Analysis Report

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

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno30.100000.10r

Measuring Date:	23-Dec-2014 13:16:37
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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: 2-Furoylglycine (42 mmol/mol Crea), Glycine ($<$ 34 mmol/mol Crea), N,N-Dimethylglycine (18 mmol/mol Crea),
Benzene and substituted derivatives: Hippuric acid (740 mmol/mol Crea),
Carboxylic acids: Trigonelline (340 mmol/mol Crea),
Keto acids and derivatives: Pyruvic acid (18 mmol/mol Crea),
Purine, Pyridine and Pyrimidine derivatives: Caffeine (140 mmol/mol Crea),
Sugars and derivatives: D-Glucose (180 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	7.5	0.3	7.485	100 🟢	0.088	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	0.28	37	31	0.278	100 🟢	0.009	≤ 54
Trimethylamine	< 0.01	< 2	2	0.005	51 ⚪	0.006	≤ 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	< 0.11	< 15	15	0.000	0 ⚪	0.262	≤ 15
2-Furoylglycine	0.31	42	39	0.312	94 🟡	0.077	≤ 40
4-Aminobutyric acid	< 0.15	< 20	20	0.000	0 ⚪	0.629	≤ 20
Alanine	0.52	69	10	0.519	89 🟡	0.215	11 - 72
Arginine	< 5.6	< 750	750	0.731	0 ⚪	2.027	≤ 750
Betaine	0.25	33	7	0.248	98 🟢	0.115	9 - 78
Creatine	< 0.37	< 50	50	0.000	100 🟢	0.088	≤ 280
Glycine	< 0.25	< 34	34	0.019	0 ⚪	0.200	38 - 440
Guanidinoacetic acid	< 0.77	< 100	100	0.711	99 🟢	0.050	≤ 140
Methionine	< 0.13	< 18	18	0.000	0 ⚪	0.541	≤ 18
N,N-Dimethylglycine	0.14	18	5	0.138	100 🟢	0.004	≤ 15
Sarcosine	< 0.01	< 2	2	0.000	0 ⚪	0.013	≤ 7
Taurine	< 1.1	< 140	140	0.566	36 ⚪	0.827	≤ 170
Valine	< 0.01	< 2	2	0.000	0 ⚪	0.622	≤ 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	< 0.07	< 10	10	0.000	0 ○	0.123	≤ 10
D-Mandelic acid	< 0.02	< 2	2	0.013	90 ●	0.040	2 - 17
Hippuric acid	5.5	740	170	5.544	99 ●	0.591	≤ 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	0.11	15	5	0.112	100 ●	0.005	≤ 51
Citric acid	2.7	350	40	2.655	97 ●	1.007	≤ 700
Formic acid	0.19	25	10	0.186	100 ●	0.008	≤ 43
Fumaric acid	< 0.01	< 2	2	0.011	80 ○	0.005	≤ 3
Imidazole	< 0.36	< 48	48	0.105	87 ●	0.068	≤ 48
Lactic acid	< 0.36	< 49	49	0.246	86 ●	0.438	≤ 110
Proline betaine	0.85	110	25	0.847	100 ●	0.042	≤ 280
Succinic acid	< 0.04	< 5	5	0.029	93 ●	0.007	≤ 39
Tartaric acid	0.11	15	5	0.114	100 ●	0.008	≤ 110
Trigonelline	2.6	340	35	2.571	100 ●	0.105	≤ 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	< 0.36	< 48	48	0.000	0 ○	0.574	≤ 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	< 0.69	< 92	92	0.033	0 ○	0.805	≤ 92
3-Hydroxybutyric acid	< 0.77	< 100	100	0.000	0 ○	1.747	≤ 100
Acetoacetic acid	0.12	16	14	0.119	33 ○	0.133	≤ 30
Acetone	0.04	6	2	0.042	96 ●	0.010	≤ 7
Oxaloacetic acid	0.27	36	17	0.270	80 ○	0.241	≤ 66
Pyruvic acid	0.14	18	9	0.135	99 ●	0.012	≤ 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	< 0.04	< 5	5	0.000	0 ○	0.489	≤ 5
1-Methylnicotinamide	< 0.24	< 32	32	0.043	76 ○	0.023	≤ 32
Adenosine	< 2.9	< 390	390	0.000	0 ○	3.349	≤ 390
Allantoin	0.14	19	17	0.142	95 ●	0.027	≤ 47
Allopurinol	< 0.07	< 10	10	0.035	95 ●	0.031	≤ 11
Caffeine	1.1	140	45	1.052	84 ○	0.946	≤ 61
Inosine	< 0.14	< 19	19	0.043	94 ●	0.049	≤ 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	< 0.32	< 43	43	0.000	0 ○	0.059	≤ 44
D-Glucose	1.3	180	34	1.340	99 ●	0.088	≤ 140
D-Lactose	< 0.72	< 96	96	0.168	81 ○	0.079	≤ 96
D-Mannitol	< 1.4	< 180	180	0.000	0 ○	4.231	≤ 180
D-Mannose	< 0.04	< 6	6	0.000	0 ○	0.286	≤ 8
Myo-Inositol	< 33	< 4400	4400	0.000	0 ○	13.62	≤ 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 $\boldsymbol{\Delta}$.

10.1 How to read the result

(a) Single signal fitting.

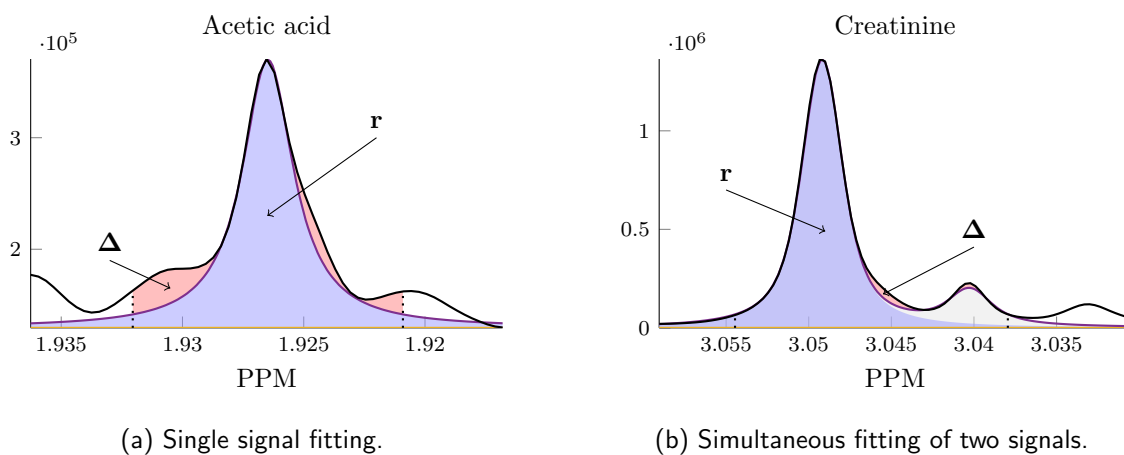(b) Simultaneous fitting of two signals.

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.

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

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) $\mathbf{\Delta}$ 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.

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