Analysis Report

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

Sample ID: ALZ_Urine_Rack03_RCM_06012015_expno740.100000.1

Measuring Date: 14-Jan-2015 14:24:30
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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: 4-Aminobutyric acid (21 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	8.7	0.3	8.691	100 ●	0.234	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	0.30	35	31	0.300	100 ●	0.011	$\leq$ 54
Trimethylamine	$<$ 0.02	$<$ 2	2	0.001	0 ○	0.016	$\leq$ 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	$<$ 0.13	$<$ 15	15	0.079	0 ○	0.182	$\leq$ 15
2-Furoylglycine	$<$ 0.33	$<$ 39	39	0.112	43 ○	0.042	$\leq$ 40
4-Aminobutyric acid	0.18	21	20	0.180	45 ○	0.218	$\leq$ 20
Alanine	0.28	32	10	0.279	100 ●	0.019	11 - 72
Arginine	$<$ 6.5	$<$ 750	750	0.718	0 ○	2.459	$\leq$ 750
Betaine	0.19	22	7	0.194	100 ●	0.027	9 - 78
Creatine	0.47	54	50	0.469	100 ●	0.234	$\leq$ 280
Glycine	0.99	110	34	0.990	100 ●	0.047	38 - 440
Guanidinoacetic acid	$<$ 0.90	$<$ 100	100	0.429	58 ○	0.222	$\leq$ 140
Methionine	$<$ 0.16	$<$ 18	18	0.000	0 ○	0.428	$\leq$ 18
N,N-Dimethylglycine	0.04	5	5	0.044	96 ●	0.008	$\leq$ 15
Sarcosine	$<$ 0.02	$<$ 2	2	0.000	0 ○	0.006	$\leq$ 7
Taurine	$<$ 1.2	$<$ 140	140	0.715	86 ●	0.292	$\leq$ 170
Valine	0.03	4	2	0.032	92 ●	0.011	$\leq$ 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	< 0.08	< 10	10	0.080	99 ●	0.007	≤ 10
D-Mandelic acid	< 0.02	< 2	2	0.000	0 ○	0.133	2 - 17
Hippuric acid	3.6	420	170	3.611	99 ●	0.282	≤ 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	0.24	28	5	0.242	100 ●	0.021	≤ 51
Citric acid	2.4	270	40	2.387	100 ●	0.249	≤ 700
Formic acid	0.33	38	10	0.329	99 ●	0.030	≤ 43
Fumaric acid	< 0.02	< 2	2	0.007	96 ●	0.001	≤ 3
Imidazole	< 0.42	< 48	48	0.077	31 ○	0.064	≤ 48
Lactic acid	< 0.42	< 49	49	0.194	96 ●	0.070	≤ 110
Proline betaine	0.32	37	25	0.322	98 ●	0.057	≤ 280
Succinic acid	0.15	18	5	0.154	99 ●	0.017	≤ 39
Tartaric acid	0.12	14	5	0.122	99 ●	0.014	≤ 110
Trigonelline	0.35	40	35	0.351	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	< 0.41	< 48	48	0.052	0 ○	0.111	≤ 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	< 0.80	< 92	92	0.046	0 ○	0.218	≤ 92
3-Hydroxybutyric acid	< 0.90	< 100	100	0.089	24 ○	0.369	≤ 100
Acetoacetic acid	0.12	14	14	0.123	94 ●	0.053	≤ 30
Acetone	0.03	3	2	0.026	99 ●	0.004	≤ 7
Oxaloacetic acid	0.23	26	17	0.227	89 ●	0.136	≤ 66
Pyruvic acid	< 0.08	< 9	9	0.035	96 ●	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	< 0.04	< 5	5	0.000	0 ○	0.144	≤ 5
1-Methylnicotinamide	< 0.27	< 32	32	0.058	99 ●	0.006	≤ 32
Adenosine	< 3.4	< 390	390	0.000	0 ○	1.740	≤ 390
Allantoin	< 0.14	< 17	17	0.109	98 ●	0.015	≤ 47
Allopurinol	< 0.09	< 10	10	0.051	77 ○	0.042	≤ 11
Caffeine	< 0.39	< 45	45	0.189	88 ●	0.226	≤ 61
Inosine	< 0.16	< 19	19	0.032	95 ●	0.039	≤ 19

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

9 Sugars and derivatives

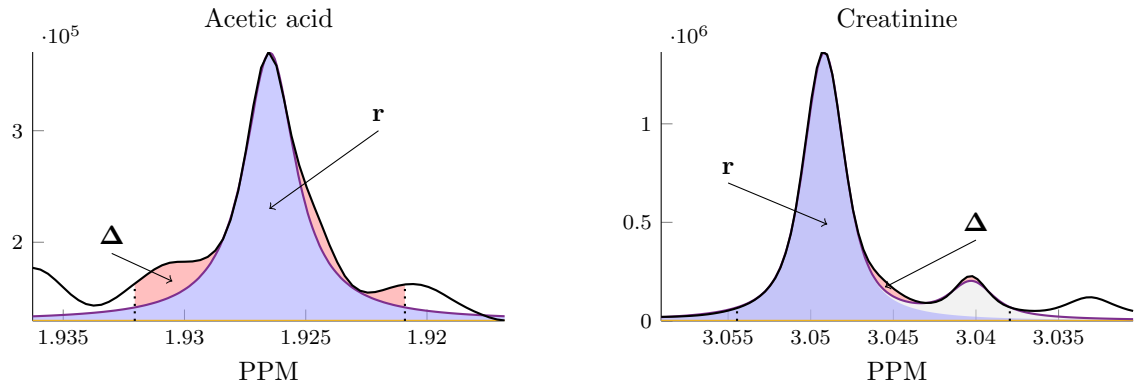
Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
D-Galactose	< 0.38	< 43	43	0.000	0 ○	0.057	≤ 44
D-Glucose	0.80	93	34	0.805	92 ●	0.147	≤ 140
D-Lactose	< 0.83	< 96	96	0.045	79 ○	0.055	≤ 96
D-Mannitol	< 1.6	< 180	180	0.000	0 ○	3.932	≤ 180
D-Mannose	< 0.05	< 6	6	0.040	0 ○	0.040	≤ 8
Myo-Inositol	< 39	< 4400	4400	0.000	0 ○	10.62	≤ 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.

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