Analysis Report

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

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno120.100000.10r

Measuring Date:	23-Dec-2014 16:53:56
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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:

Creatinine: *Creatinine (20 mmol/L),*
Amino acids and derivatives: *Alanine (< 10 mmol/mol Crea),*
Keto acids and derivatives: *Acetoacetic acid (87 mmol/mol Crea), Acetone (16 mmol/mol Crea),*
Sugars and derivatives: *D-Lactose (110 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	20	0.3	20.03	100 ●	0.382	1 - 19

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

2 Amines and derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
Dimethylamine	$<$ 0.61	$<$ 31	31	0.544	100 ●	0.013	$\leq$ 54
Trimethylamine	$<$ 0.04	$<$ 2	2	0.002	0 ○	0.011	$\leq$ 3

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

3 Amino acids and derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
1-Methylhistidine	$<$ 0.30	$<$ 15	15	0.069	49 ○	0.085	$\leq$ 15
2-Furoylglycine	$<$ 0.77	$<$ 39	39	0.000	0 ○	0.098	$\leq$ 40
4-Aminobutyric acid	$<$ 0.40	$<$ 20	20	0.000	0 ○	3.019	$\leq$ 20
Alanine	$<$ 0.21	$<$ 10	10	0.177	99 ●	0.026	11 - 72
Arginine	$<$ 15	$<$ 750	750	1.132	23 ○	2.697	$\leq$ 750
Betaine	0.31	16	7	0.314	97 ●	0.090	9 - 78
Creatine	$<$ 1.00	$<$ 50	50	0.152	100 ●	0.382	$\leq$ 280
Glycine	0.92	46	34	0.919	99 ●	0.123	38 - 440
Guanidinoacetic acid	$<$ 2.1	$<$ 100	100	0.853	71 ○	0.573	$\leq$ 140
Methionine	$<$ 0.36	$<$ 18	18	0.075	0 ○	0.208	$\leq$ 18
N,N-Dimethylglycine	$<$ 0.10	$<$ 5	5	0.076	50 ○	0.045	$\leq$ 15
Sarcosine	$<$ 0.04	$<$ 2	2	0.023	0 ○	0.053	$\leq$ 7
Taurine	$<$ 2.9	$<$ 140	140	0.990	97 ●	0.447	$\leq$ 170
Valine	0.08	4	2	0.076	41 ○	0.074	$\leq$ 7

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

4 Benzene and substituted derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
Benzoic acid	< 0.19	< 10	10	0.010	9	0.206	≤ 10
D-Mandelic acid	< 0.04	< 2	2	0.028	53	0.028	2 - 17
Hippuric acid	< 3.4	< 170	170	2.036	99	0.231	≤ 660

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

5 Carboxylic acids

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
Acetic acid	< 0.10	< 5	5	0.057	95	0.013	≤ 51
Citric acid	5.7	280	40	5.700	100	0.695	≤ 700
Formic acid	< 0.19	< 10	10	0.079	100	0.004	≤ 43
Fumaric acid	0.06	3	2	0.058	100	0.002	≤ 3
Imidazole	< 0.96	< 48	48	0.000	0	0.629	≤ 48
Lactic acid	< 0.97	< 49	49	0.619	45	0.613	≤ 110
Proline betaine	< 0.50	< 25	25	0.321	97	0.052	≤ 280
Succinic acid	0.14	7	5	0.144	94	0.034	≤ 39
Tartaric acid	1.5	76	5	1.517	100	0.057	≤ 110
Trigonelline	< 0.69	< 35	35	0.147	100	0.004	≤ 67

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

6 Fatty acids and derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
2-Methylsuccinic acid	< 0.96	< 48	48	0.000	0	0.826	≤ 48

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

7 Keto acids and derivatives

Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
2-Oxoglutaric acid	< 1.8	< 92	92	0.643	61	0.642	≤ 92
3-Hydroxybutyric acid	< 2.1	< 100	100	1.626	96	0.581	≤ 100
Acetoacetic acid	1.7	87	14	1.746	100	0.055	≤ 30
Acetone	0.33	16	2	0.327	100	0.023	≤ 7
Oxaloacetic acid	< 0.34	< 17	17	0.120	0	0.329	≤ 66
Pyruvic acid	< 0.18	< 9	9	0.116	97	0.025	≤ 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. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
1-Methyladenosine	< 0.10	< 5	5	0.000	0	0.178	≤ 5
1-Methylnicotinamide	< 0.63	< 32	32	0.458	100	0.017	≤ 32
Adenosine	< 7.8	< 390	390	0.000	0	3.937	≤ 390
Allantoin	< 0.33	< 17	17	0.063	77	0.029	≤ 47
Allopurinol	< 0.20	< 10	10	0.113	87	0.095	≤ 11
Caffeine	< 0.91	< 45	45	0.572	61	0.542	≤ 61
Inosine	< 0.38	< 19	19	0.160	72	0.107	≤ 19

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

9 Sugars and derivatives

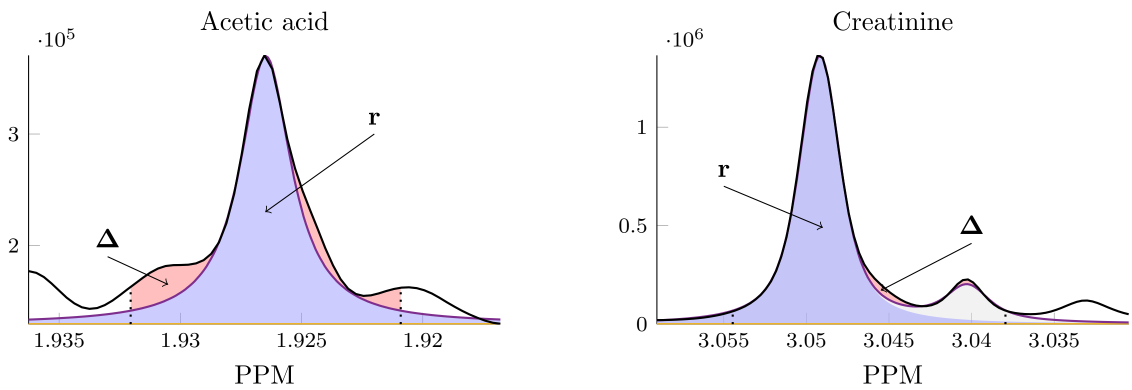
Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
D-Galactose	< 0.87	< 43	43	0.697	100	0.012	≤ 44
D-Glucose	0.82	41	34	0.817	93	0.196	≤ 140
D-Lactose	2.2	110	96	2.196	70	1.509	≤ 96
D-Mannitol	< 3.7	< 180	180	0.000	0	9.404	≤ 180
D-Mannose	< 0.12	< 6	6	0.000	0	0.114	≤ 8
Myo-Inositol	< 89	< 4400	4400	0.000	0	9.057	≤ 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 $\boldsymbol{\Delta}$.

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 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) $\mathbf{\Delta}$ 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.

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

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) $\mathbf{\Delta}$ 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.

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