	0 ○	0.017	≤ 10
D-Mandelic acid	< 0.01	< 2	2	0.000	0 ○	0.043	2 - 17
Hippuric acid	0.90	440	170	0.903	100 ●	0.064	≤ 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	0.08	38	5	0.077	98 ●	0.011	≤ 51
Citric acid	2.0	980	40	1.990	100 ●	0.136	≤ 700
Formic acid	0.13	64	10	0.131	100 ●	0.003	≤ 43
Fumaric acid	< 0.01	< 2	2	0.004	99 ●	0.000	≤ 3
Imidazole	< 0.10	< 48	48	0.034	81 ○	0.017	≤ 48
Lactic acid	< 0.10	< 49	49	0.042	99 ●	0.100	≤ 110
Proline betaine	0.16	78	25	0.159	89 ●	0.045	≤ 280
Succinic acid	0.06	27	5	0.055	99 ●	0.005	≤ 39
Tartaric acid	< 0.01	< 5	5	0.000	0 ○	0.009	≤ 110
Trigonelline	0.08	41	35	0.083	100 ●	0.003	≤ 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	< 0.10	< 48	48	0.000	0 ○	0.140	≤ 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	< 0.19	< 92	92	0.052	40 ○	0.129	≤ 92
3-Hydroxybutyric acid	< 0.21	< 100	100	0.060	27 ○	0.130	≤ 100
Acetoacetic acid	0.16	77	14	0.156	100 ●	0.012	≤ 30
Acetone	0.02	9	2	0.019	99 ●	0.002	≤ 7
Oxaloacetic acid	0.11	56	17	0.114	93 ●	0.051	≤ 66
Pyruvic acid	< 0.02	< 9	9	0.010	98 ●	0.002	≤ 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 ○	0.070	≤ 5
1-Methylnicotinamide	< 0.06	< 32	32	0.031	89 ●	0.014	≤ 32
Adenosine	< 0.79	< 390	390	0.000	0 ○	0.540	≤ 390
Allantoin	< 0.03	< 17	17	0.020	98 ●	0.003	≤ 47
Allopurinol	< 0.02	< 10	10	0.019	81 ○	0.014	≤ 11
Caffeine	< 0.09	< 45	45	0.060	92 ●	0.048	≤ 61
Inosine	< 0.04	< 19	19	0.015	86 ●	0.014	≤ 19

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

9 Sugars and derivatives

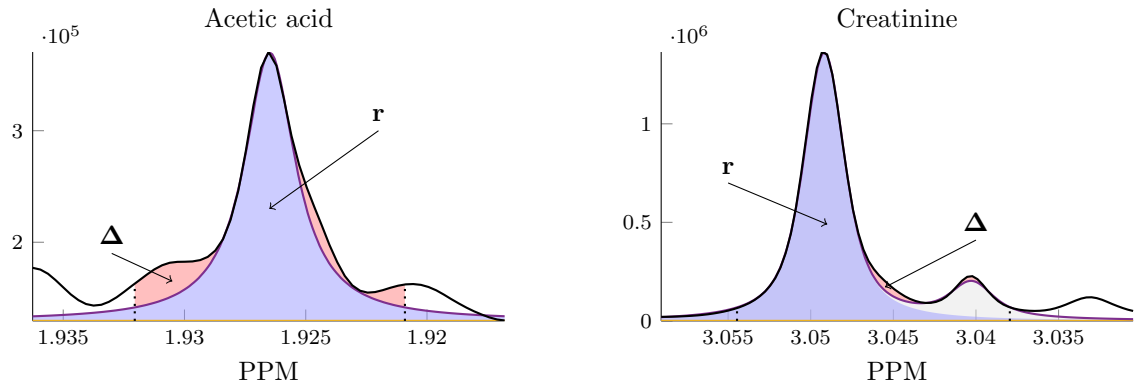
Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
D-Galactose	< 0.09	< 43	43	0.000	0 ○	0.028	≤ 44
D-Glucose	0.17	85	34	0.173	84 ○	0.041	≤ 140
D-Lactose	< 0.19	< 96	96	0.047	64 ○	0.040	≤ 96
D-Mannitol	< 0.37	< 180	180	0.000	0 ○	1.068	≤ 180
D-Mannose	< 0.01	< 6	6	0.000	0 ○	0.042	≤ 8
Myo-Inositol	< 9.0	< 4400	4400	0.000	0 ○	2.375	≤ 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.

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