Analysis Report

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

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno10.100000.10r

Measuring Date: 23-Dec-2014 12:47:24
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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: Creatine (780 mmol/mol Crea),
Carboxylic acids: Trigonelline (84 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	5.2	0.3	5.245	99 ●	0.531	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	< 0.16	< 31	31	0.140	100 ●	0.001	≤ 54
Trimethylamine	< 0.01	< 2	2	0.002	97 ●	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	< 0.08	< 15	15	0.000	0 ○	0.041	≤ 15
2-Furoylglycine	< 0.20	< 39	39	0.053	60 ○	0.023	≤ 40
4-Aminobutyric acid	< 0.10	< 20	20	0.033	18 ○	0.064	≤ 20
Alanine	0.08	15	10	0.079	99 ●	0.008	11 - 72
Arginine	< 3.9	< 750	750	0.256	48 ○	0.364	≤ 750
Betaine	0.07	14	7	0.074	100 ●	0.006	9 - 78
Creatine	4.1	780	50	4.091	99 ●	0.531	≤ 280
Glycine	0.26	49	34	0.259	100 ●	0.012	38 - 440
Guanidinoacetic acid	< 0.54	< 100	100	0.132	0 ○	0.258	≤ 140
Methionine	< 0.09	< 18	18	0.000	0 ○	3.659	≤ 18
N,N-Dimethylglycine	0.03	6	5	0.032	72 ○	0.015	≤ 15
Sarcosine	< 0.01	< 2	2	0.004	0 ○	0.008	≤ 7
Taurine	< 0.75	< 140	140	0.160	37 ○	0.293	≤ 170
Valine	< 0.01	< 2	2	0.009	93 ●	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	< 0.05	< 10	10	0.045	22 ○	0.028	≤ 10
D-Mandelic acid	< 0.01	< 2	2	0.008	63 ○	0.005	2 - 17
Hippuric acid	2.4	460	170	2.387	99 ●	0.221	≤ 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	0.03	6	5	0.029	97 ●	0.006	≤ 51
Citric acid	1.1	210	40	1.087	100 ●	0.082	≤ 700
Formic acid	< 0.05	< 10	10	0.037	100 ●	0.002	≤ 43
Fumaric acid	< 0.01	< 2	2	0.004	79 ○	0.001	≤ 3
Imidazole	< 0.25	< 48	48	0.034	34 ○	0.048	≤ 48
Lactic acid	< 0.25	< 49	49	0.075	82 ○	0.068	≤ 110
Proline betaine	0.27	52	25	0.273	98 ●	0.033	≤ 280
Succinic acid	< 0.03	< 5	5	0.019	64 ○	0.008	≤ 39
Tartaric acid	0.42	80	5	0.418	100 ●	0.004	≤ 110
Trigonelline	0.44	84	35	0.439	100 ●	0.014	≤ 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	< 0.25	< 48	48	0.000	0 ○	0.134	≤ 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	< 0.48	< 92	92	0.001	64 ○	0.136	≤ 92
3-Hydroxybutyric acid	< 0.54	< 100	100	0.000	0 ○	0.477	≤ 100
Acetoacetic acid	< 0.07	< 14	14	0.043	79 ○	0.025	≤ 30
Acetone	0.01	2	2	0.010	99 ●	0.002	≤ 7
Oxaloacetic acid	< 0.09	< 17	17	0.038	83 ○	0.030	≤ 66
Pyruvic acid	< 0.05	< 9	9	0.029	88 ●	0.007	≤ 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	< 0.03	< 5	5	0.000	0 ○	0.099	≤ 5
1-Methylnicotinamide	< 0.17	< 32	32	0.025	90 ●	0.009	≤ 32
Adenosine	< 2.0	< 390	390	0.000	0 ○	1.150	≤ 390
Allantoin	< 0.09	< 17	17	0.057	99 ●	0.004	≤ 47
Allopurinol	< 0.05	< 10	10	0.013	82 ○	0.029	≤ 11
Caffeine	< 0.24	< 45	45	0.106	96 ●	0.102	≤ 61
Inosine	< 0.10	< 19	19	0.013	43 ○	0.037	≤ 19

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

9 Sugars and derivatives

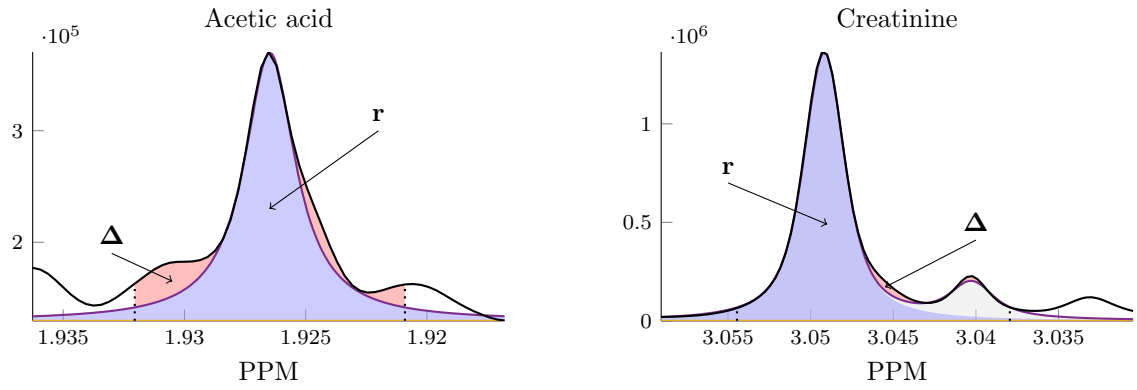
Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
D-Galactose	< 0.23	< 43	43	0.000	0 ○	0.022	≤ 44
D-Glucose	0.22	42	34	0.218	89 ●	0.048	≤ 140
D-Lactose	< 0.50	< 96	96	0.037	28 ○	0.055	≤ 96
D-Mannitol	< 0.96	< 180	180	0.000	0 ○	1.734	≤ 180
D-Mannose	< 0.03	< 6	6	0.000	0 ○	0.092	≤ 8
Myo-Inositol	< 23	< 4400	4400	0.000	0 ○	4.354	≤ 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.

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