The impact of temperature on the transformation of illicit drug biomarkers in wastewater

Ramin, Pedram; Polesel, Fabio; Brock, Andreas Libonati; Plósz, Benedek G.

Published in:
Science of the Total Environment

Link to article, DOI:
[10.1016/j.scitotenv.2018.06.307](https://doi.org/10.1016/j.scitotenv.2018.06.307)

Publication date:
2018

Document Version
Peer reviewed version

[Link back to DTU Orbit](#)

Citation (APA):
Ramin, P., Polesel, F., Brock, A. L., & Plósz, B. G. (2018). The impact of temperature on the transformation of illicit drug biomarkers in wastewater. *Science of the Total Environment*, 644, 1612-1616.
<https://doi.org/10.1016/j.scitotenv.2018.06.307>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

The impact of temperature on the transformation of illicit drug biomarkers in wastewater

Pedram Ramin^{1,2}, Fabio Polesel¹, Andreas Libonati Brock¹, Benedek Gy. Plósz^{1,3}

¹DTU Environment, Technical University of Denmark, Bygningstorvet 115, 2800 Kongens Lyngby,
Denmark

²Process and Systems Engineering Centre (PROSYS), Department of Chemical and Biochemical
Engineering, Technical University of Denmark, DK-2800 Kgs. Lyngby, Denmark

³Department of Chemical Engineering, University of Bath, Claverton Down, Bath BA2 7AY, UK

Corresponding authors:

Pedram Ramin: pear@kt.dtu.dk; Benedek Gy. Plósz: b.g.plosz@bath.ac.uk;

*Graphical Abstract

Highlights:

- Transformation of illicit drug biomarkers in wastewater can be temperature-dependent.
- Relevant published scientific literature were systematically reviewed and selected for data collection.
- Arrhenius equation was used to describe temperature-dependent transformation kinetics of selected biomarkers in wastewater under aerobic conditions.
- The study can facilitate comparative assessments of drug stability in wastewater and more accurate estimation of drug consumption, especially in multi-catchment studies covering wide geographical area

The impact of temperature on the transformation of illicit drug biomarkers in wastewater

Pedram Ramin^{1,2}, Fabio Polesel¹, Andreas Libonati Brock¹, Benedek Gy. Plósz^{1,3}

¹DTU Environment, Technical University of Denmark, Bygningstorvet 115, 2800 Kongens Lyngby, Denmark

²Process and Systems Engineering Centre (PROSYS), Department of Chemical and Biochemical Engineering, Technical University of Denmark, DK-2800 Kgs. Lyngby, Denmark

³Department of Chemical Engineering, University of Bath, Claverton Down, Bath BA2 7AY, UK

Corresponding authors:

Pedram Ramin: pear@kt.dtu.dk; Benedek Gy. Plósz: b.g.plosz@bath.ac.uk;

15

16 **Abstract**

17 Temperature is well-known as a key factor, influencing the transformation kinetics of organic
18 chemicals. In the context of wastewater-based epidemiology; however, temperature differences among
19 sewer catchments and within the same catchment (due, e.g., to seasonal variations) have been neglected
20 to date as a factor influencing the estimation of illicit drug consumption.

21 In this study, we assessed the influence of temperature on the transformation of drug biomarkers
22 occurring at trace levels in wastewater, based on laboratory-scale experimental evidence, and its
23 ensuing implications for back-calculation of chemical consumption rate. Existing literature on the
24 stability of drug biomarkers in untreated wastewater was systematically reviewed, and transformation
25 rates obtained at different temperatures were collected. Arrhenius-based equations were fitted to
26 empirical data and identified to describe the transformation of selected cocaine and morphine
27 biomarkers at applicability temperature range (from 2–9°C to 30–31°C). These empirically-derived
28 relationships were used to assess the influence of temperature on the transformation of drug biomarkers
29 during in-sewer transport and its effect on the back-calculation of drug consumption rate in urban
30 catchments. Findings from this study can help reduce the uncertainty intrinsic to wastewater-based
31 epidemiology studies, and will be beneficial in generalizing consumption estimates from different
32 catchments worldwide.

33

34 **Keywords:** Wastewater-based epidemiology, stability, temperature, biotransformation, Arrhenius
35 equation

36

37

38 **Highlights:**

- 39 • Transformation of illicit drug biomarkers in wastewater can be temperature-dependent.
- 40 • Relevant published scientific literature were systematically reviewed and selected for data
- 41 collection.
- 42 • Arrhenius equation was used to describe temperature-dependent transformation kinetics of
- 43 selected biomarkers in wastewater under aerobic conditions.
- 44 • The study can facilitate comparative assessments of drug stability in wastewater and more
- 45 accurate estimation of drug consumption, especially in multi-catchment studies covering wide
- 46 geographical areas.

47 **1. Introduction**

48 Wastewater-based epidemiology (WBE) is a growing research field to improve social behavior
49 predictions in an epidemiological context. It is based on the analysis of substance residues (biomarkers)
50 in wastewater and back-calculation of population consumption/exposure at catchment level. Substance
51 use biomarkers, such as illicit drugs, have been the main focus of WBE studies (Gracia-Lor et al.,
52 2017). A number of uncertainties (e.g., chemical analysis, determination of catchment population) have
53 been associated to the determination of community drug use (Castiglioni et al., 2013). Furthermore,
54 neglecting in-sewer transformation can also be a significant source of bias since biomarker
55 concentration levels at the excretion point can differ from the sampling point (Li et al., 2018). In-sewer
56 stability of drugs is mainly associated to abiotic transformation (without the presence of biomass) and
57 biotransformation in the presence of suspended and attached biomass.

58 In WBE studies, two main approaches have been used to translate measured concentration to
59 consumption rate: (i) lumped correction factors that include e.g., excretion ratios and in-sewer
60 transformation; (ii) in-sewer process kinetic models together with excretion ratios. The first approach is
61 commonly used due to its simplicity, with the major drawback of lacking catchment specificity.
62 Conversely, process models explicitly rely on first- or second-order equations (McCall et al., 2016;
63 Plósz et al., 2013; Ramin et al., 2016) to describe transformation kinetics, therefore allowing to account
64 for a number of influencing factors (e.g. redox conditions, in-sewer residence time, transformation
65 pathways and biomarker concentrations) depending on the complexity level. A factor known to
66 influence microbial activity—hence biomarker stability—is temperature. The impact of temperature on
67 the transformation of organic micropollutants has been assessed in activated sludge (Li et al., 2005) and
68 in anaerobic digestion (Carballa et al., 2007). As to illicit drug biomarkers, stability studies in untreated
69 wastewater (Bisceglia and Lippa, 2014b; Devault et al., 2017) have overall revealed enhanced

transformation kinetics with increasing temperature. While the effect of temperature on microbial growth kinetics is considered in models for conventional pollutants (e.g., activated sludge models), very few examples exist on quantifying the temperature dependence of kinetic model parameters for trace organic chemical transformation (Li et al., 2005; Wick et al., 2009).

In sewers, wastewater temperature exhibits seasonal and geographical variations and may further vary within the same catchment. During a recent Europe-wide sampling campaign (conducted simultaneously in 47 cities), the temperature of raw wastewater at sampling points was reported in the range between 7 °C and 28°C (Ort et al., 2014). Consequently, the impact of temperature on the stability of drug biomarkers in sewers may significantly vary from catchment to catchment, and the associated uncertainties propagating to the back-calculated consumption rate could be reduced in WBE approaches using more robust temperature models – the main focal area chosen for this study.

Considering existing limitations, the objectives of this study were: (i) to assess the effect of temperature on in-sewer drug biomarker stability, based on findings from published literature; (ii) Use empirical equations to describe temperature-dependent transformation kinetics of selected biomarkers in wastewater under aerobic conditions; (iii) to assess the influence of temperature on the in-sewer removal of drug biomarkers in a hypothetical urban catchment.

87 2. Materials and methods

88 2.1. Literature review and data treatment

89 Published scientific literature was reviewed (last update: 31/03/2018) to select drug biomarker stability
90 studies in untreated wastewater, i.e. without the influence of biofilm. Further screening was performed
91 to identify studies that fulfilled the following criteria: (i) stability studies were performed under aerobic
92 conditions; (ii) biomarker transformation kinetics were explicitly reported or could be derived
93 (calculated) based on presented results (e.g., concentration profiles in batch experiments); (iii)
94 estimation of model parameters (see Eq. 1) was associated with good match between measured and
95 predicted concentration profiles ($R^2 > 0.7$). Ten literature studies were eventually selected (Table 1),
96 providing relevant information on stability of cocaine (COC), ecgonine methyl ester (EME),
97 cocaethylene (CE), norcocaine (NorCOC) and 6-monoacetylmorphine (6-MAM).

98 The first-order transformation rate coefficient (k , d^{-1}) was used as indicator of biomarker stability in
99 wastewater. Notably, k accounts for both abiotic and biotransformation kinetics, given that abiotic
100 control experiments were absent in most of the selected studies. When k values were not explicitly
101 reported, they were estimated by fitting experimental data with a first-order kinetic equation (Eq. 1):

$$102 \quad C(t) = C_0 e^{-kt} \quad (\text{Eq. 1})$$

103 where C_0 and $C(t)$ are biomarker concentrations at time 0 and at time t , respectively.

104 In two cases (McCall et al., 2016; Ramin et al., 2016), abiotic and biotransformation kinetics were
105 separately assessed and quantified by estimating the first-order rate coefficients (k_{abio} , d^{-1}) and pseudo-
106 first-order rate coefficients (k_{bio} , $L g^{-1} d^{-1}$), respectively. The two kinetic indicators were combined to
107 obtain k (Eq. 2):

$$108 \quad k = k_{abio} + k_{bio} X_{TSS} \quad (\text{Eq. 2})$$

109 where X_{TSS} (g L⁻¹) denotes the concentration of total suspended solids (TSS) in the experiments. Data
 110 from concentration profiles were extracted, when necessary, using the software *PlotDigitizer*.
 111 For each biomarker, the Arrhenius equation (Eq. 3) was used to describe variations in transformation
 112 rates as a function of temperature:

$$113 \quad k_T = k_{25} \theta^{(T-25)} \quad (\text{Eq. 3})$$

114 where T(°C) denotes the temperature, at which a specific k_T value was derived, k_{25} the transformation
 115 rate at 25°C and θ (-) the exponential Arrhenius coefficient. Parameters θ and k_{25} were estimated for
 116 each biomarker using particle swarm optimization in MATLAB 2016b. A temperature of 25°C was
 117 selected as reference to improve the identifiability of both estimated parameters, as previously
 118 suggested (Schwaab et al., 2007).

119 <Table 1>

120 2.2. Back-calculation procedure

121 To back-calculate drug concentration at the release point e.g. after toilet flush (unknown), drug
 122 concentration at the influent of wastewater treatment plant (known) is considered in a hypothetical
 123 catchment. In-sewer transformation was simulated using Eq. 1 and assuming an average residence time
 124 of 4.5 h, corresponding to the average residence time in a recent European monitoring campaign (Ort et
 125 al., 2014). To reflect on the uncertainty of the estimated model parameters (e.g. k_T (d⁻¹) and θ) Monte
 126 Carlo simulations with Latin hypercube sampling (LHS) were performed. To evaluate the impact of
 127 temperature on the removal of the selected drugs, three temperature conditions were considered, being
 128 representative of low (T=5°C), medium (T=15°C) and high (T=25°C) temperature.

129

130

131 **3. Results and discussion**

132 *3.1. Temperature-dependent transformation*

133 Considerable data variability in k rate values found in literature was noticed for most all selected drugs
134 (Fig. 1), even considering the same temperature (e.g., 6-MAM) as a result of factors such as,
135 differences in stability test conditions used in literature. Nevertheless, overall increase of k with
136 increasing temperature was observed, especially when considering the mean of multiple measurements
137 for each unique temperature.

138 Additionally, for each biomarker, Figure 1 presents plots of fitted Arrhenius equations (and associated
139 95% confidence intervals, shaded areas). Interestingly, many of the calculated data points (not reported
140 in the original study) and estimated ones (reported in the original study) fall out of the confidence
141 interval. Besides the previously discussed inherent data variability, this may have resulted from the
142 limited applicability of first-order transformation kinetics e.g. due to significant microbial growth
143 during batch experiments (Ramin et al., 2016).

144 Estimated parameter values k_T (d^{-1}) and Θ for the selected biomarkers are reported in Table 2. It can be
145 noticed that the estimated relative error was low, below 50%, except for NorCOC (0.78%) and
146 parameter collinearity was low expect for EME (-0.75). This seems to suggest good parameter
147 identifiability, based on criteria (error < 50% and collinearity < 0.7) set by (Frutiger et al., 2016).
148 Nevertheless, these thresholds are subjective and the consideration of 25°C as reference temperature
149 allowed for the improvement of parameter identifiability (achieving lower correlation).

150 Estimated Θ coefficient values were between 1.04 and 1.18, in agreement with previously reported
151 values. That is, for primary metabolic processes (relevant for biomass growth) in sewers, Arrhenius-
152 based temperature corrections have been suggested, with Θ values of 1.07 and 1.05 for aerobic water

153 phase and biofilm processes, respectively (Hvitved-Jacobsen et al., 2013). Henze et al. (2000) also
154 suggested similar coefficients to describe temperature dependency of biological processes in the
155 Activated sludge model No. 2 (ASM2). These coefficients are ranging from low ($\theta = 1.04$) for
156 hydrolysis by phosphate-accumulating biomass to high ($\theta = 1.12$) for nitrification. Similar θ values
157 were also estimated for 17- β estradiol (E2) transformation by activated sludge, ranging from 1.03 to
158 1.09 for different biomass concentrations (Li et al., 2005). Wick et al. (2009) considered temperature-
159 dependent biotransformation for successful prediction of season-dependent pharmaceutical and illicit
160 drugs removal in WWTPs. The correction factor, θ , for organic micropollutants such as
161 pharmaceuticals was estimated in the range of 1.03–1.09 (Joss et al., 2006). Overall, previous and
162 current findings demonstrate that temperature can have considerable impact on transformation, the
163 extent of which is compound-dependent.

164

165 3.2. *Influence of temperature on back-calculation of drug use*

166 As expected, higher temperature resulted in higher in-sewer removal, with 40% (6-MAM) to almost 4-
167 fold (EME) increase of removal efficiency from medium to high temperature. Consistently, 6-MAM
168 and EME have lowest and highest θ values (Table 2).

169 These results indicate that accounting for in-sewer transformation is important especially at elevated
170 temperatures (above 15°C). Consequently, the temperature dependency of k should be accounted for
171 explicitly in steady-state and dynamic model simulations. From this stand point, the Arrhenius equation
172 can be included in existing modeling frameworks for removal of drug biomarkers in wastewater such
173 as WATS—ASM-X (Ramin et al., 2016). We note that, in this study, the estimation of in-sewer
174 removal was performed based on individual biomarkers, and the transformation of biomarkers
175 into/from other biomarkers was neglected. It is common practice to back-calculate the consumption of

176 COC based on the concentration of its metabolite benzoylecgonine (BE) and COC itself. It has been
177 found that BE, beside formation, also under go transformation (McCall et al., 2016; Ramin et al.,
178 2016), although some studies reported negligible in-sewer BE transformation (Bisceglia and Lippa,
179 2014b; Thai et al., 2014). Further discussion on back-calculation of illicit drug consumption interested
180 readers are referred to available literature (Castiglioni et al., 2013; Khan and Nicell, 2011).

181 It is evident that further research is crucial for obtaining new evidence on drug stability at different
182 temperatures, especially for new psychoactive substances. This is generally relevant for other types of
183 biomarkers beyond illicit drugs which wastewater-based epidemiology has gained interests (Gracia-Lor
184 et al., 2017). We encourage authors to report conditions at which stability tests were performed,
185 similarly to Table 1. This would allow for better comparison and consistency evaluation among
186 different studies.

187

188 **4. Conclusions**

189 This study represents a first attempt to describe temperature-dependent transformation (abiotic and
190 biotic) of five illicit drug biomarkers (COC, EME, CE, NorCOC, 6-MAM) in untreated wastewater
191 under aerobic conditions. Following conclusions are made:

- 192 • Although affected by the considerable variability of measured transformation kinetics, the
193 Arrhenius equation could capture trends of increasing transformation rates with increasing
194 temperature within the applicability domain (from 2–9°C to 30–31°C).
- 195 • Arrhenius-based equations were estimated for each biomarker and used for removal predictions
196 during transport in ideal sewers. Up to almost 4-fold removal efficiency was observed when
197 temperature was changed from 15 °C to 25°C.

- These findings have considerable implications for back-calculation of drug consumption based on the analysis of untreated wastewater influents, especially for multi-catchment studies covering wide geographical areas. Further research should extend the investigation of temperature effects to (i) a larger number biomarkers; (ii) anaerobic conditions; and (iii) sewer biofilms.

Acknowledgments

This study was supported by the European Union's Seventh Framework Programme for research, technological development, and demonstration [grant agreement 317205, the SEWPROF MC ITN project].

208 **References**

209

210 Baker, D.R., Kasprzyk-Hordern, B., 2011. Critical evaluation of methodology commonly used in
211 sample collection, storage and preparation for the analysis of pharmaceuticals and illicit drugs in
212 surface water and wastewater by solid phase extraction and liquid chromatography-mass
213 spectrometry. *J. Chromatogr. A* 1218, 8036–59. doi:10.1016/j.chroma.2011.09.012

214 Bisceglia, K.J., Lippa, K. a, 2014a. Stability of cocaine and its metabolites in municipal wastewater -
215 the case for using metabolite consolidation to monitor cocaine utilization. *Environ. Sci. Pollut.*
216 *Res.* 21, 4453–4460. doi:10.1007/s11356-013-2403-5

217 Bisceglia, K.J., Lippa, K. a., 2014b. Stability of cocaine and its metabolites in municipal wastewater -
218 the case for using metabolite consolidation to monitor cocaine utilization. *Environ. Sci. Pollut.*
219 *Res.* 21, 4453–4460. doi:10.1007/s11356-013-2403-5

220 Carballa, M., Omil, F., Ternes, T., Lema, J.M., 2007. Fate of pharmaceutical and personal care
221 products (PPCPs) during anaerobic digestion of sewage sludge. *Water Res.* 41, 2139–2150.
222 doi:10.1016/j.watres.2007.02.012

223 Castiglioni, S., Bijlsma, L., Covaci, A., Emke, E., Hernández, F., Reid, M., Ort, C., Thomas, K. V.,
224 Van Nuijs, A.L.N., De Voogt, P., Zuccato, E., 2013. Evaluation of uncertainties associated with
225 the determination of community drug use through the measurement of sewage drug biomarkers.
226 *Environ. Sci. Technol.* 47, 1452–1460. doi:10.1021/es302722f

227 Chen, C., Kostakis, C., Irvine, R.J., Felgate, P.D., White, J.M., 2013. Evaluation of pre-analysis loss of
228 dependent drugs in wastewater: Stability and binding assessments. *Drug Test. Anal.* 5, 716–721.
229 doi:10.1002/dta.1428

230 Devault, D.A., Lévi, Y., Karolak, S., 2017. Applying sewage epidemiology approach to estimate illicit

231 drug consumption in a tropical context: Bias related to sewage temperature and pH. *Sci. Total*
 232 *Environ.* 584-585, 252–258. doi:10.1016/j.scitotenv.2017.01.114
 233 Frutiger, J., Marcarie, C., Abildskov, J., Sin, G., 2016. A Comprehensive Methodology for
 234 Development, Parameter Estimation, and Uncertainty Analysis of Group Contribution Based
 235 Property Models-An Application to the Heat of Combustion. *J. Chem. Eng. Data* 61, 602–613.
 236 doi:10.1021/acs.jced.5b00750
 237 Gracia-Lor, E., Castiglioni, S., Bade, R., Been, F., Castrignanò, E., Covaci, A., González-Mariño, I.,
 238 Hapeshi, E., Kasprzyk-Hordern, B., Kinyua, J., Lai, F.Y., Letzel, T., Lopardo, L., Meyer, M.R.,
 239 O'Brien, J., Ramin, P., Rousis, N.I., Rydevik, A., Ryu, Y., Santos, M.M., Senta, I., Thomaidis,
 240 N.S., Veloutsou, S., Yang, Z., Zuccato, E., Bijlsma, L., 2017. Measuring biomarkers in
 241 wastewater as a new source of epidemiological information: Current state and future perspectives.
 242 *Environ. Int.* 99, 131–150. doi:10.1016/j.envint.2016.12.016
 243 Henze, M., Gujer, W., Mino, T., Loosdrecht, M. van, 2000. Activated Sludge Models ASM1, ASM2,
 244 ASM2d AND ASM3, cientific and Technical Report No 9, IWA Publishing. London.
 245 Hvitved-Jacobsen, T., Vollertsen, J., Nielsen, A.H., 2013. Sewer Processes: Microbial and Chemical
 246 Process Engineering of Sewer Networks, second. ed. CRC Press.
 247 Joss, A., Carballa, M., Kreuzinger, N., Siegrist, H., Zabczynski, S., 2006. Human pharmaceuticals,
 248 hormones and fragrances: The challenge of micropollutants in urban water management, *Science*
 249 *of The Total Environment*. IWA Publishing, London. doi:10.1016/j.scitotenv.2006.10.031
 250 Khan, U., Nicell, J.A., 2011. Refined sewer epidemiology mass balances and their application to
 251 heroin, cocaine and ecstasy. *Environ. Int.* 37, 1236–1252. doi:10.1016/j.envint.2011.05.009
 252 Li, F., Yuasa, A., Obara, A., Mathews, A.P., 2005. Aerobic batch degradation of 17-beta estradiol (E2)
 253 by activated sludge: Effects of spiking E2 concentrations, MLVSS and temperatures. *Water Res.*

254 39, 2065–2075. doi:10.1016/j.watres.2005.02.009

255 Li, J., Gao, J., Thai, P.K., Sun, X., Mueller, J.F., Yuan, Z., Jiang, G., 2018. Stability of Illicit Drugs as

256 Biomarkers in Sewers: From Lab to Reality. *Environ. Sci. Technol.* acs.est.7b05109.

257 doi:10.1021/acs.est.7b05109

258 Mardal, M., Kinyua, J., Ramin, P., Miserez, B., van Nuijs, A.L.N., Covaci, A., Meyer, M.R., 2016.

259 Screening for illicit drugs in pooled human urine and urinated soil samples and studies on the

260 stability of urinary excretion products of cocaine, MDMA, and MDEA in wastewater by

261 hyphenated mass spectrometry techniques. *Drug Test. Anal.* doi:10.1002/dta.1957

262 McCall, A.K., Scheidegger, A., Madry, M.M., Steuer, A.E., Weissbrodt, D.G., Vanrolleghem, P.A.,

263 Kraemer, T., Morgenroth, E., Ort, C., 2016. Influence of different sewer biofilms on

264 transformation rates of drugs. *Environ. Sci. Technol.* 50, 13351–13360.

265 doi:10.1021/acs.est.6b04200

266 Ort, C., van Nuijs, A.L.N., Berset, J.D., Bijlsma, L., Castiglioni, S., Covaci, A., de Voogt, P., Emke, E.,

267 Fatta-Kassinos, D., Griffiths, P., Hernández, F., González-Mariño, I., Grabic, R., Kasprzyk-

268 Hordern, B., Mastroianni, N., Meierjohann, A., Nefau, T., Östman, M., Pico, Y., Racamonde, I.,

269 Reid, M., Slobodnik, J., Terzic, S., Thomaidis, N., Thomas, K. V., 2014. Spatial differences and

270 temporal changes in illicit drug use in Europe quantified by wastewater analysis. *Addiction* 109,

271 1338–1352. doi:10.1111/add.12570

272 Plósz, B.G., Reid, M.J., Borup, M., Langford, K.H., Thomas, K. V., 2013. Biotransformation kinetics

273 and sorption of cocaine and its metabolites and the factors influencing their estimation in

274 wastewater. *Water Res.* 47, 2129–2140. doi:10.1016/j.watres.2012.12.034

275 Ramin, P., Brock, A.L., Polesel, F., Causanilles, A., Emke, E., de Voogt, P., Plósz, B.G., 2016.

276 Transformation and sorption of illicit drug biomarkers in sewer systems : understanding the role of

277 suspended solids in raw wastewater. *Environ. Sci. Technol.* 50, 13397–13408.

278 Schwaab, M., Lemos, L.P., Pinto, J.C., 2007. Optimum reference temperature for reparameterization of
279 the Arrhenius equation. Part 1: Problems involving one kinetic constant. *Chem. Eng. Sci.* 62,
280 2750–2764. doi:10.1016/j.ces.2008.03.010

281 Senta, I., Krizman, I., Ahel, M., Terzic, S., 2014. Assessment of stability of drug biomarkers in
282 municipal wastewater as a factor influencing the estimation of drug consumption using sewage
283 epidemiology. *Sci. Total Environ.* 487, 659–665. doi:10.1016/j.scitotenv.2013.12.054

284 Thai, P.K., Jiang, G., Gernjak, W., Yuan, Z., Lai, F.Y., Mueller, J.F., 2014. Effects of sewer conditions
285 on the degradation of selected illicit drug residues in wastewater. *Water Res.* 48, 538–547.
286 doi:10.1016/j.watres.2013.10.019

287 van Nuijs, A.L.N., Abdellati, K., Bervoets, L., Blust, R., Jorens, P.G., Neels, H., Covaci, A., 2012. The
288 stability of illicit drugs and metabolites in wastewater, an important issue for sewage
289 epidemiology? *J. Hazard. Mater.* 239-240, 19–23. doi:10.1016/j.jhazmat.2012.04.030

290 Wick, A., Fink, G., Joss, A., Siegrist, H., Ternes, T.A., 2009. Fate of beta blockers and psycho-active
291 drugs in conventional wastewater treatment. *Water Res.* 43, 1060–1074.
292 doi:10.1016/j.watres.2008.11.031

293

295

296 **Figure 1.** Arrhenius equation fits for degradation rates k (d^{-1}) as a function of temperature ($^{\circ}\text{C}$). These
 297 are based on the reported (full circles) and the estimated (empty circles) empirical values from
 298 literature. Lines are the best prediction and the shaded band is the 95% confidence interval of the
 299 prediction.

Figure 2. Estimated removal efficiencies from excretion point to WWTP influent (in-sewer residence time = 4.5 h) for selected drug biomarkers, based on the identified Arrhenius regressions. Error bars represent 95% confidence interval following Monte Carlo simulation. Asterics (*) indicates that the temperature is out of applicability range.

305 **Table 1.** Overview of selected biomarker stability studies from published literature.

	Reference	Chemical	Data source for extraction of <i>k</i>	Temp. (°C)	pH	DO (mg L ⁻¹)	Duration of experiment (h)	No. of samples taken	C ₀ (µg L ⁻¹)	TSS (g L ⁻¹)
1	(Baker and Kasprzyk-Hordern, 2011)	COC, CE, 6MAM, NorCOC	Table	2, 19	7.4	-	72	4	1.0	-
2	(van Nuijs et al., 2012)	COC, EME, 6MAM	Graph	20	7.5	-	26	13	0.06–0.60	-
3	(Chen et al., 2013)	6MAM	Graph	4	7.4	-	336	6	>0.1	-
4	(Bisceglia and Lippa, 2014a)	COC, EME, CE, NorCOC	Values reported	9, 23, 31	7.4	-	26	16	1.5–3.0	-
5	(Senta et al., 2014)	COC, 6MAM	Graph, values reported	20	7.5	-	72	7	0.2	-
6	(Thai et al., 2014)	COC, 6MAM	Values reported	20	7.5	-	12	9	10	-
7	(Mardal et al., 2016)	COC, EME, CE	Graph, Table	23	7–8	-	24	9	0.5–100	-
8	(Ramin et al., 2016)	COC, EME, CE, 6MAM	Values reported	14	8.6–8.8	10	48	9	10	0.32 ± 0.04
9	(McCall et al., 2016)	COC, CE, 6MAM, NorCOC	Values reported	21	8.0–8.9	5–8	24	11	2.0–3.0	0.14–0.29
10	(Devault et al., 2017)	COC, 6MAM	Values reported	20, 30	6.6, 7.6	-	24	7	1.0–3.0	-

¹Used silanized amber glass bottles stored in the dark.

²Stability test performed in silanized glass flasks which were hand-shaken app. 10 times per hour.

³Bottles at 20°C were placed under fume cupboard uncapped and gently stirred 3 times per day (distilled water was used to compensate for evaporation). Bottle at 4°C was stored with cap on.

⁴Used Erlenmeyer flask equipped with foam stopper to allow air transfer. Reactor was shaken at 180 rpm in the dark.

⁵Glass bottles were capped with cotton plugs and placed in a thermostated cabinet.

⁶Used gravity sewer reactor with continuous mixing with magnetic stirrer (250 rpm) to enhance surface aeration.

⁷Urinary samples collected at a music festival was diluted with wastewater and incubated in a temperature water bath

⁸Transformation study was performed in a covered jacketed reactor equipped with an agitator and oxygen diffuser.

⁹Transformaiton study was conducted in Erlenmeyer flask on a shaker table in the dark. Autoclaved wastewater was chosen to represent abiotic transformation.

¹⁰Glass bottles were placed in the dark and aerobic conditinos was maintained by shaking with a magnetic stir bar.

306 **Table 2.** Estimated k_{T25} (d^{-1}) and θ and their correlation for the selected drugs. Parameters are estimated
 307 as the best fitted value together with 95% confidence interval. The predictions are valid in the reported
 308 temperature range.

	k_{T25} (d^{-1})	θ	Correlation (k_{T25} and θ)	Temperature range ($^{\circ}\text{C}$)
COC	1.48 (1.23, 1.75)	1.07 (1.04, 1.11)	0.06	9–31
EME	1.78 (1.03, 2.54)	1.18 (1.09, 1.28)	-0.75	9–31
CE	0.73 (0.61, 0.85)	1.10 (1.06, 1.13)	0.07	2–31
6MAM	0.64 (0.49, 0.78)	1.04 (1.00, 1.07)	0.49	2–30
NorCOC	1.44 (0.32, 2.57)	1.04 (0.90, 1.18)	0.29	9–31

309

310

Table 1. Overview of selected biomarker stability studies from published literature.

	Reference	Chemical	Data source for extraction of <i>k</i>	Temp. (°C)	pH	DO (mg L ⁻¹)	Duration of experiment (h)	No. of samples taken	C ₀ (µg L ⁻¹)	TSS (g L ⁻¹)
1	(Baker and Kasprzyk-Hordern, 2011)	COC, CE, 6MAM, NorCOC	Table	2, 19	7.4	-	72	4	1.0	-
2	(van Nuijs et al., 2012)	COC, EME, 6MAM	Graph	20	7.5	-	26	13	0.06–0.60	-
3	(Chen et al., 2013)	6MAM	Graph	4	7.4	-	336	6	>0.1	-
4	(Bisceglia and Lippa, 2014a)	COC, EME, CE, NorCOC	Values reported	9, 23, 31	7.4	-	26	16	1.5–3.0	-
5	(Senta et al., 2014)	COC, 6MAM	Graph, values reported	20	7.5	-	72	7	0.2	-
6	(Thai et al., 2014)	COC, 6MAM	Values reported	20	7.5	-	12	9	10	-
7	(Mardal et al., 2016)	COC, EME, CE	Graph, Table	23	7-8	-	24	9	0.5-100	-
8	(Ramin et al., 2016)	COC, EME, CE, 6MAM	Values reported	14	8.6–8.8	10	48	9	10	0.32 ± 0.04
9	(McCall et al., 2016)	COC, CE, 6MAM, NorCOC	Values reported	21	8.0–8.9	5–8	24	11	2.0–3.0	0.14–0.29
10	(Devault et al., 2017)	COC, 6MAM	Values reported	20, 30	6.6, 7.6	-	24	7	1.0–3.0	-

¹Used silanized amber glass bottles stored in the dark.

²Stability test performed in silanized glass flasks which were hand-shaken app. 10 times per hour.

³Bottles at 20°C were placed under fume cupboard uncapped and gently stirred 3 times per day (distilled water was used to compensate for evaporation). Bottle at 4°C was stored with cap on.

⁴Used Erlenmeyer flask equipped with foam stopper to allow air transfer. Reactor was shaken at 180 rpm in the dark.

⁵Glass bottles were capped with cotton plugs and placed in a thermostated cabinet.

⁶Used gravity sewer reactor with continuous mixing with magnetic stirrer (250 rpm) to enhance surface aeration.

⁷Urinary samples collected at a music festival was diluted with wastewater and incubated in a temperature water bath

⁸Transformation study was performed in a covered jacketed reactor equipped with an agitator and oxygen diffuser.

⁹Transformation study was conducted in Erlenmeyer flask on a shaker table in the dark. Autoclaved wastewater was chosen to represent abiotic transformation.

¹⁰Glass bottles were placed in the dark and aerobic conditions was maintained by shaking with a magnetic stir bar.

Table 2. Estimated k_{T25} (d^{-1}) and θ and their correlation for the selected drugs. Parameters are estimated as the best fitted value together with 95% confidence interval. The predictions are valid in the reported temperature range.

	k_{T25} (d^{-1})	θ	Correlation (k_{T25} and θ)	Temperature range ($^{\circ}\text{C}$)
COC	1.48 (1.23, 1.75)	1.07 (1.04, 1.11)	0.06	9–31
EME	1.78 (1.03, 2.54)	1.18 (1.09, 1.28)	-0.75	9–31
CE	0.73 (0.61, 0.85)	1.10 (1.06, 1.13)	0.07	2–31
6MAM	0.64 (0.49, 0.78)	1.04 (1.00, 1.07)	0.49	2–30
NorCOC	1.44 (0.32, 2.57)	1.04 (0.90, 1.18)	0.29	9–31

Figure 1. Arrhenius equation fits for degradation rates k (d⁻¹) as a function of temperature (°C). These are based on the reported (full circles) and the estimated (empty circles) empirical values from literature. Lines are the best prediction and the shaded band is the 95% confidence interval of the prediction.

Figure 2. Estimated removal efficiencies from excretion point to WWTP influent (in-sewer residence time = 4.5 h) for selected drug biomarkers, based on the identified Arrhenius regressions. Error bars represent 95% confidence interval following Monte Carlo simulation. Asterisks (*) indicates that the temperature is out of applicability range.