Analysis Report

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

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno370.100000.10r

Measuring Date:	23-Dec-2014 22:35:04
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Quantification Method Version:	Quant-UR B.1.1.0

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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 (24 mmol/mol Crea),*
Carboxylic acids: *Formic acid (52 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	4.8	0.3	4.775	100	0.102	1 - 19

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

2 Amines and derivatives

Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{mmol}{mol\ Crea}$
Dimethylamine	0.17	35	31	0.168	100	0.004	$\leq$ 54
Trimethylamine	< 0.01	< 2	2	0.005	99	0.001	$\leq$ 3

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

3 Amino acids and derivatives

Compound	Conc. mmol/L	Conc. $\frac{mmol}{mol\ Crea}$	LOD $\frac{mmol}{mol\ Crea}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{mmol}{mol\ Crea}$
1-Methylhistidine	< 0.07	< 15	15	0.000	0	0.209	$\leq$ 15
2-Furoylglycine	< 0.18	< 39	39	0.119	96	0.019	$\leq$ 40
4-Aminobutyric acid	0.12	24	20	0.116	55	0.108	$\leq$ 20
Alanine	0.17	36	10	0.173	100	0.011	11 - 72
Arginine	< 3.6	< 750	750	0.400	0	2.231	$\leq$ 750
Betaine	0.12	26	7	0.123	100	0.012	9 - 78
Creatine	< 0.24	< 50	50	0.052	100	0.102	$\leq$ 280
Glycine	0.62	130	34	0.623	100	0.023	38 - 440
Guanidinoacetic acid	< 0.49	< 100	100	0.267	7	0.277	$\leq$ 140
Methionine	< 0.09	< 18	18	0.000	0	0.220	$\leq$ 18
N,N-Dimethylglycine	0.04	8	5	0.040	49	0.027	$\leq$ 15
Sarcosine	< 0.01	< 2	2	0.004	0	0.008	$\leq$ 7
Taurine	< 0.68	< 140	140	0.391	80	0.206	$\leq$ 170
Valine	0.02	3	2	0.016	86	0.010	$\leq$ 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	$<$ 0.05	$<$ 10	10	0.000	0	0.040	$\leq$ 10
D-Mandelic acid	$<$ 0.01	$<$ 2	2	0.000	0	0.086	2 - 17
Hippuric acid	2.5	530	170	2.537	99	0.221	$\leq$ 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	0.05	11	5	0.054	93	0.021	$\leq$ 51
Citric acid	2.6	530	40	2.552	100	0.223	$\leq$ 700
Formic acid	0.25	52	10	0.249	100	0.011	$\leq$ 43
Fumaric acid	$<$ 0.01	$<$ 2	2	0.004	78	0.002	$\leq$ 3
Imidazole	$<$ 0.23	$<$ 48	48	0.000	0	0.136	$\leq$ 48
Lactic acid	$<$ 0.23	$<$ 49	49	0.105	88	0.044	$\leq$ 110
Proline betaine	0.19	40	25	0.192	98	0.044	$\leq$ 280
Succinic acid	0.04	8	5	0.038	79	0.013	$\leq$ 39
Tartaric acid	0.14	29	5	0.138	100	0.010	$\leq$ 110
Trigonelline	0.20	42	35	0.202	100	0.005	$\leq$ 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	$<$ 0.23	$<$ 48	48	0.000	0	0.193	$\leq$ 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	$<$ 0.44	$<$ 92	92	0.077	35 ○	0.230	$\leq$ 92
3-Hydroxybutyric acid	$<$ 0.49	$<$ 100	100	0.000	0 ○	0.761	$\leq$ 100
Acetoacetic acid	0.10	21	14	0.102	92 ●	0.068	$\leq$ 30
Acetone	0.01	3	2	0.015	99 ●	0.004	$\leq$ 7
Oxaloacetic acid	0.17	35	17	0.168	84 ○	0.135	$\leq$ 66
Pyruvic acid	$<$ 0.04	$<$ 9	9	0.017	71 ○	0.010	$\leq$ 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	$<$ 0.02	$<$ 5	5	0.000	0 ○	0.100	$\leq$ 5
1-Methylnicotinamide	$<$ 0.15	$<$ 32	32	0.036	94 ●	0.011	$\leq$ 32
Adenosine	$<$ 1.9	$<$ 390	390	0.000	0 ○	1.216	$\leq$ 390
Allantoin	$<$ 0.08	$<$ 17	17	0.055	98 ●	0.007	$\leq$ 47
Allopurinol	$<$ 0.05	$<$ 10	10	0.032	63 ○	0.036	$\leq$ 11
Caffeine	$<$ 0.22	$<$ 45	45	0.189	98 ●	0.133	$\leq$ 61
Inosine	$<$ 0.09	$<$ 19	19	0.017	70 ○	0.043	$\leq$ 19

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

9 Sugars and derivatives

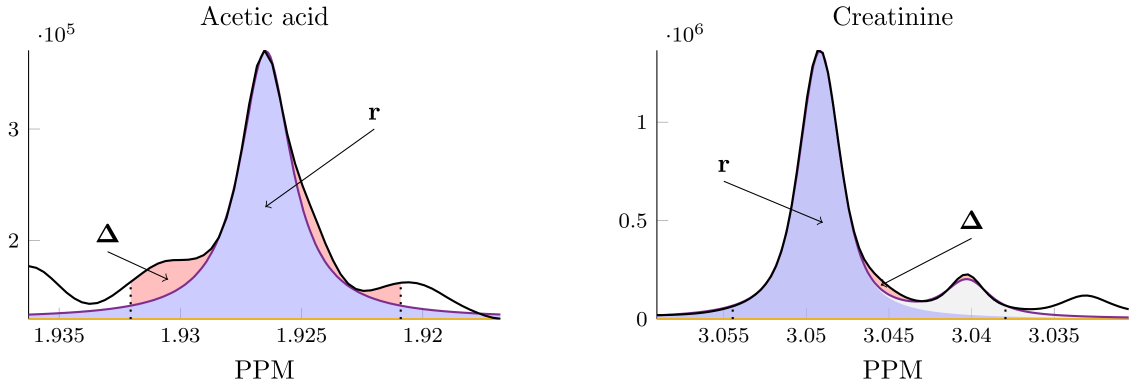
Compound	Conc. mmol/L	Conc. mmol/mol Crea	LOD mmol/mol Crea	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/mol Crea
D-Galactose	$<$ 0.21	$<$ 43	43	0.097	96 ●	0.005	$\leq$ 44
D-Glucose	0.19	39	34	0.188	83 ○	0.074	$\leq$ 140
D-Lactose	$<$ 0.46	$<$ 96	96	0.175	81 ○	0.684	$\leq$ 96
D-Mannitol	$<$ 0.87	$<$ 180	180	0.396	47 ○	0.744	$\leq$ 180
D-Mannose	$<$ 0.03	$<$ 6	6	0.023	96 ●	0.002	$\leq$ 8
Myo-Inositol	$<$ 21	$<$ 4400	4400	0.000	0 ○	5.611	$\leq$ 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) $\boldsymbol{\Delta}$ 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.

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

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) $\boldsymbol{\Delta}$ 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.

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