Analysis Report

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

Sample ID:	ALZ_Urine_Rack01_RCM_221214_expno840.100000.10r

Measuring Date:	24-Dec-2014 09:45:10
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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:

Carboxylic acids: Trigonelline (140 mmol/mol Crea).

Further detailed information is provided on the following pages.

Contents

1 Creatinine

Compound	Conc.	LOD	r	ρ	Δ	95% Range[*]
	mmol/L	mmol/L	mmol/L	%	mmol/L	mmol/L
Creatinine	6.0	0.3	5.986	100 🟢	0.096	1 - 19

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

2 Amines and derivatives

Compound	Conc.	Conc.	LOD	r	ρ	Δ	95% Range[*]
	mmol/L	$\frac{mmol}{mol\ Crea}$	$\frac{mmol}{mol\ Crea}$	mmol/L	%	mmol/L	$\frac{mmol}{mol\ Crea}$
Dimethylamine	< 0.18	< 31	31	0.156	100 🟢	0.004	≤ 54
Trimethylamine	< 0.01	< 2	2	0.001	0 ⚪	0.002	≤ 3

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

3 Amino acids and derivatives

| Compound	Conc.	Conc.	LOD	r	ρ	Δ	95% Range[*]
	mmol/L	$\frac{mmol}{mol\ Crea}$	$\frac{mmol}{mol\ Crea}$	mmol/L	%	mmol/L	$\frac{mmol}{mol\ Crea}$
1-Methylhistidine	< 0.09	< 15	15	0.000	0 ⚪	0.086	≤ 15
2-Furoylglycine	< 0.23	< 39	39	0.000	0 ⚪	0.046	≤ 40
4-Aminobutyric acid	< 0.12	< 20	20	0.026	15 ⚪	0.072	≤ 20
Alanine	0.13	22	10	0.135	100 🟢	0.008	11 - 72
Arginine	< 4.5	< 750	750	0.397	4 ⚪	0.642	≤ 750
Betaine	0.26	44	7	0.262	99 🟢	0.033	9 - 78
Creatine	0.52	87	50	0.519	100 🟢	0.096	≤ 280
Glycine	0.40	67	34	0.400	100 🟢	0.015	38 - 440
Guanidinoacetic acid	< 0.62	< 100	100	0.248	94 🟡	0.073	≤ 140
Methionine	< 0.11	< 18	18	0.000	0 ⚪	0.127	≤ 18
N,N-Dimethylglycine	0.04	7	5	0.042	92 🟡	0.012	≤ 15
Sarcosine	< 0.01	< 2	2	0.004	0 ⚪	0.009	≤ 7
Taurine	< 0.85	< 140	140	0.561	77 ⚪	0.296	≤ 170
Valine	0.01	3	2	0.015	86 🟡	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. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range[*] $\frac{mmol}{mol\ Crea}$
Benzoic acid	< 0.06	< 10	10	0.000	0 ⚪	0.032	≤ 10
D-Mandelic acid	< 0.01	< 2	2	0.000	0 ⚪	0.008	2 - 17
Hippuric acid	3.6	600	170	3.575	100 🟢	0.256	≤ 660

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

5 Carboxylic acids

| Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range[*] $\frac{mmol}{mol\ Crea}$
Acetic acid	0.04	7	5	0.042	97 🟢	0.010	≤ 51
Citric acid	2.1	350	40	2.120	100 🟢	0.120	≤ 700
Formic acid	0.17	28	10	0.167	100 🟢	0.003	≤ 43
Fumaric acid	< 0.01	< 2	2	0.002	96 🟢	0.000	≤ 3
Imidazole	< 0.29	< 48	48	0.045	47 ⚪	0.035	≤ 48
Lactic acid	< 0.29	< 49	49	0.063	92 🟡	0.031	≤ 110
Proline betaine	< 0.15	< 25	25	0.081	16 ⚪	0.077	≤ 280
Succinic acid	0.06	9	5	0.056	99 🟢	0.006	≤ 39
Tartaric acid	< 0.03	< 5	5	0.011	96 🟢	0.004	≤ 110
Trigonelline	0.87	140	35	0.868	100 🟢	0.027	≤ 67

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

6 Fatty acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range[*] $\frac{mmol}{mol\ Crea}$
2-Methylsuccinic acid	< 0.29	< 48	48	0.000	0 ⚪	0.154	≤ 48

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

7 Keto acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range[*] $\frac{mmol}{mol\ Crea}$
2-Oxoglutaric acid	< 0.55	< 92	92	0.075	42 ○	0.106	≤ 92
3-Hydroxybutyric acid	< 0.62	< 100	100	0.065	47 ○	0.114	≤ 100
Acetoacetic acid	< 0.09	< 14	14	0.048	96 ●	0.014	≤ 30
Acetone	0.01	2	2	0.014	99 ●	0.003	≤ 7
Oxaloacetic acid	< 0.10	< 17	17	0.031	49 ○	0.044	≤ 66
Pyruvic acid	< 0.05	< 9	9	0.022	84 ○	0.009	≤ 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. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range[*] $\frac{mmol}{mol\ Crea}$
1-Methyladenosine	< 0.03	< 5	5	0.000	0 ○	0.084	≤ 5
1-Methylnicotinamide	< 0.19	< 32	32	0.073	98 ●	0.009	≤ 32
Adenosine	< 2.3	< 390	390	0.000	0 ○	0.952	≤ 390
Allantoin	< 0.10	< 17	17	0.038	95 ●	0.008	≤ 47
Allopurinol	< 0.06	< 10	10	0.025	92 ●	0.033	≤ 11
Caffeine	< 0.27	< 45	45	0.105	98 ●	0.083	≤ 61
Inosine	< 0.11	< 19	19	0.019	97 ●	0.032	≤ 19

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

9 Sugars and derivatives

Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range[*] $\frac{mmol}{mol\ Crea}$
D-Galactose	< 0.26	< 43	43	0.000	0 ○	0.021	≤ 44
D-Glucose	0.22	37	34	0.221	59 ○	0.139	≤ 140
D-Lactose	< 0.57	< 96	96	0.296	67 ○	2.960	≤ 96
D-Mannitol	< 1.1	< 180	180	0.000	0 ○	1.245	≤ 180
D-Mannose	< 0.04	< 6	6	0.000	0 ○	0.052	≤ 8
Myo-Inositol	< 27	< 4400	4400	0.000	0 ○	4.119	≤ 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 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.

$$\rho = \max\left(0, \mathrm{corr}\left(\overline{s}, \overline{f+b}\right)\right),$$

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) $\mathbf{\Delta}$ 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.

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