Analysis Report

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

Sample ID: ALZ_Urine_Rack01_RCM_221214_expno630.100000.10r

Measuring Date: 24-Dec-2014 04:57:55
Reporting Date: 12-Dec-2020 15:47:54, 7 page(s), Version 1.1.0
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:

Benzene and substituted derivatives: Hippuric acid (780 mmol/mol Crea).

Further detailed information is provided on the following pages.

Geschäftsführer: Dr. Falko Busse | Patrick Minhorst

Silberstreifen 4
76287 Rheinstetten, Germany
Tel. +49(0)721 5161-0
Fax. +49(0)721 517101
nmr@bruker-biospin.com
www.bruker-biospin.com

Deutsche Bank AG Karlsruhe
Konto 13 15 16 · BLZ 660 700 04
IBAN: DE87 6607 0004 0013 1516 00
SWIFT-BIC: DEUTDESM660

USt-Ident.-Nr DE 143 239 759
WEEE-Reg.-Nr. DE 43 181 702
Steuer-Nr. 31190/39205
Handelsregister Mannheim HRB 10 23 68
Sitz der Gesellschaft: 76287 Rheinstetten

Contents

1 Creatinine

Compound	Conc. mmol/L	LOD mmol/L	r mmol/L	ρ %	Δ mmol/L	95% Range(*) mmol/L
Creatinine	5.5	0.3	5.468	100 ●	0.085	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	0.19	34	31	0.188	100 ●	0.006	$\leq$ 54
Trimethylamine	$<$ 0.01	$<$ 2	2	0.005	83 ○	0.003	$\leq$ 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	$<$ 0.08	$<$ 15	15	0.042	0 ○	0.069	$\leq$ 15
2-Furoylglycine	$<$ 0.21	$<$ 39	39	0.065	0 ○	0.105	$\leq$ 40
4-Aminobutyric acid	$<$ 0.11	$<$ 20	20	0.084	54 ○	0.098	$\leq$ 20
Alanine	0.18	34	10	0.185	100 ●	0.012	11 - 72
Arginine	$<$ 4.1	$<$ 750	750	0.423	0 ○	1.506	$\leq$ 750
Betaine	0.15	27	7	0.147	99 ●	0.045	9 - 78
Creatine	$<$ 0.27	$<$ 50	50	0.097	100 ●	0.085	$\leq$ 280
Glycine	0.47	87	34	0.474	100 ●	0.042	38 - 440
Guanidinoacetic acid	$<$ 0.56	$<$ 100	100	0.494	87 ●	0.150	$\leq$ 140
Methionine	$<$ 0.10	$<$ 18	18	0.000	0 ○	0.156	$\leq$ 18
N,N-Dimethylglycine	0.07	14	5	0.075	97 ●	0.011	$\leq$ 15
Sarcosine	$<$ 0.01	$<$ 2	2	0.010	0 ○	0.014	$\leq$ 7
Taurine	$<$ 0.78	$<$ 140	140	0.611	84 ○	0.316	$\leq$ 170
Valine	0.02	3	2	0.017	95 ●	0.004	$\leq$ 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	< 0.05	< 10	10	0.000	0 ○	0.023	≤ 10
D-Mandelic acid	< 0.01	< 2	2	0.000	0 ○	0.093	2 - 17
Hippuric acid	4.2	780	170	4.250	99 ●	0.500	≤ 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	0.06	10	5	0.056	97 ●	0.010	≤ 51
Citric acid	3.1	570	40	3.143	100 ●	0.271	≤ 700
Formic acid	0.06	11	10	0.060	98 ●	0.012	≤ 43
Fumaric acid	< 0.01	< 2	2	0.007	96 ●	0.001	≤ 3
Imidazole	< 0.26	< 48	48	0.041	29 ○	0.052	≤ 48
Lactic acid	< 0.27	< 49	49	0.132	50 ○	0.105	≤ 110
Proline betaine	0.47	85	25	0.466	100 ●	0.017	≤ 280
Succinic acid	0.12	22	5	0.119	100 ●	0.006	≤ 39
Tartaric acid	0.17	31	5	0.171	99 ●	0.025	≤ 110
Trigonelline	< 0.19	< 35	35	0.070	100 ●	0.003	≤ 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	< 0.26	< 48	48	0.000	0 ○	0.348	≤ 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	< 0.50	< 92	92	0.000	0 ○	0.266	≤ 92
3-Hydroxybutyric acid	< 0.56	< 100	100	0.023	0 ○	0.368	≤ 100
Acetoacetic acid	0.08	14	14	0.077	68 ○	0.047	≤ 30
Acetone	0.01	2	2	0.011	93 ●	0.004	≤ 7
Oxaloacetic acid	0.13	23	17	0.127	63 ○	0.128	≤ 66
Pyruvic acid	< 0.05	< 9	9	0.039	85 ●	0.015	≤ 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	< 0.03	< 5	5	0.000	0 ○	0.114	≤ 5
1-Methylnicotinamide	< 0.17	< 32	32	0.029	90 ●	0.011	≤ 32
Adenosine	< 2.1	< 390	390	0.000	0 ○	1.441	≤ 390
Allantoin	< 0.09	< 17	17	0.075	95 ●	0.016	≤ 47
Allopurinol	< 0.05	< 10	10	0.039	79 ○	0.035	≤ 11
Caffeine	0.28	52	45	0.284	91 ●	0.195	≤ 61
Inosine	< 0.10	< 19	19	0.022	97 ●	0.030	≤ 19

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

9 Sugars and derivatives

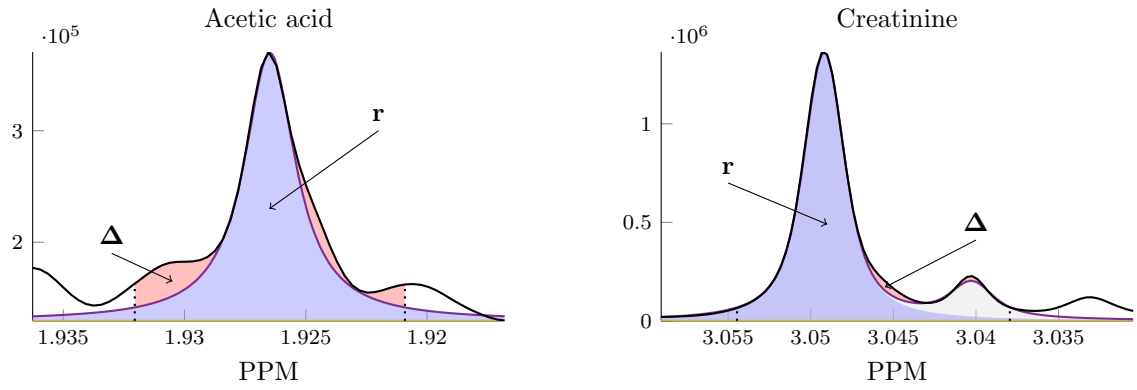
Compound	Conc. mmol/L	Conc. $\frac{\text{mmol}}{\text{mol Crea}}$	LOD $\frac{\text{mmol}}{\text{mol Crea}}$	r mmol/L	ρ %	Δ mmol/L	95% Range(*) $\frac{\text{mmol}}{\text{mol Crea}}$
D-Galactose	< 0.24	< 43	43	0.041	52 ○	0.017	≤ 44
D-Glucose	0.29	53	34	0.289	85 ●	0.085	≤ 140
D-Lactose	< 0.52	< 96	96	0.152	85 ●	0.061	≤ 96
D-Mannitol	< 1.00	< 180	180	0.000	0 ○	3.399	≤ 180
D-Mannose	< 0.03	< 6	6	0.018	0 ○	0.008	≤ 8
Myo-Inositol	< 24	< 4400	4400	0.000	0 ○	5.400	≤ 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.

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