Analysis Report

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

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno140.100000.10r

Measuring Date:	23-Dec-2014 17:08:39
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Quantification Method Version:	Quant-UR B.1.1.0

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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: Dimethylamine (290 mmol/mol Crea).

Further detailed information is provided on the following pages.

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Contents

1 Creatinine

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/L
Creatinine	7.9	0.3	7.915	100 ●	0.154	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	2.3	290	31	2.310	100 ●	0.108	≤ 54
Trimethylamine	0.02	3	2	0.021	100 ●	0.000	≤ 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	< 0.12	< 15	15	0.000	0 ○	0.223	≤ 15
2-Furoylglycine	< 0.30	< 39	39	0.028	21 ○	0.027	≤ 40
4-Aminobutyric acid	< 0.16	< 20	20	0.000	0 ○	0.369	≤ 20
Alanine	0.22	28	10	0.223	100 ●	0.017	11 - 72
Arginine	< 5.9	< 750	750	0.572	0 ○	1.373	≤ 750
Betaine	0.21	27	7	0.212	100 ●	0.346	9 - 78
Creatine	< 0.40	< 50	50	0.239	100 ●	0.154	≤ 280
Glycine	0.62	78	34	0.616	100 ●	0.026	38 - 440
Guanidinoacetic acid	< 0.82	< 100	100	0.623	98 ●	0.102	≤ 140
Methionine	< 0.14	< 18	18	0.000	0 ○	0.369	≤ 18
N,N-Dimethylglycine	0.04	5	5	0.041	56 ○	0.024	≤ 15
Sarcosine	< 0.01	< 2	2	0.000	0 ○	0.009	≤ 7
Taurine	< 1.1	< 140	140	0.928	99 ●	0.183	≤ 170
Valine	0.04	5	2	0.035	95 ●	0.007	≤ 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	< 0.08	< 10	10	0.000	0 ○	0.036	≤ 10
D-Mandelic acid	< 0.02	< 2	2	0.000	0 ○	0.080	2 - 17
Hippuric acid	2.8	360	170	2.815	99 ●	0.292	≤ 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	10	5	0.080	94 ●	0.022	≤ 51
Citric acid	2.6	320	40	2.551	100 ●	0.178	≤ 700
Formic acid	0.20	25	10	0.198	100 ●	0.010	≤ 43
Fumaric acid	< 0.01	< 2	2	0.004	93 ●	0.001	≤ 3
Imidazole	< 0.38	< 48	48	0.000	0 ○	0.156	≤ 48
Lactic acid	< 0.38	< 49	49	0.088	85 ●	0.144	≤ 110
Proline betaine	< 0.20	< 25	25	0.066	88 ●	0.059	≤ 280
Succinic acid	< 0.04	< 5	5	0.029	86 ●	0.009	≤ 39
Tartaric acid	0.22	28	5	0.224	100 ●	0.008	≤ 110
Trigonelline	< 0.27	< 35	35	0.063	100 ●	0.002	≤ 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	< 0.38	< 48	48	0.000	0 ○	0.302	≤ 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	< 0.73	< 92	92	0.124	45 ○	0.242	≤ 92
3-Hydroxybutyric acid	< 0.82	< 100	100	0.000	0 ○	1.022	≤ 100
Acetoacetic acid	< 0.11	< 14	14	0.085	94 ●	0.039	≤ 30
Acetone	< 0.01	< 2	2	0.015	94 ●	0.004	≤ 7
Oxaloacetic acid	0.20	26	17	0.202	90 ●	0.108	≤ 66
Pyruvic acid	< 0.07	< 9	9	0.038	85 ●	0.014	≤ 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	< 0.04	< 5	5	0.000	0 ○	0.115	≤ 5
1-Methylnicotinamide	< 0.25	< 32	32	0.058	99 ●	0.005	≤ 32
Adenosine	< 3.1	< 390	390	0.000	0 ○	1.293	≤ 390
Allantoin	< 0.13	< 17	17	0.053	99 ●	0.007	≤ 47
Allopurinol	< 0.08	< 10	10	0.073	92 ●	0.084	≤ 11
Caffeine	< 0.36	< 45	45	0.108	92 ●	0.122	≤ 61
Inosine	< 0.15	< 19	19	0.018	93 ●	0.085	≤ 19

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

9 Sugars and derivatives

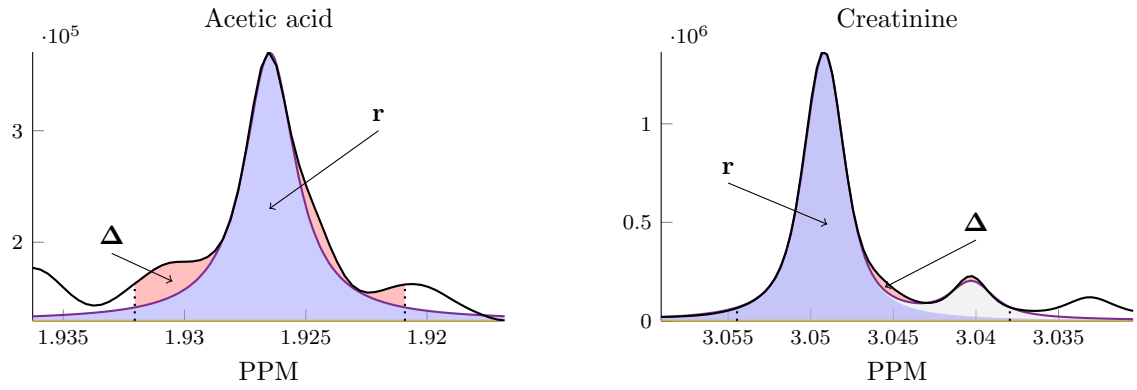
Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
D-Galactose	< 0.34	< 43	43	0.009	73 ○	0.003	≤ 44
D-Glucose	< 0.27	< 34	34	0.253	88 ●	0.059	≤ 140
D-Lactose	< 0.76	< 96	96	0.128	83 ○	0.102	≤ 96
D-Mannitol	< 1.4	< 180	180	0.000	0 ○	2.641	≤ 180
D-Mannose	< 0.05	< 6	6	0.031	95 ●	0.007	≤ 8
Myo-Inositol	< 35	< 4400	4400	0.000	0 ○	127.2	≤ 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.

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