# Supplement

# Impact of the antidiabetic drug metformin and its transformation product guanylurea on the health of the big ramshorn snail (*Planorbarius corneus*)

### Measurement of the concentrations of metformin and guanylurea in the exposure medium

Tab. S. 1: Operating parameters of the triple quadrupole mass spectrometer (QqQ-MS) for the quantification of the metformin and guanylurea concentrations in the test medium.

|  |  |
| --- | --- |
| **Parameter** | **Set point** |
| Gas temperature | 150 °C |
| Gas flow | 16 L/min |
| Nebulizer | 45 psi |
| Sheath gas heater | 400 °C |
| Sheath gas flow | 12 L/min |
|  |  |
| Capillary voltage | 1500 V |
| Ion funnel high/low pressure RF | 90/70 V |
| Fragmentor voltage | 380 V |

Tab. S. 2: Operating parameters of the triple quadrupole mass spectrometer (QqQ-MS).

|  |  |  |  |
| --- | --- | --- | --- |
|  | metformin | metformin D6 | guanylurea |
| Precursor ion (m/z) | 130 | 136 | 103.1 |
| Product ion (Quan/Qual) (m/z) | 60/71.1 | 60/77.1 | 60/86 |
| Collision energy (setpoint in V) | 10/30 | 10/30 | 10/5 |
| Cell accelerator voltage (V) | 6/6 | 6/6 | 5/5 |

Tab. S. 3: Intraday variations (RSDr) and interday variations (RSDR) of a 1 µg/L standard with metformin (MF) and guanylurea (GU) respectively measured by QqQ-MS

|  |  |  |
| --- | --- | --- |
|  | RSDr [%] | RSDR [%) |
|  | (n=4) | (MF n=6; GU n=4) |
| metformin | 1.5 | 5.5 |
| guanylurea | 6.6 | 9.5 |

Tab. S. 4: Mean metformin water concentrations of the test aquaria per treatment for the experiment with the big Ramshorn snail exposed to MF, measured with LC-MS

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **metformin** | | 0 µg/l | 10 µg/l | 100 µg/l | 1000 µg/l | 10000 µg/l |
| start | 11.11.2016 | < LoQ | 7.6 | 69 | 825 | 8958 |
| before w.e. | 18.11.2016 | < LoQ | 12.0 | 98 | 1120 | 10579 |
| after w.e. | 18.11.2016 | < LoQ | 10.8 | 119 | 1153 | 11418 |
| before w.e. | 02.12.2016 | < LoQ | 9.9 | 127 | 1121 | 11293 |
| after w.e. | 02.12.2016 | < LoQ | 10.5 | 99 | 1113 | 11939 |
| end | 16.12.2016 | < LoQ | 9.7 | 74 | 1095 | 11584 |
| before / after w.e.= before / after water exchange; LoQ = limit of quantification | | | | | | |

Tab. S. 5: Mean guanylurea water concentrations of the test aquaria per treatment for the experiment with the big Ramshorn snail exposed to MF, measured with LC-MS

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **guanylurea** | | 0 µg/L | 100 µg/L | 10.000 µg/L | 100.000 µg/L |
| start | 02.06.2017 | 0.10 | 110 | 10723 | 113096 |
| before w.e. | 08.06.2017 | 0.73 | 122 | 12044 | 108887 |
| after w.e. | 08.06.2017 | 0.30 | 100 | 11714 | 114516 |
| before w.e. | 14.06.2017 | 0.98 | 97 | 8639 | 117104 |
| after w.e. | 14.06.2017 | 0.24 | 94 | 10995 | 143593 |
| end | 23.06.2017 | 1.33 | 91 | 12131 | 115471 |
| before / after w.e.= before / after water exchange | | | | | |

### Histopathological examination

Tab. S. 6: Haematoxylin-Eosin staining protocol

|  |  |
| --- | --- |
| **medium** | **duration** |
| Roti® -Histol | 5 min |
| Roti® -Histol | 5 min |
| 100% ethanol | 5 min |
| 90% ethanol | 5 min n |
| 80% ethanol | 5 min n |
| 70% ethanol | 5 min |
| distilled water | 5 min |
| Haematoxylin | 4 min |
| distilled water | 4 s |
| running tap water | 20 min |
| Eosin | 5 min |
| 70% ethanol | 10 s |
| 80% ethanol | 5 min |
| 90% ethanol | 5 min |
| 96% ethanol | 5 min |
| 100% ethanol | 5 min |
| Roti® -Histol | 5 min |
| Roti® -Histol | 5 min |

Tab. S. 7: Supporting information for Tab. S. 10: qualitative examination of the samples: Histopathological findings in the hepatopancreas of big ramshorn snail

|  |  |  |  |
| --- | --- | --- | --- |
|  | Dark grey | Grey | White |
| Lumen | enlarged lumen | partially enlarged lumen | narrow lumen |
| digestive cells | bulging of apices | partially bulging of apices | smooth apices |
| disturbed compartmentation | partially disturbed compartmentation | regular  compartmentation |
| many deformed nuclei | few deformed nuclei | no deformed nuclei |
| crypt cells | irregular shape and number | - | normal shape and number |
| many deformed nuclei | few deformed nuclei | no deformed nuclei |
| vacuolisation | partially vacuolisation | no vacuolisation |

Tab. S. 8: Detailed information for the histopathological findings in the hepatopancreas of big ramshorn snails exposed to metformin or guanylurea (for the qualitative examination)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **metformin** | 0 µg/L | | | 10 µg/L | | | 100 µg/L | | | 1000 µg/L | | | 10 000 µg/L | | |
| enlarged lumen | 1 | 6 | 7 | 4 | 5 | 5 | 2 | 6 | 7 | 7 | 5 | 3 | 5 | 5 | 4 |
| bulging of apices DC | 3 | 9 | 2 | 10 | 4 | 0 | 8 | 5 | 2 | 9 | 6 | 0 | 13 | 1 | 0 |
| compartmentation DC | 0 | 0 | 14 | 0 | 0 | 14 | 0 | 0 | 15 | 0 | 0 | 15 | 1 | 0 | 13 |
| deformed nucleus DC | 0 | 0 | 14 | 0 | 0 | 14 | 0 | 0 | 15 | 0 | 0 | 15 | 0 | 0 | 14 |
| irregular shape and number of CC | 0 | - | 14 | 0 | - | 14 | 1 | - | 14 | 4 | - | 11 | 5 | - | 9 |
| deformed nucleus CC | 0 | 0 | 14 | 0 | 0 | 14 | 0 | 0 | 15 | 0 | 0 | 15 | 0 | 0 | 15 |
| vacuolisation CC | 0 | 3 | 11 | 2 | 4 | 8 | 1 | 4 | 10 | 2 | 5 | 8 | 6 | 3 | 6 |
|  | | | | | | | | | | | | | | | |
| **guanylurea** | 0 µg/L | | | 100 µg/L | | | 10 000 µg/L | | | 100 000 µg/L | | |  | | |
| enlarged lumen | 3 | 5 | 7 | 0 | 6 | 9 | 1 | 9 | 5 | 6 | 8 | 0 |
| bulging of apices DC | 0 | 0 | 15 | 0 | 2 | 13 | 0 | 4 | 11 | 1 | 3 | 10 |
| compartmentation DC | 0 | 0 | 15 | 2 | 2 | 11 | 1 | 2 | 12 | 7 | 0 | 7 |
| deformed nucleus DC | 0 | 0 | 15 | 0 | 0 | 15 | 0 | 1 | 14 | 0 | 1 | 13 |
| irregular shape and number of CC | 0 | - | 15 | 0 | - | 15 | 0 | - | 15 | 8 | - | 6 |
| deformed nucleus CC | 0 | 3 | 12 | 0 | 3 | 12 | 0 | 7 | 8 | 7 | 7 | 0 |
| vacuolisation CC | 0 | 0 | 15 | 2 | 0 | 13 | 1 | 2 | 12 | 7 | 0 | 7 |

### Statistical details

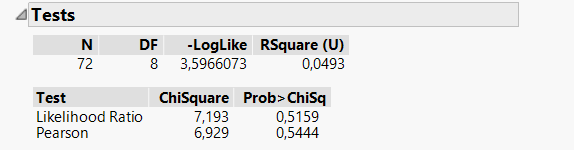
Tab. S. 9: Number of individuals investigated

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Metformin | | | | | |
| **Nominal water concentrations** | 0 µg/L | 10 µg/L | 100 µg/L | 1000 µg/L | 10 000 µg/L |
| **Weight [g]** | n=20 | n=21 | n=21 | n=20 | n=18 |
| **Relative Hsp70 level [rel. grey value]** | n=14 | n=15 | n=13 | n=15 | n=15 |
| **Lipid peroxide level [CHP-equiv./mg wet weight]** | n=15 | n=15 | n=15 | n=15 | n=15 |
| Guanylurea | | | | | |
| **Nominal water concentrations** | 0 µg/L | 100 µg/L | 10 000 µg/L | 100 000 µg/L |  |
|  |
|  |
| **Weight [g]** | n=21 | n=21 | n=20 | n=19 |  |
| **Relative Hsp70 level [rel. grey value]** | n=14 | n=14 | n=11 | n=14 |  |
| **Lipid peroxide level [CHP-equiv./mg wet weight]** | n=14 | n=15 | n=15 | n=15 |  |

Tab. S. 10: Details for the statistical analyses of the experiments with big ramshorn snail exposed to metformin or guanylurea

|  |  |
| --- | --- |
| Mortality | metformin: COX-regression: df=4; χ2=1.09036\*10-8; p=1; |
| guanylurea: COX-regression: df=3; χ2= 2.65 \*10-9; p=1 |
| Body weight | metformin: nested ANOVA: df=4/8569; F=0.4503; p=0.7719; transformation with square root; |
| guanylurea: nested ANOVA: df=11/69; F= 3.6227; p=0.0172; transformation with log; Dunnett’s test: all p-values > 0.05 |
| Stress protein level | metformin: nested ANOVA: df=4/57; F=1.9976; p=0.1071; |
| guanylurea: nested ANOVA: df=11/41; F=4.3880; p=0.0091; Dunnett’s test: all p-values > 0.05 |
| Lipid peroxide level | metformin: nested ANOVA: df=4/59; F=1.6092; p=0.1264; |
| guanylurea: nested ANOVA: df=11/47; F=0.4929; p=0.6889 |
| Histopathology of hepatopancreas | metformin: Likelihood-ratio-χ2-test df=8; χ2=7.193; p=0.5159; |
| guanylurea: Likelihood-ratio-χ2-test: df=6; χ2=31.044; p<0.0001; pairwise comparison: (0 µg/L|100 000 µg/L): p=0.0018 |
| Fig. S. 1: Statistical analysis - the histopathological analysis of the hepatopancreas of big ramshorn snail exposed to guanylurea (comparison of all groups) | | |
| Fig. S. 2: Single comparison of the control group with the exposure group of 100 000 µg/L guanylurea | | |

Fig. S. 3: Statistical analysis - the histopathological analysis of the hepatopancreas of big ramshorn snail exposed to metformin



### CRED-criteria

Tab. S. 11: Details about the fulfilment of the criteria for reporting and evaluation ecotoxicity data (CRED) according to Moermond, Kase et al. (2016) for the experiment with *Planorbarius corneus* exposed to metformin

|  |  |  |  |
| --- | --- | --- | --- |
| **CRED-criteria: Exposure of big Ramshorn snail to metformin** | | | |
| **1. General information** | | | |
| a. Purpose | | | Aim of the study was to investigate the effect of metformin on the health of big Ramshorn snail. |
| b. Endpoints | | | Histopathological investigation of the hepatopancreas, analyses of stress protein (Hsp70) and lipid peroxide level, analysis of weight |
| **2. Test design** | | | |
| a. Standard | | | Not performed according to a standard procedure |
| b. GLP | | | Not GLP-accredited |
| c. Controls | | | Laboratory negative control |
| d. Validity | | | The mortality of the control was 0 %. |
| **3. Test compound** | | | |
| a. Identification | | 1,1-Dimethylbiguanide hydrochloride; CAS: 1115-70-4 | | |
| b. Physico-chemical characteristics | | 16.56 g/L (TOCRIS, 2017) | | |
| c. Source | | Sigma-Aldrich, Product Number: D150959; Batch Number: BCBP0558V | | |
| d. Purity | | 99.9% according to the Certificate of Analysis from Sigma-Aldrich | | |
| e. Formulation | | no formulation, no impurities | | |
| **4. Test organism** | | | | |
| a. Scientific name | | *Planorbarius corneus* | | |
| b. Body weight | | mean= 3.92 g ± 1.61 g | | |
| c. Age/life stage | | adults | | |
| d. Reproductive condition | | in reproductive condition | | |
| e. Sex | | hermaphroditic | | |
| f. Strain/clone | | no defined clone | | |
| g. Source | | progeny of snails obtained from Kölle Zoo Stuttgart, Germany and Bachflohkrebse.de, Stuttgart, Germany | | |
| h. Acclimatisation | | acclimatisation to temperature for two days | | |
| **5. Exposure conditions** | | | | |
| a. Schedule | | semi-static design with water exchange once a week | | |
| b. System | | closed | | |
| c. Test medium | | Filtered tap water (iron filter, active charcoal filter, particle filter) cooled to 11°C and aerated | | |
| d. Temperature | | Climate chamber set to 11°C, measured at the beginning and the end of the experiment;  mean=10.30 °C ± 0.13 °C | | |
| e. pH | | measured at the beginning and the end of the experiment; mean=8.16 ± 0.09 | | |
| f. Hardness | | not measured | | |
| g. Conductivity | | measured at the beginning and the end of the experiment; mean=460.73 µS/cm ± 6.60 µS/cm | | |
| h. Dissolved oxygen | | measured at the beginning and the end of the experiment; mean=10.03 mg/L ± 0.27 mg/L | | |
| i. Light intensity/quality | | 10 h : 14 h light : dark cycle | | |
| j. Feeding | | Once per day with Novo Tabs from JBL | | |
| k. Aquaria | | 25 L glass aquaria filled with 10 L of medium, covered with glass plane, silicone tubing, aerated with airstones (JBL ProSilent Aeras Micro S2) | | |
| l. Sand/sediment | | no sediment tested | | |
| m. Stock solutions | | Stock solution 1 (10 g/L) prepared from 14.803 g guanylurea sulfate in 1 L dest. water, stock solution 2 (0.1 g/L) produced from stock solution 1 via 1:100 dilution | | |
| n. Nominal concentrations | | 0, 10, 100, 1000, 10 000 μg/L | | |
| o. Measured concentration | | Water samples were taken and analysed at the beginning and the end of the experiment as well as two times during the experiments, before and after the water exchange. mean: <LoQ; 10.08 µg/L; 97.6 µg/L; 1071 µg/L; 10962 µg/L | | |
| p. Method | | HPLC-MS (QqQ-MS) (LoD = 1 ng/L) | | |
| q. Duration | | 35 d (11.11.2016 – 16.12.2016) | | |
| r. Observations | | Mortality, at the end of the experiment body weight was determined and samples were taken for biochemical and histological analyses | | |
| s. Results | | summary table in article | | |
| t. Biomass loading | | mean: 2.74 g/L | | |
| **6. Statistical Design and Biological Response** | | | | |
| a. Replicates | Three replicate aquaria per test concentration | | | |
| b. Number of organisms | 7 snails exposed per replicate, 5 of them were used for the histological and biochemical analyses, the other 2 were given to the chemical analysis of metformin and guanylurea in the tissue (analyses not finished yet) | | | |
| c. Design | Three blocks, one replicate per treatment present in each block, arranged in randomized order | | | |
| d. Statistical methods | mortality: nested COX-regression; body mass, stress proteins, lipid peroxides: nested ANOVA; histology: likelihood ratio test | | | |
| e. Biological response | no effects on mortality, weight, levels of stress proteins and lipid peroxides; trend to increased number of reactions in the hepatopancreas of snails exposed to 10 000 µg/L metformin | | | |
| f. Dose-response | not observable | | | |
| g. Statistical significances | no statistical significances | | | |
| h. Significance level | α = 0.05, in cases of multiple comparisons adjusted via sequential Bonferroni | | | |
| i. Variability | not estimated | | | |
| j. Raw data | provided on request | | | |

Tab. S. 12: Details about the fulfilment of the criteria for reporting and evaluation ecotoxicity data (CRED) according to Moermond, Kase et al. (2016) for the experiment with *Planorbarius corneus* exposed to guanylurea

|  |  |  |  |
| --- | --- | --- | --- |
| **CRED-criteria: Exposure of big Ramshorn snail to guanylurea** | | | |
| **1. General information** | | | |
| a. Purpose | | | Aim of the study was to investigate the effect of guanylurea on the health of big Ramshorn snail. |
| b. Endpoints | | | Histopathological investigation of the hepatopancreas, analyses of stress protein (Hsp70) and lipid peroxide level, analysis of weight |
| **2. Test design** | | | |
| a. Standard | | | Not performed according to a standard procedure |
| b. GLP | | | Not GLP-accredited |
| c. Controls | | | Laboratory negative control |
| d. Validity | | | The mortality of the control was 0 %. |
| **3. Test compound** | | | |
| a. Identification | | Guanylurea Sulfate; CAS: 591-01-5 | | |
| b. Physico-chemical characteristics | | 5.00\*104 mg/L (ChemIDplus) by toxnet | | |
| c. Source | | TCI, Product Number: D0433; Batch Number: AKJLG & WIA7F | | |
| d. Purity | | >98% according to the Certificate of Analysis from TCI | | |
| e. Formulation | | no formulation, no impurities | | |
| **4. Test organism** | | | | |
| a. Scientific name | | *Planorbarius corneus* | | |
| b. Body weight | | mean=2.12 g ± 0.75 g | | |
| c. Age/life stage | | adults | | |
| d. Reproductive condition | | in reproductive condition | | |
| e. Sex | | hermaphroditic | | |
| f. Strain/clone | | no defined clone | | |
| g. Source | | progeny of snails obtained from Kölle Zoo Stuttgart, Germany and Bachflohkrebse.de, Stuttgart, Germany | | |
| h. Acclimatisation | | acclimatisation to temperature for two days | | |
| **5. Exposure conditions** | | | | |
| a. Schedule | | semi-static design with water exchange once a week | | |
| b. System | | closed | | |
| c. Test medium | | Filtered tap water (iron filter, active charcoal filter, particle filter) cooled to 11°C and aerated | | |
| d. Temperature | | Climate chamber set to 11°C, measured at the beginning and the end of the experiment; mean=10.55 °C ± 0.23 °C | | |
| e. pH | | measured at the beginning and the end of the experiment; mean=8.32 ± 0.04 | | |
| f. Hardness | | not measured | | |
| g. Conductivity | | measured at the beginning and the end of the experiment; mean=499.42 µS/cm ± 26.93 µS/cm | | |
| h. Dissolved oxygen | | measured at the beginning and the end of the experiment; mean=10.58 mg/L ± 0.17 mg/L | | |
| i. Light intensity/quality | | 10 h : 14 h light : dark cycle | | |
| j. Feeding | | Once per day with Novo Tabs from JBL | | |
| k. Aquaria | | 25 L glass aquaria filled with 10 L of medium, covered with glass plane, silicone tubing, aerated with airstones (JBL ProSilent Aeras Micro S2) | | |
| l. Sand/sediment | | no sediment tested | | |
| m. Stock solutions | | Stock solution 1 (10 g/L) prepared from 14.803 g guanylurea sulfate in 1 L dest. water, stock solution 2 (0.1 g/L) produced from stock solution 1 via 1:100 dilution | | |
| n. Nominal concentrations | | 0, 100, 10,000, 100 000 μg/L | | |
| o. Measured concentration | | Water samples were taken and analysed at the beginning and the end of the experiment as well as two times during the experiments, before and after the water exchange. mean: 0.61 µg/L; 102.2 µg/L; 11041 µg/L; 118778 µg/L | | |
| p. Method | | HPLC-MS (QqQ-MS) (LoD = 10 ng/L) | | |
| q. Duration | | 21 d (02.06.17 – 23.06.17) | | |
| r. Observations | | Mortality, at the end of the experiment body weight was determined and samples were taken for biochemical and histological analyses | | |
| s. Results | | summary table in article | | |
| t. Biomass loading | | mean: 1.49 g/L | | |
| **6. Statistical Design and Biological Response** | | | | |
| a. Replicates | Three replicate aquaria per test concentration | | | |
| b. Number of organisms | 7 snails exposed per replicate, 5 of them were used for the histological and biochemical analyses, the other 2 were given to the chemical analysis of metformin and guanylurea in the tissue (analyses not finished yet) | | | |
| c. Design | Three blocks, one replicate per treatment present in each block, arranged in randomized order | | | |
| d. Statistical methods | mortality: nested COX-regression; body mass, stress proteins, lipid peroxides: nested ANOVA; histology: likelihood ratio test | | | |
| e. Biological response | no effects on mortality, weight, levels of stress proteins and lipid peroxides; significantly increased number of reactions in the hepatopancreas of snails exposed to 100 000 µg/L guanylurea | | | |
| f. Dose-response | not observable | | | |
| g. Statistical significances | Histopathology hepatopancreas: LOEC= 100 000 µg/L | | | |
| h. Significance level | α = 0.05, in cases of multiple comparisons adjusted via sequential Bonferroni | | | |
| i. Variability | not estimated | | | |
| j. Raw data | provided on request | | | |

### Water quality parameters

Tab. S. 13: Limnological parameters of the experiment with the big ramshorn snail exposed to metformin

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| metformin concentration [µg/L] | replicate | oxygen concentration [mg/L] | pH | conductivity [µS/cm] | temperature [°C] | time point |
| 0 | 1 | 10.32 | 8.06 | 455 | 10.2 | start |
| 0 | 2 | 9.19 | 8.07 | 460 | 10.2 | start |
| 0 | 3 | 10.19 | 8.08 | 457 | 10.2 | start |
| 10 | 1 | 10.24 | 8.11 | 456 | 10.4 | start |
| 10 | 2 | 10.24 | 8.12 | 454 | 10.3 | start |
| 10 | 3 | 10.21 | 8.14 | 461 | 10.4 | start |
| 100 | 1 | 10.37 | 8.30 | 456 | 10.3 | start |
| 100 | 2 | 10.21 | 8.28 | 457 | 10.3 | start |
| 100 | 3 | 10.31 | 8.29 | 457 | 10.0 | start |
| 1000 | 1 | 10.26 | 8.27 | 457 | 10.6 | start |
| 1000 | 2 | 10.27 | 8.27 | 452 | 10.3 | start |
| 1000 | 3 | 10.29 | 8.25 | 458 | 10.3 | start |
| 10 000 | 1 | 9.45 | 8.17 | 463 | 10.2 | start |
| 10 000 | 2 | 10.16 | 8.16 | 462 | 10.2 | start |
| 10 000 | 3 | 10.24 | 8.20 | 462 | 10.4 | start |
| 0 | 1 | 9.95 | 7.97 | 464 | 10.3 | end |
| 0 | 2 | 9.98 | 8.01 | 454 | 10.3 | end |
| 0 | 3 | 10.00 | 8.03 | 463 | 10.2 | end |
| 10 | 1 | 9.81 | 8.06 | 469 | 10.5 | end |
| 10 | 2 | 9.92 | 8.06 | 463 | 10.3 | end |
| 10 | 3 | 9.93 | 8.07 | 467 | 10.5 | end |
| 100 | 1 | 10.07 | 8.18 | 452 | 10.2 | end |
| 100 | 2 | 9.85 | 8.19 | 459 | 10.3 | end |
| 100 | 3 | 10.01 | 8.19 | 479 | 10.0 | end |
| 1000 | 1 | 10.00 | 8.22 | 458 | 10.5 | end |
| 1000 | 2 | 9.99 | 8.22 | 455 | 10.3 | end |
| 1000 | 3 | 9.99 | 8.22 | 460 | 10.3 | end |
| 10 000 | 1 | 9.56 | 8.16 | 463 | 10.2 | end |
| 10 000 | 2 | 9.86 | 8.16 | 471 | 10.3 | end |
| 10 000 | 3 | 9.90 | 8.19 | 478 | 10.4 | end |

Tab. S. 14: Limnological parameters of the experiment with the big ramshorn snail exposed to guanylurea

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| guanylurea concentration [µg/L] | replicate | oxygen concentration [mg/L] | pH | conductivity [µS/cm] | temperature [°C] | time point |
| 0 | 1 | 10.61 | 8.37 | 484 | 10.6 | start |
| 0 | 2 | 10.5 | 8.36 | 482 | 10.4 | start |
| 0 | 3 | 10.63 | 8.36 | 482 | 10.1 | start |
| 100 | 1 | 10.41 | 8.36 | 489 | 10.6 | start |
| 100 | 2 | 10.65 | 8.35 | 481 | 10.3 | start |
| 100 | 3 | 10.63 | 8.35 | 482 | 10.1 | start |
| 10 000 | 1 | 10.04 | 8.29 | 492 | 10.7 | start |
| 10 000 | 2 | 10.17 | 8.3 | 491 | 10.4 | start |
| 10 000 | 3 | 10.86 | 8.33 | 489 | 10.3 | start |
| 100 000 | 1 | 10.7 | 8.31 | 540 | 10.7 | start |
| 100 000 | 2 | 10.63 | 8.32 | 540 | 10.6 | start |
| 100 000 | 3 | 10.76 | 8.31 | 539 | 10.4 | start |
| 0 | 1 | 10.65 | 8.26 | 479 | 10.7 | end |
| 0 | 2 | 10.68 | 8.26 | 483 | 10.6 | end |
| 0 | 3 | 10.71 | 8.27 | 479 | 10.4 | end |
| 100 | 1 | 10.59 | 8.27 | 479 | 10.9 | end |
| 100 | 2 | 10.52 | 8.27 | 478 | 10.6 | end |
| 100 | 3 | 10.66 | 8.27 | 476 | 10.5 | end |
| 10 000 | 1 | 10.55 | 8.3 | 490 | 10.6 | end |
| 10 000 | 2 | 10.76 | 8.33 | 490 | 10.5 | end |
| 10 000 | 3 | 10.64 | 8.35 | 489 | 10.5 | end |
| 100 000 | 1 | 10.54 | 8.39 | 549 | 11 | end |
| 100 000 | 2 | 10.56 | 8.38 | 548 | 10.9 | end |
| 100 000 | 3 | 10.54 | 8.37 | 555 | 10.8 | end |