

Lijekovi u okolišu

Valerije Vrček

***Farmaceutsko-biokemijski fakultet
Sveučilište u Zagrebu***



Lana Petrinec, mag. pharm.

Županijski skup nastavnika
kemije/biologije osnovnih škola
Zagrebačke županije - istok i zapad.

Zagreb, 14. ožujka 2023.

Klaus Kümmerer
Editor

Pharmaceuticals in the Environment

Sources,
Fate,
Effects
and Risks

Third, revised and enlarged edition

 Springer

PHARMA- ECOLOGY

*The Occurrence and Fate of
Pharmaceuticals and Personal Care
Products in the Environment*



PATRICK K. JJEMBA

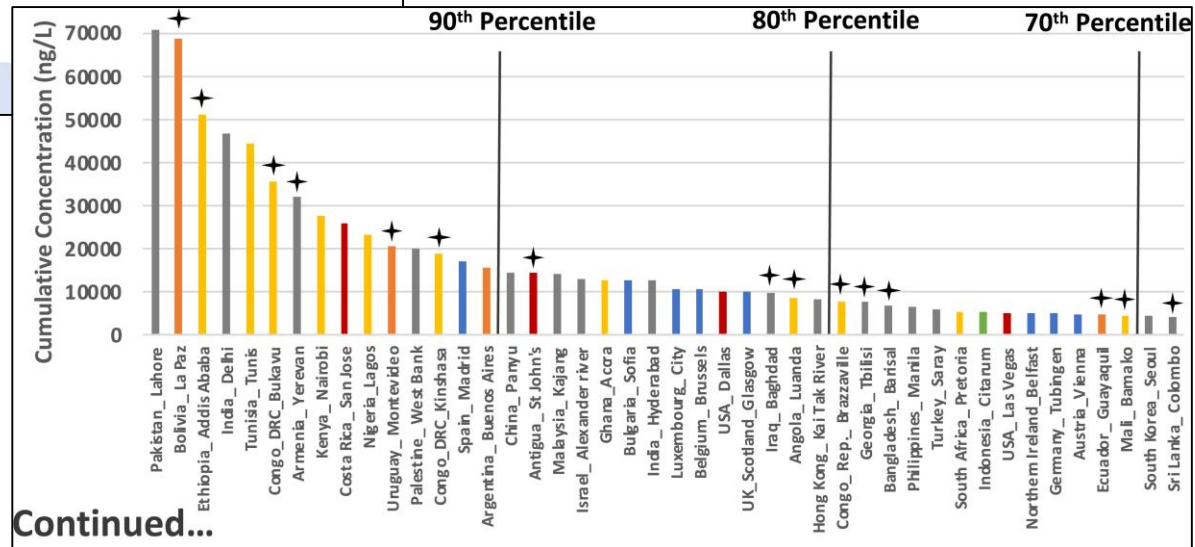
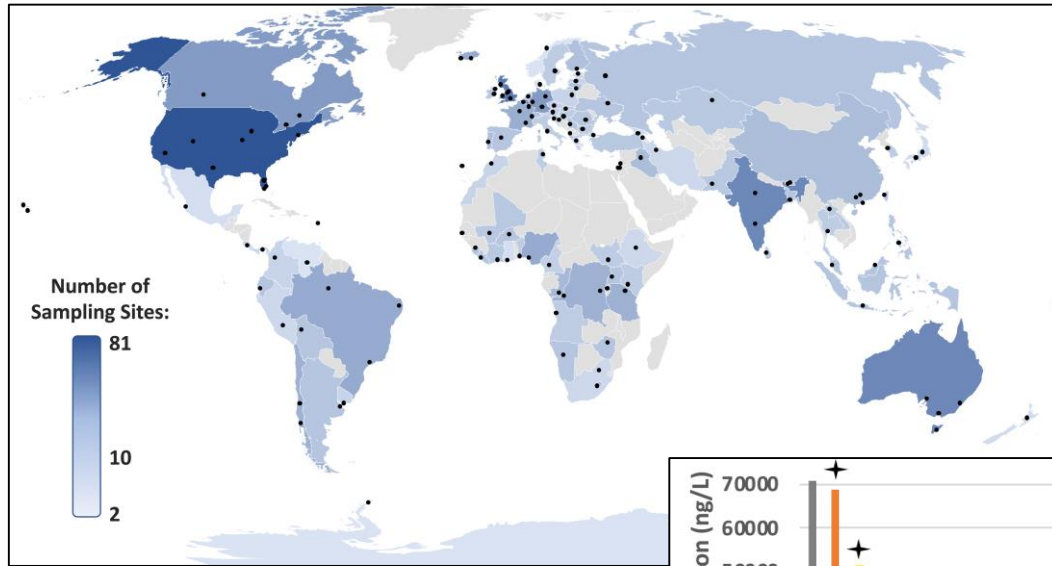
 WILEY

Pharmaceutical pollution of the world's rivers

John L. Wilkinson  , Alistair B. A. Boxall , Dana W. Kolpin ,  +123, and Charles Teta  [Authors Info & Affiliations](#)

Edited by Andrea Rinaldo, School of Architecture, Civil and Environmental Engineering, Laboratory of Ecohydrology, Ecole Polytechnique Federale de Lausanne, Lausanne, Switzerland; received August 11, 2021; accepted December 10, 2021

February 14, 2022 | 119 (8) e2113947119 | <https://doi.org/10.1073/pnas.2113947119>



-  Africa
-  Antarctica
-  Asia
-  Europe
-  North America
-  Oceania
-  South America
-  Country not previously monitored

Pharmaceuticals: a threat to drinking water?

Oliver A. Jones, John N. Lester and Nick Voulvoulis

Department of Environmental Science and Technology, Faculty of Life Sciences, Imperial College, London, SW7 2BP, UK

Pijemo li lijekove svojih susjeda?



The New York Times
Expect the World®



Toxic Waters
A series about the worsening pollution in American waters and regulators' response

December 17, 2009

That Tap Water Is Legal but May Be Unhealthy

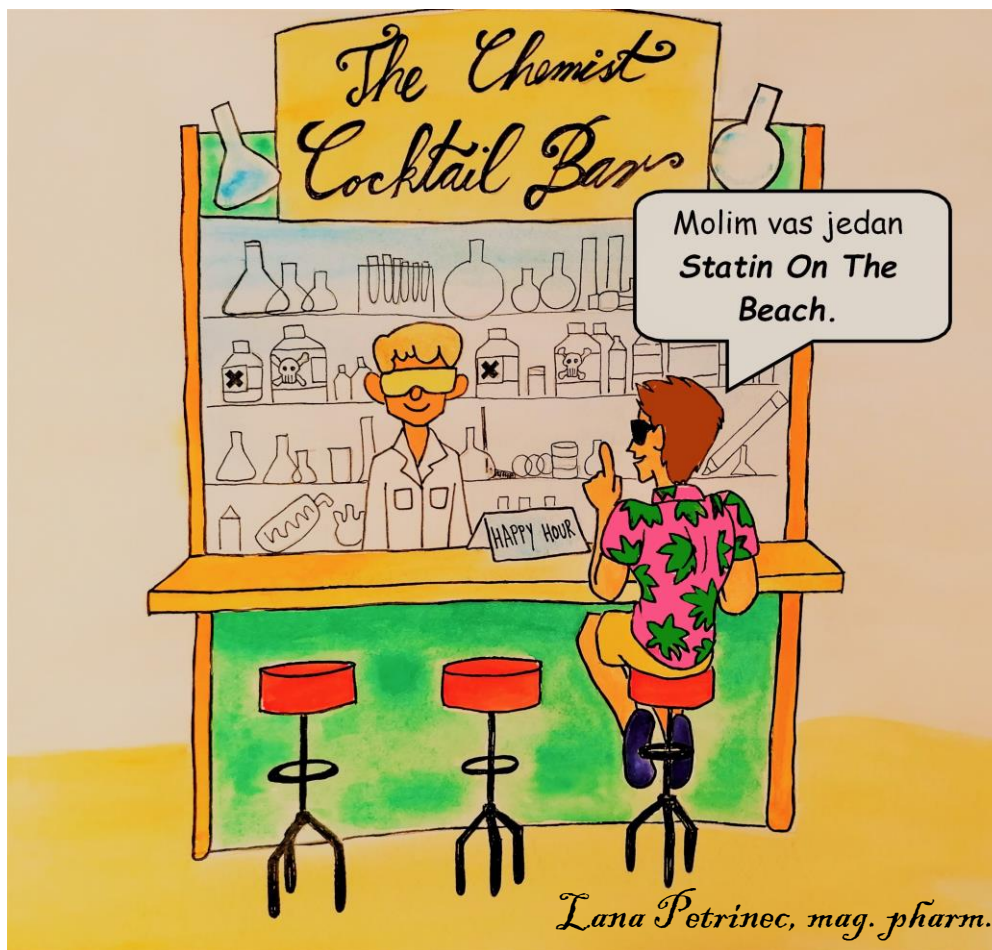
By [CHARLES DUHIGG](#)

Meprobamat, anksiolitik:	~ 40 ng / L pitke vode
Fenazon, analgetik:	~ 400 ng / L pitke vode
Karbamazepin, antiepileptik:	~ 260 ng / L pitke vode
Klofibrična kiselina, regulator lipida:	~ 300 ng / L pitke vode

1 μg / L pitke vode

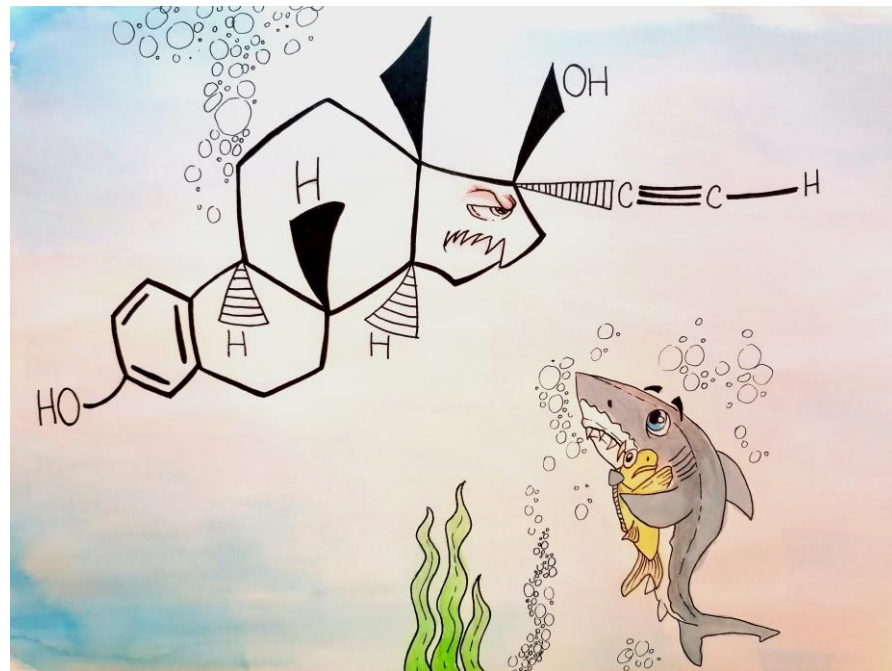
Farmaceutski kokteli (ili kaljuže)

1. Lijekovi (ni)su obične kemikalije
2. (Eko)toksikologija vrlo niskih doza
3. (Eko)toksikologija smjese
4. Kumulativni učinak lijekova





Karen Kidd, Canadian Rivers Institute, University of New Brunswick: "If you can measure the synthetic estrogen in the water, then that's enough to cause an effect, and we can measure it at very low parts-per-trillion concentrations."



Lana Petrinec, mag. pharm.

PNAS | May 22, 2007 | vol. 104 | no. 21 | 8897–8901

Collapse of a fish population after exposure to a synthetic estrogen

Karen A. Kidd^{*†}, Paul J. Blanchfield^{*}, Kenneth H. Mills^{*}, Vince P. Palace^{*}, Robert E. Evans^{*}, James M. Lazorchak[‡], and Robert W. Flick[‡]

^{*}Fisheries and Oceans Canada, Freshwater Institute, 501 University Crescent, Winnipeg, Manitoba, Canada R3T 2N6; and [†]Molecular Indicators Research Branch, United States Environmental Protection Agency, 26 West Martin Luther King Drive, Cincinnati, OH 45268

Edited by Deborah Swackhamer, University of Minnesota, Minneapolis, MN, and accepted by the Editorial Board March 29, 2007 (received for review October 27, 2006)

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Diclofenac residues as the cause of vulture population decline in Pakistan

J. Lindsay Oaks¹, Martin Gilbert², Munir Z. Virani², Richard T. Watson², Carol U. Meteyer³, Bruce A. Rideout⁴, H. L. Shivaprasad⁵, Shakeel Ahmed⁶, Muhammad Jamshed Iqbal Chaudhry⁶, Muhammad Arshad⁶, Shahid Mahmood⁶, Ahmad Ali⁶ & Aleem Ahmed Khan⁶

¹*Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, Washington 99164-7040, USA*

²*The Peregrine Fund, 5668 West Flying Hawk Lane, Boise, Idaho 83709, USA*

³*USGS–National Wildlife Health Center, 6006 Schroeder Road, Madison, Wisconsin 53711-6223, USA*

⁴*Center for Reproduction of Endangered Species, Zoological Society of San Diego, PO Box 120551, San Diego, California 92112, USA*

⁵*California Animal Health and Food Safety Laboratory System–Fresno Branch, University of California at Davis, 2789 S. Orange Avenue, Fresno, California 93725, USA*

⁶*Zoology Division, Institute of Pure and Applied Biology, Bahauddin Zakariya University, Multan, Pakistan*

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Zaboravljena lekcija ?

Science of the Total Environment 782 (2021) 146890



Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv



First diclofenac intoxication in a wild avian scavenger in Europe

Marta Herrero-Villar^{a,*}, Émilie Delepoulle^b, Laura Suárez-Regalado^b, Carlos Solano-Manrique^c, Carles Juan-Sallés^d, Juan J. Iglesias-Lebrija^b, Pablo R. Camarero^a, Fernando González^b, Ernesto Álvarez^b, Rafael Mateo^a

^a Instituto de Investigación en Recursos Cinegéticos (IREC), CSIC-UCLM-JCCM, 13005 Ciudad Real, Spain

^b Grupo de Rehabilitación de la Fauna Autóctona y su Hábitat (GREFA), 28220 Majadahonda, Spain

^c Centre de Fauna Valcaient, Departament de Territori i Sostenibilitat, Generalitat de Catalunya, 25199 Lleida, Spain

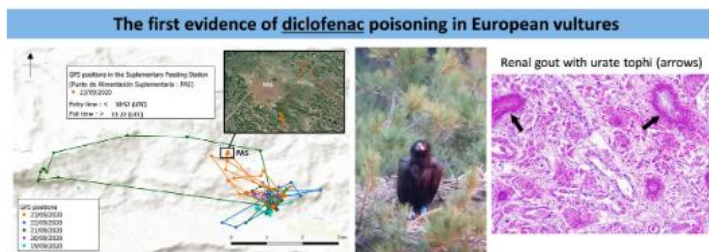
^d Noah's Path, 03203 Elche, Spain



HIGHLIGHTS

- First case of diclofenac poisoning in a European vulture
- Diclofenac intoxication has been detected for the first time in cinereous vulture.
- The fledgling presented extended visceral gout and no signs of other pathologies.
- Diclofenac concentrations were 26.5 ng/g in liver and 51.4 ng/g in kidney.
- This evidences the need of close vigilance and stronger regulation on diclofenac.

GRAPHICAL ABSTRACT



Lana Petrinec, mag. pharm.

Dilute Concentrations of a Psychiatric Drug Alter Behavior of Fish from Natural Populations

T. Brodin *et al.*

Science **339**, 814 (2013);

DOI: 10.1126/science.1226850



T. Brodin,^{1*} J. Fick,² M. Jonsson,¹ J. Klaminder¹

Environmental pollution by pharmaceuticals is increasingly recognized as a major threat to aquatic ecosystems worldwide. A variety of pharmaceuticals enter waterways by way of treated wastewater effluents and remain biochemically active in aquatic systems. Several ecotoxicological studies have been done, but generally, little is known about the ecological effects of pharmaceuticals. Here we show that a benzodiazepine anxiolytic drug (oxazepam) alters behavior and feeding rate of wild European perch (*Perca fluviatilis*) at concentrations encountered in effluent-influenced surface waters. Individuals exposed to water with dilute drug concentrations (1.8 micrograms liter⁻¹) exhibited increased activity, reduced sociality, and higher feeding rate. As such, our results show that anxiolytic drugs in surface waters alter animal behaviors that are known to have ecological and evolutionary consequences.



UPUTA O LIJEKU:

„Neuobičajene nuspojave...koje mogu dovesti do agresivnog i socijalno neprihvatljivog ponašanja“

H A L M E D

21 - 12 - 2011

ODOBRENO

Transformation of Acetaminophen by Chlorination Produces the Toxicants 1,4-Benzoquinone and *N*-Acetyl-*p*-benzoquinone Imine

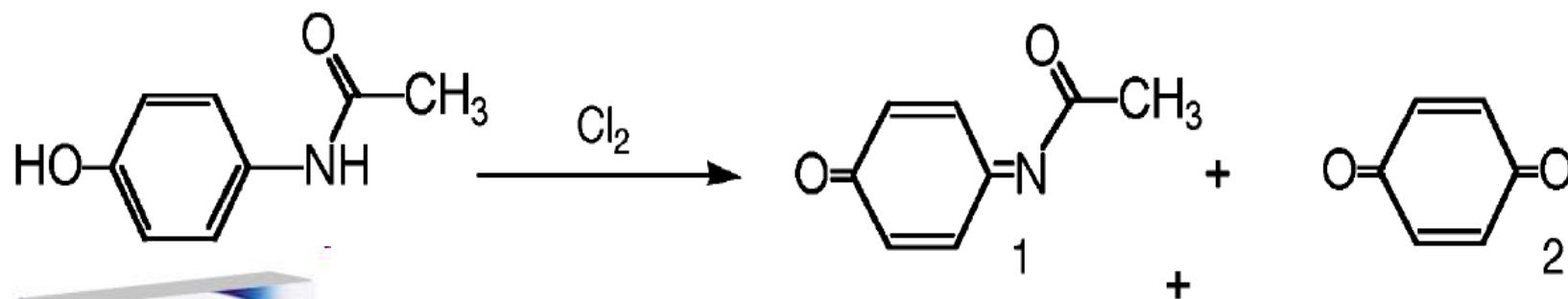
MARY BEDNER* AND
WILLIAM A. MACCREHAN

Analytical Chemistry Division, National Institute of
Standards and Technology, Mailstop 8392,
Gaithersburg, Maryland 20899-8392

CHART 1



liver microsomes oxidize acetaminophen to *N*-acetyl-*p*-benzoquinone imine (NAPQI; II), a toxic metabolite that results in hepatic necrosis (1). NAPQI, however, is known to be fairly unstable and readily hydrolyzes to the toxicant 1,4-benzoquinone (III) in aqueous solution (2). The wide use and potentially nefarious chemistry exhibited by acetaminophen render it an important pharmaceutical compound to investigate in the environment. Acetaminophen has



Five unidentified products

Methadone Contributes to *N*-Nitrosodimethylamine Formation in Surface Waters and Wastewaters during Chloramination

David Hanigan,^{*,†} E. Michael Thurman,[‡] Imma Ferrer,[‡] Yang Zhao,[§] Susan Andrews,[§] Jinwei Zhang,^{||} Pierre Herckes,^{||} and Paul Westerhoff[†]

[†]School of Sustainable Engineering and the Built Environment, Arizona State University, Box 3005, Tempe, Arizona 85287-3005, United States

[‡]Center for Environmental Mass Spectrometry, Department of Environmental Engineering, University of Colorado at Boulder, Boulder, Colorado 80309-0428, United States

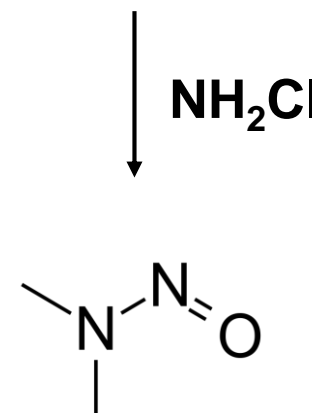
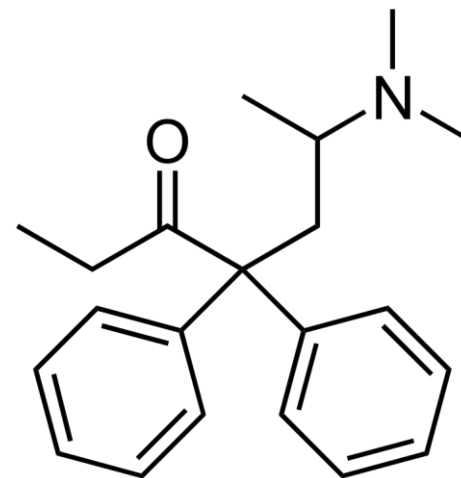
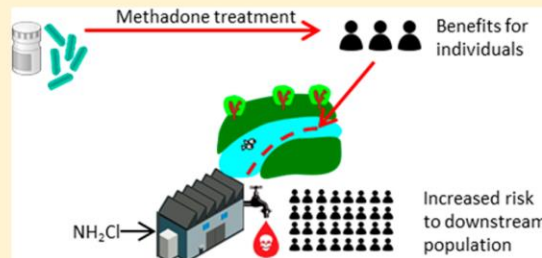
[§]Department of Civil Engineering, University of Toronto, 35 St. George Street, Toronto, ON, Canada M5S 1A4

^{||}Department of Chemistry and Biochemistry, Arizona State University, Tempe, Arizona 85287-1604, United States

S Supporting Information

ABSTRACT: *N*-Nitrosodimethylamine (NDMA) is a probable human carcinogen that forms in drinking water as a disinfection byproduct. Several specific precursor chemicals present during chloramination are known but cannot account for the total observed NDMA formation potential (FP) in drinking waters. We discovered a pharmaceutical precursor of NDMA with high FP using a liquid chromatography/quadrupole/time-of-flight mass spectrometry (LC/QTOF-MS) screening procedure. The pharmaceutical methadone, which is used to mitigate heroin withdrawal symptoms and is also prescribed for chronic pain, contains a dimethylisopropylamine functional group that reacts to

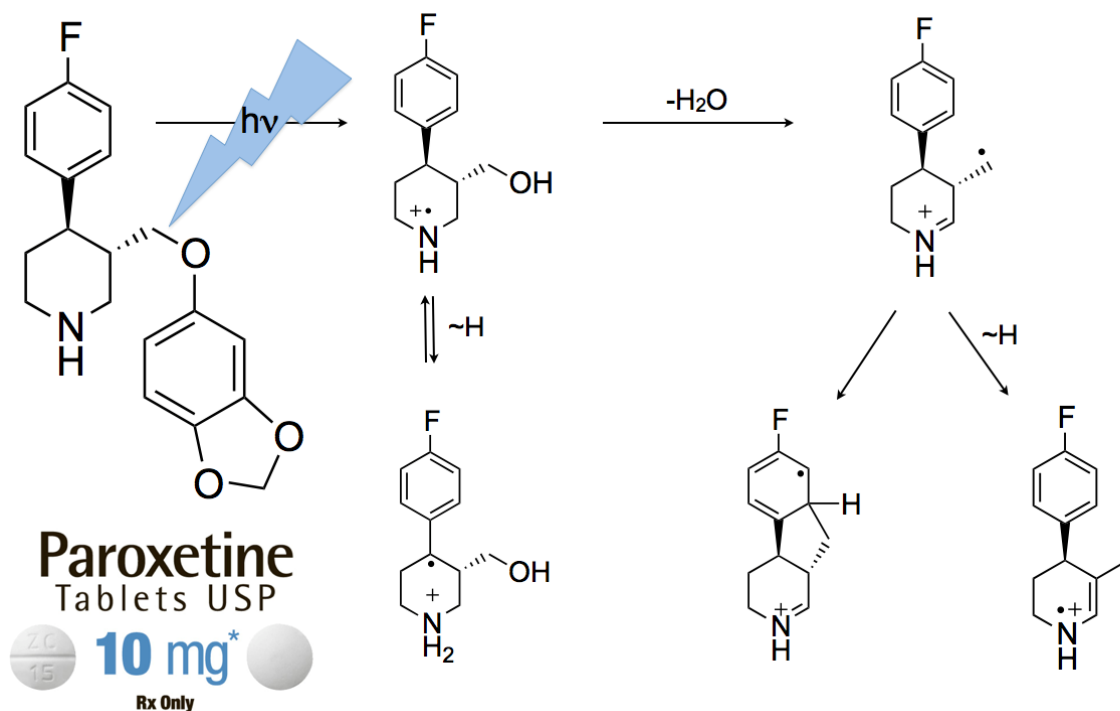
form large amounts of NDMA upon chloramination. In this study, methadone had a molar NDMA yield ranging from 23 to 70% depending on chloramine dose (1–150 mg of Cl₂/L) and was responsible for between 1 and 10% of NDMA FP in most raw surface waters in which it was detected and up to 62% of NDMA FP in wastewater. Samples with higher methadone concentrations had greater NDMA FP. We measured a median methadone concentration of 23 ng/L with a range of 1–2256 ng/L among detections, which was consistent with high occurrence rates and environmental persistence for methadone in the published literature for surface waters and wastewaters. A literature review of methadone use, metabolism, and fate in the United States resulted in a prediction of low nanogram per liter levels of methadone-associated NDMA FP at drinking water treatment plants (DWTPs) downstream of communities using methadone. Medicinal use of methadone potentially displaces and transforms the health risks associated with heroin use by individuals to possible cancer risk for populations served by downstream DWTPs. This work is among the first to contrast known public health benefits of pharmaceutical-taking patients against the potential exposure of millions of people to physiologically relevant levels of carcinogenic NDMA in chloraminated drinking water.



The chemical fate of paroxetine metabolites. Dehydration of radicals derived from 4-(4-fluorophenyl)-3-(hydroxymethyl)piperidinet†

Davor Šakić,^a Florian Achrainer,^b Valerije Vrčec^{*a} and Hendrik Zipse^b

Cite this: *Org. Biomol. Chem.*, 2013, **11**, 4232



Farmaceutski profil vode na izvoru Jadra

Samanta Šubić, Valerije Vrčec

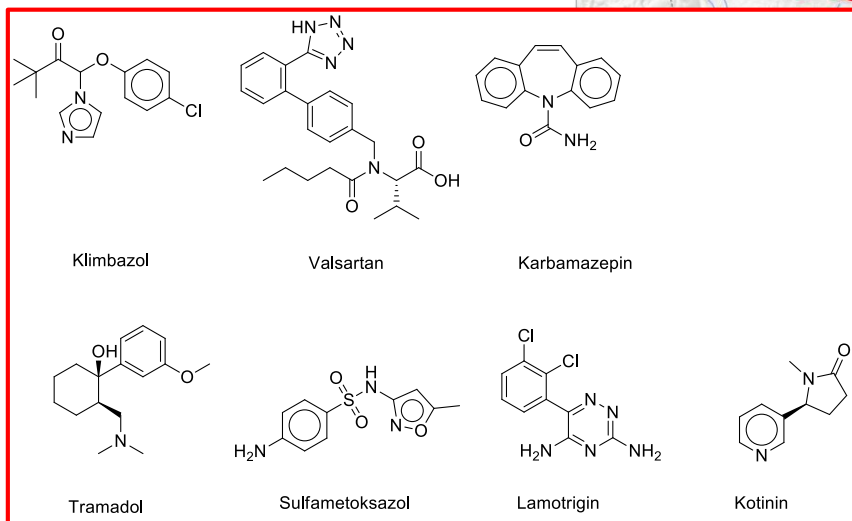
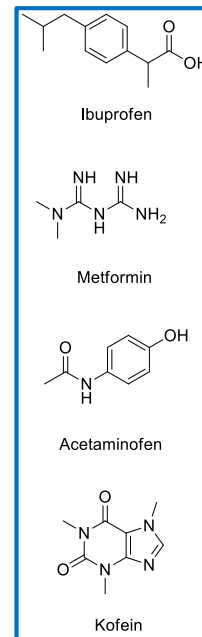
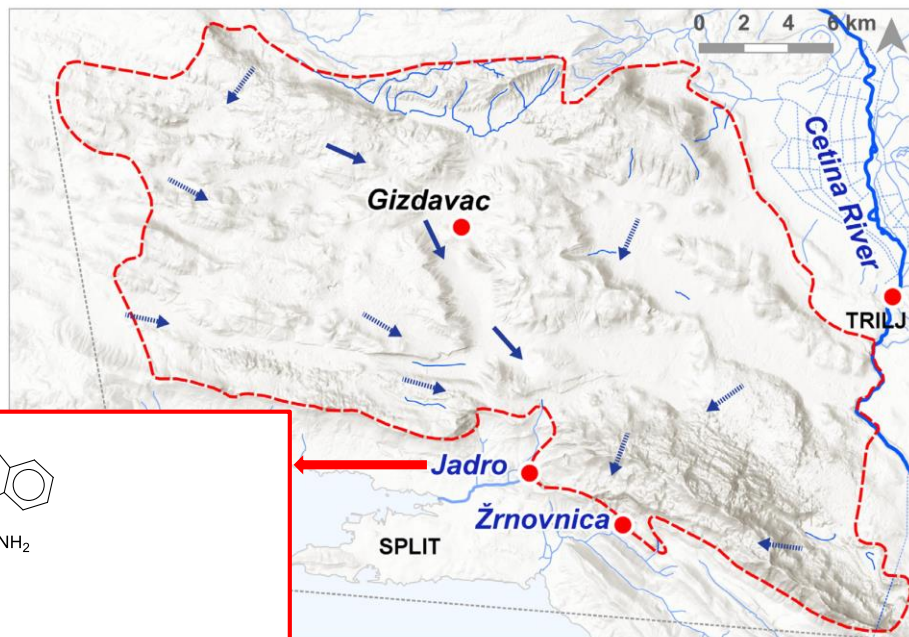


JAVNA TRIBINA

izvor jadra
naša voda

17/01/2023 @ FGAG

05. siječnja 2023.

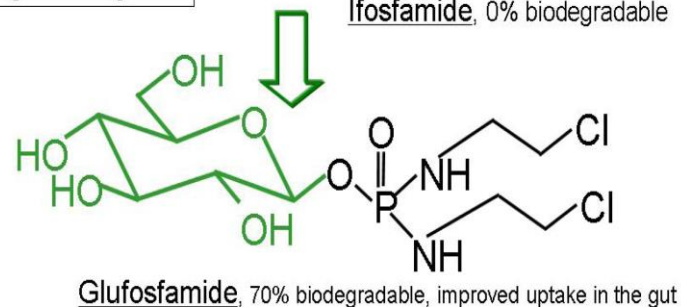
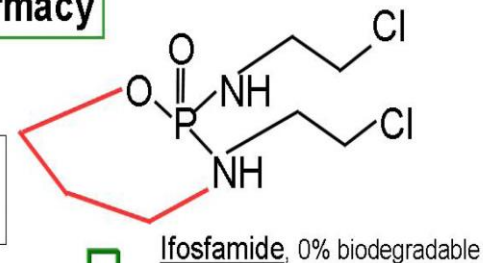


- Podzemni tokovi
- Mjesta uzorkovanja
- - - Područje sliva

Zelena farmacija –
dizajn lijekova istog
terapijskog, ali boljeg
ekotoksikološkog profila

Green Pharmacy

Example for the
Development of a
"green" drug



PERGAMON

Chemosphere 40 (2000) 767–773

CHEMOSPHERE

Biodegradability of antineoplastic compounds in screening tests: influence of glucosidation and of stereochemistry

K. Kümmerer^{a,*}, A. Al-Ahmad^a, B. Bertram^b, M. Wießler^b

^a *Institute of Environmental Medicine and Hospital Epidemiology, University Hospital University of Freiburg, Hugstetter Straße 55, D-79106, Freiburg, Germany*

^b *Deutsches Krebsforschungszentrum, Abt. Molekulare Toxikologie, Im Neuenheimer Feld 280, D-69 120, Heidelberg, Germany*

Postoje li zombi-lijekovi?

REPORT

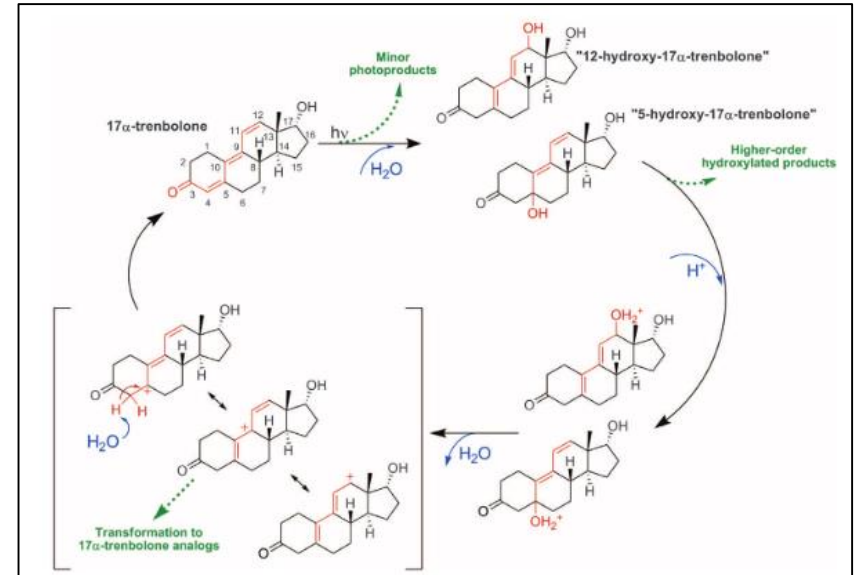
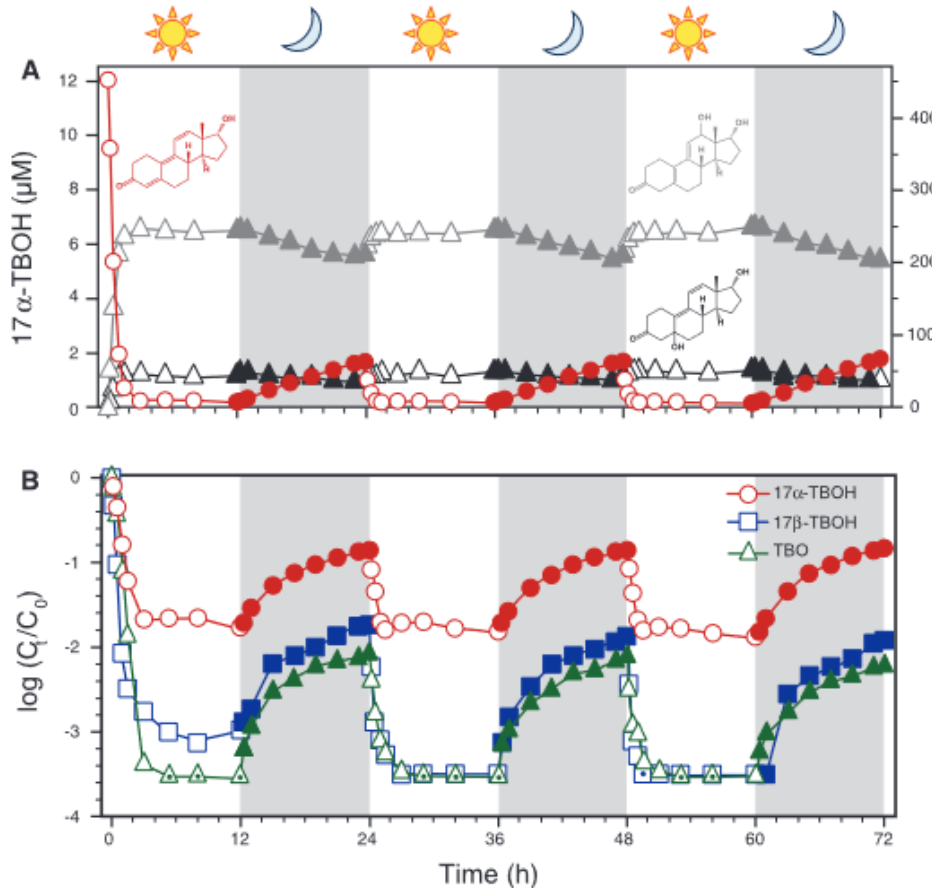


Product-to-Parent Reversion of Trenbolone: Unrecognized Risks for Endocrine Disruption

SHEN QU, EDWARD P. KOLODZIEJ, SARAH A. LONG, JAMES B. GLOER, ERIC V. PATTERSON, JONAS BALTRUSAITIS, GERRAD D. JONES, PETER V. BENCHETLER, EMILY A. COLE, [...]

AND DAVID M. CWIERTNY [+2 authors](#) [Authors Info & Affiliations](#)

SCIENCE • 26 Sep 2013 • Vol 342, Issue 6156 • pp. 347-351 • DOI: 10.1126/science.1243192



Irrigation of Root Vegetables with Treated Wastewater: Evaluating Uptake of Pharmaceuticals and the Associated Human Health Risks

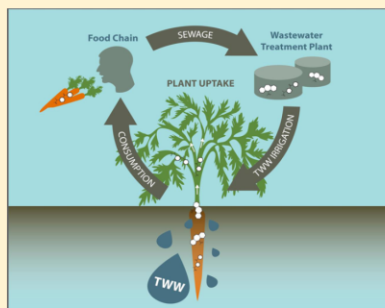
Tomer Malchi,^{†,‡} Yehoshua Maor,[‡] Galit Tadmor,^{†,‡} Moshe Shenker,[†] and Benny Chefetz^{*,†,‡}

[†]Department of Soil and Water Sciences, Faculty of Agriculture, Food and Environment, The Hebrew University of Jerusalem, Rehovot 76100, Israel

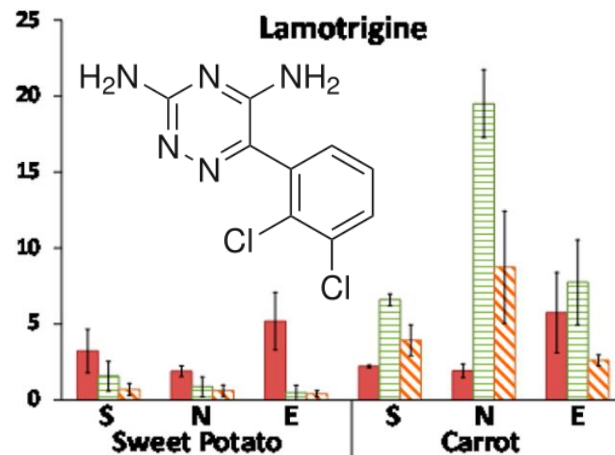
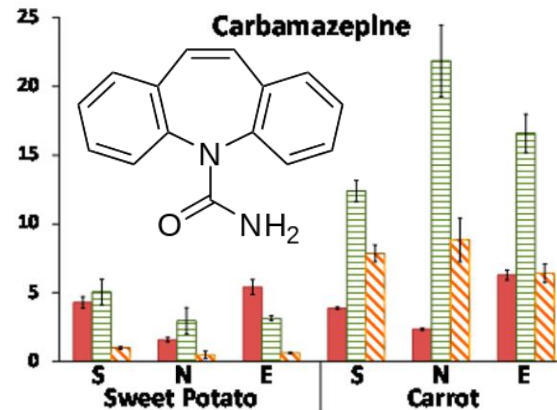
[‡]The Hebrew University Center of Excellence in Agriculture and Environmental Health, P.O. Box 12, Rehovot 76100, Israel

S Supporting Information

ABSTRACT: To meet mounting water demands, treated wastewater has become an important source of irrigation. Thus, contamination of treated wastewater by pharmaceutical compounds (PCs) and the fate of these compounds in the agricultural environment are of increasing concern. This field study aimed to quantify PC uptake by treated wastewater-irrigated root crops (carrots and sweet potatoes) grown in lysimeters and to evaluate potential risks. In both crops, the nonionic PCs (carbamazepine, caffeine, and lamotrigine) were detected at significantly higher concentrations than ionic PCs (metoprolol, bezafibrate, clofibrac acid, diclofenac, gemfibrozil, ibuprofen, ketoprofen, naproxen, sulfamethoxazole, and sildenafil). PCs in leaves were found at higher concentrations than in the roots. Carbamazepine metabolites were found mainly in the leaves, where the concentration of the metabolite 10,11-epoxycarbamazepine was significantly higher than the parent compound. The health risk associated with consumption of wastewater-irrigated root vegetables was estimated using the threshold of toxicological concern (TTC) approach. Our data show that the TTC value of lamotrigine can be reached for a child at a daily consumption of half a carrot (~60 g). This study highlights that certain PCs accumulated in edible organs at concentrations above the TTC value should be categorized as contaminants of emerging concern.



ng / g



Tko je dezinficirao vodu ?



Increased Use of Quaternary Ammonium Compounds during the SARS-CoV-2 Pandemic and Beyond: Consideration of Environmental Implications

Priya I. Hora, Sarah G. Pati, Patrick J. McNamara, and William A. Arnold*

Cite This: *Environ. Sci. Technol. Lett.* 2020, 7, 622–631

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ABSTRACT: Quaternary ammonium compounds (QACs) are active ingredients in over 200 disinfectants currently recommended by the U.S. EPA for use to inactivate the SARS-CoV-2 (COVID-19) virus. The amounts of these compounds used in household, workplace, and industry settings has very likely increased, and usage will continue to be elevated given the scope of the pandemic. QACs have been previously detected in wastewater, surface waters, and sediments, and effects on antibiotic resistance have been explored. Thus, it is important to assess potential environmental and engineering impacts of elevated QAC usage, which may include disruption of wastewater treatment unit operations, proliferation of antibiotic resistance, formation of nitrosamine disinfection byproducts, and impacts on biota in surface waters. The threat caused by COVID-19 is clear, and a reasonable response is elevated use of QACs to mitigate spread of infection. Exploration of potential effects, environmental fate, and technologies to minimize environmental releases of QACs, however, is warranted.



Disinfectants – as emergent (and pandemic) issue. Tenfold (“1000 %”) increase of production and consumption in the last two years.

Quats may: A. be transformed to carcinogenic nitroso compounds in water. B. induce antibiotic resistance in the environment



Lana Petrinec, mag. pharm.

Hvala na pažnji