

# Bulletin Board

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## Regulatory Update

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## ASIA PACIFIC

**Proposed Philippine bill targets single-use plastic waste**

2023-05-17

On May 7, 2023, the Editorial Board of the Manila Times published an editorial outlining concerns about the management of solid waste in the Philippines and encouraging Filipinos to "have more policy discussions on improving the management of solid wastes in the country." The Board brought up three measures already on the books in the Philippines: The Ecological Solid Waste Management Act of 2000, the Philippine Action Plan for Sustainable Consumption and Production, and the Extended Producer Responsibility (EPR) Act of 2022.

The Ecological Solid Waste Management Act is seen as deficient, as plastic waste continues to be a pervasive problem due to the lack of capacity of the nation's infrastructure. According to the World Bank, the Philippines generates 2.7 million tons of plastic waste annually, with an estimated 20% ending up in the ocean. The government's Action Plan for Sustainable Consumption and Production "is designed to promote sustainable practices and behaviors across sectors and throughout government" and the editorial board call for "an early review of how those plans can be implemented faster."

Meanwhile, the Extended Producer Responsibility Act of 2022, scheduled to go into effect later this year, is considered "a positive note." However, "the EPR law does not apply to 99.6 percent of registered firms, [the] micro, small, and medium enterprises" (FPF reported).

In April 2023, The Manila Bulletin reported that Paulo Duterte of the Philippines House of Representatives is still pushing to pass the single-use plastics bill he introduced on July 26, 2022. House Bill (HB) No.507 would "regulate the manufacture, sale, use, and importation of single-use plastic products... [as well as] the distribution, recovery, collection, recycling, and disposal." The bill would thus, "develop an integrated and comprehensive policy for plastic waste management," said Duterte. Further highlighting that while the House of Representatives has approved an excise tax on single-use plastic bags, HB 507 includes packaging, utensils, and other common single-use items.

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Read More

FPF, 17-05-23

<https://www.foodpackagingforum.org/news/proposed-philippine-bill-targets-single-use-plastic-waste>

### Philippines watchdog urges ban on PFAS

2023-05-23

In March 2022, EcoWaste Coalition, a civil society toxics watchdog in the Philippines, called on the nation's Environmental Management Bureau to implement a nationwide ban on per- and polyfluoroalkyl substances (PFAS). The reason is the "global contamination crisis linked to the largely unregulated production and use" of PFAS. EcoWaste specifically asked the Bureau to:

1. Add PFAS to the Philippines Priority Chemicals List.
2. Draft and issue a Chemical Control Order specifically for PFAS.
3. Support the global ban on the production and use of PFAS as a class.

EcoWaste highlighted multiple studies on the extensive presence of PFAS in the global environment (FPF reported) but particularly highlighted a 2022 study from the University of the Philippines Institute of Biology that detected elevated levels of PFAS in women with breast cancer living in the Greater Manila Area. The study additionally found that women from "a heavily industrialized region" had significantly higher levels of long-chain PFAS compared to other regions around Manila.

According to the press release, certain PFAS chemicals are listed in the Philippine Inventory of Chemical and Chemical Substances. However, there are no comprehensive regulations governing the thousands of PFAS compounds used in various consumer, commercial, and industrial products. PFAS and its derivatives are also not included in the Philippine "list of banned, restricted, severely restricted, and regulated chemicals as per the National Profile on Chemical Management prepared by the Department of Health and the University of the Philippines."

Read More

FPF, 16-05-23

<https://www.foodpackagingforum.org/news/philippines-watchdog-urges-ban-on-pfas>

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### Chinese Pesticide Registration Made Easy: A Step-by-Step Guide for Successful Registration

2023-05-19

Pesticides are essential substances used in agriculture and forestry to prevent or control the spread of diseases, insects, weeds, rodents, and other harmful organisms. They regulate plant growth and insect behavior, helping to maintain the integrity of crops and forests.

However, the use of pesticides also carries potential risks and hazards to human health and the environment. Therefore, China implements a rigorous pesticide registration management system. Under the Regulation on the Administration of Pesticide, all pesticides are required to be registered before they can be produced, sold, or used.

To help companies navigate the complex and demanding process of pesticide registration in China, REACH24H launched a step-by-step guide for successful pesticide registration in China. This guide aims to address three main questions:

- What are the requirements for applicants?
- Before applying for pesticide registration, what preparations are required?
- What is the application process?

The registration process is divided into five stages, with detailed breakdowns and summaries of key points and strategies for each stage.

#### Stage 1: Applicant Qualification Review

Overseas companies that produce pesticides and export to China must have a domestic office or a qualified agency to assist with the application. This requirement is essential to ensure that companies comply with China's pesticide registration laws and regulations.

Read More

REACH24H, 19-05-23

<https://www.reach24h.com/en/news/industry-news/agrochemical/chinese-pesticide-registration-guide.html>

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### AMERICA

#### EPA Opens Public Comment on Draft Guidance for Pesticide Application Submissions that Require Endangered Species Act Reviews

2023-05-18

The U.S. Environmental Protection Agency (EPA) is seeking public comment on draft guidance to improve the efficiency of EPA's Endangered Species Act (ESA) analyses for new pesticide active ingredient applications and active ingredients undergoing registration review. This guidance, when finalized, fulfills requirements outlined in the Pesticide Registration Improvement Act of 2022 (PRIA 5) and furthers goals outlined in EPA's 2022 ESA Workplan to protect listed species from exposure to pesticides.

Among other requirements, PRIA 5 mandates that EPA develop and issue guidance to registrants regarding analyses necessary to support the evaluation of potential adverse effects from outdoor uses of pesticide products on listed species and designated critical habitat. PRIA 5 specifies that the draft guidance be available for public comment and be finalized within nine months of PRIA 5 issuance.

The draft guidance applies to:

- New conventional pesticides and biopesticides that are intended for outdoor use; and
- Existing conventional pesticides and biopesticides that are intended for outdoor use that are being reevaluated under registration review.

Although this document does not create new requirements for applicants, the recommendations in the guidance will help applicants address potential effects to listed species for new active ingredients and registration review actions. In particular, the recommendations focus on actions that applicants can voluntarily pursue to inform their proposed mitigation measures for listed species. These actions include identifying where a pesticide will be used, how species may be exposed to the pesticide, and how to select mitigation to reduce the exposure. If followed, these recommendations should expedite the FIFRA action and improve the efficiency of the overall ESA-FIFRA process.

Guidance for new uses of existing active ingredients will be made available at a later date.

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The draft guidance, which incorporates lessons EPA has learned over the past several years as it has worked to implement EPA's ESA workplan, is available for public comment in docket EPA-HQ-OPP-2023-0281 at [www.regulations.gov](http://www.regulations.gov) for 30 days.

Read More

EPA, 18-05-23

EPA-HQ-OPP-2023-0281

#### How the "Halliburton Loophole" lets fracking companies pollute water with no oversight

2023-05-18

Fracking companies used more than 282 million pounds of hazardous chemicals from 2014 to 2021 with no federal oversight, according to a new study.

The study, published in *Environmental Pollution*, is the first to examine the "Halliburton Loophole," which exempts fracking from federal regulation under the Safe Drinking Water Act.

The provision, passed by Congress as part of the Energy Policy Act of 2005, was endorsed by then-Vice President Dick Cheney, who formerly served as the CEO of Halliburton. The company patented fracking technologies in the 1940s and is still one of the top suppliers of fracking fluids in the world.

The study found that from 2014 through 2021, 62% to 73% of reported fracking jobs each year used at least one chemical that's categorized as harmful to human health and the environment under the Safe Drinking Water Act.

These chemicals include carcinogens like formaldehyde, arsenic and benzene; possible carcinogens like acrylamide and naphthalene; and ethylene glycol, which can damage the kidneys, nerves and respiratory system.

Read More

EHN, 18-05-23

<https://www.ehn.org/halliburton-loophole-2659983182.html>

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MAY. 26, 2023

### How did nonstick “forever chemicals” get into our food? Blame pesticides

2023-05-16

Pesticides have come under increased scrutiny in recent years. From the discovery that the herbicide glyphosate is in 80 percent of Americans’ urine to concerns that weedkillers’ neonicotinoids in pesticides are killing off bees, scientists keep amassing alarming information about the products ostensibly intended to protect our food. Now a recent study by a nonprofit focused on protecting the environment reveals a new problem with pesticides: They are filled with forever chemicals, a class of compound that is typically used in nonstick and waterproof surfaces. These chemicals aren’t used as pesticides and shouldn’t be in them, a fact which at first puzzled scientists who discovered the contamination.

The findings come courtesy of the Center for Biological Diversity in their March report on the most widely used pesticides in the United States. The authors find that “dangerous” PFAS (per- and polyfluoroalkyl substances) that are linked to cancer, kidney disease, high blood pressure, thyroid disease, autoimmune disease, birth defects and other serious health problems — even when people are only exposed at low levels.

PFAS are popularly known as “forever chemicals” because they never organically degrade, meaning once in the environment they linger there permanently. The authors of the report express concern that, because these PFAS were found in three out of the seven most commonly used pesticides, they could be covering our food and leaching into our water supply.

Read More

Sallon, 16-05-23

<https://www.salon.com/2023/05/16/how-did-nonstick-forever-chemicals-get-into-our-food-pesticides/>

### New York’s New Environmental Justice Law

2023-05-18

Unless amended or carefully implemented, there’s a risk the law could hurt the communities it’s meant to serve.

New York has enacted what may be the country’s most stringent environmental justice law. The state deserves credit for its commitment to remedying the unfair pollution burdens placed on disadvantaged

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communities. The law is so broadly worded, however, that it may have the potential to prevent economic development that would aid those communities, or even new facilities like hospitals that are urgently needed by the community. It might also impede New York’s clean energy program, including its effort to direct green spending to disadvantaged communities.

This language is the core of the New York law:

“The department shall not issue an applicable permit for a new project if it determines that the project will cause or contribute more than a de minimis amount of pollution to a disproportionate pollution burden on the disadvantaged community.”

There are also provisions that require more extensive environmental study if a facility “may” cross over the de minimis level. (“De minimis” is lawyerese for “trivial”).

One thing to note is that the trigger is whether the facility would cause pollution in a disadvantaged community, not whether it is located there. So any ban on new air pollution sources would apply not in the community but upwind.

Why might this provision be a problem: Consider a disadvantaged community that has disproportionate air pollution and also lacks good access to a hospital. If read strictly, the provision might prohibit putting a new hospital in or near the community. Hospitals generate vehicle traffic from patients, staff, supply delivery, ambulances, and visitors. That traffic would add to local air pollution.

Read More

Legal Planet, 18-05-23

<https://legal-planet.org/2023/05/18/new-yorks-new-environmental-justice-law/>

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### EUROPE

#### EFSA seeks data on plasticizers in food contact materials

2023-05-18

On May 5, 2023, the European Food Safety Authority (EFSA) opened another round of data collection on phthalates and structurally similar substances used as plasticizers in food contact materials (FCMs). A previous input round ran from June to November 2022 (FPF reported). The initiative is part of a European Commission mandate that requires EFSA to re-evaluate these substances and assess the migration data in the context of dietary exposure.

National food authorities, research institutions, academia, food business operators, and other stakeholders are invited to submit data on the migration, occurrence, and/or quantities of plasticizers, such as phthalates, terephthalates, citrates, and benzoates, in FCMs. EFSA aims to gather results generated from experimental studies on FCMs before their actual use, including migration test using food simulants.

The list of substances identified as potential plasticizers and considered within this call for data is provided. Stakeholders interested in submitting data are requested to contact EFSA, preferably by June 30th, 2023. The deadline for submission is August 31st, 2023.

Read More

FPF, 18-05-23

<https://www.foodpackagingforum.org/news/efsa-seeks-data-on-plasticizers-in-food-contact-materials>

#### Schedule of retained EU law

2023-05-17

Schedule of retained EU Law that will be revoked or sunset by 31 December 2023.

Retained EU law (REUL) was established by The European Union (Withdrawal) Act 2018 to ensure legal certainty and continuity immediately after Brexit, by preserving all EU and EU-derived law as it stood immediately before the UK's departure. However, retained EU law was never intended to sit on the statute book indefinitely.

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The Retained EU Law (Revocation and Reform) Bill allows the United Kingdom to take the next step in reasserting the sovereignty of Parliament. It will end the special status of retained EU law in the UK statute book and will enable retained EU law to be more easily amended, revoked and replaced.

On 10 May an amendment was tabled to replace the current sunset in the Bill with a list of the retained EU laws that we intend to revoke under the Bill at the end of 2023.

The list covers each piece of legislation being revoked and the reason it is being removed from the statute book at the end of 2023. It includes a significant amount of REUL that is defunct and unnecessary now we have left the EU. This is an efficient way of removing such legacy regulation from our statute book and represents good lawmaking.

The schedule removes items of REUL that are burdensome and duplicative. For example, we will be removing some items of REUL relating to the National Air Pollution Control Plan (NAPCP). The current format of the NAPCP is long, complicated, resource intensive and duplicative, and does nothing to improve the quality of the air we breathe. By revoking this item, we can better focus on what will actually help clean up our air, such as by delivering on the ambitious air quality targets we have set in statute through the Environmental Act.

The schedule also includes some REUL which we can now remove which had been designed in a way which was clearly contrary to the needs and requirements of the UK. For example, The Port Services Regulations set out reporting and consultation requirements designed for the largely publicly owned EU ports sector, which place unnecessary burdens on the predominantly private-sector UK port operators.

The government has already revoked or reformed over 1,000 EU laws since our exit. In addition to the list of around 600 we propose to revoke directly through the schedule to the REUL Bill, the Financial Services and Markets Bill and the Procurement Bill will revoke around a further 500 pieces of REUL.

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We are committed to lightening the regulatory burden on businesses and helping to spur economic growth, and our Edinburgh Reforms of UK financial services include over 30 regulatory reforms to unlock investment and boost growth in towns and cities across the UK.

Read More

Gov.uk, 17-05-23

<https://www.gov.uk/government/publications/schedule-of-retained-eu-law>

## INTERNATIONAL

### The Daunting Task of Cutting Heavy Metals from Baby Food

2023-05-15

RICE CEREAL IS a staple in many American babies' diets and is often the first solid food an infant eats. In recent years, however, it has also become one of many baby foods that has been raising alarm among lawmakers and parents.

Most cultivated rice grows submerged in paddy fields, primarily in South and Southeast Asia, although it is also grown in the United States and many other countries. These flooded fields provide a cool, fertile environment for a healthy crop, but that same environment also allows contamination from toxic heavy metals, including arsenic, cadmium, lead, and mercury.

At least some heavy metals appear to harm brain development and cognition; and have also been linked to ailments including lung disease, kidney disease, skin lesions, and cancer. Heavy metal exposure is especially dangerous for infants because, compared to adults, they eat more food relative to their body weight and their diet is less varied. Babies are also particularly sensitive to the toxic effects of heavy metals because their bodies are still developing.

In February 2021, the U.S. House Oversight and Reform Subcommittee on Economic and Consumer Policy released a report on heavy metals in baby food produced by several of the country's largest manufacturers. The 59-page document ended with a call for immediate action from the Food and Drug Administration. Two months later, the FDA announced the Closer to Zero initiative, which uses an iterative approach to reduce heavy metal

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exposure among babies and children. The FDA issued draft guidance on lead in fruit and vegetable juice in April 2022 and in baby food more broadly in January 2023. Action plans for arsenic, cadmium, and mercury aren't scheduled to be completed until 2024 at the earliest.

In the meantime, botanists, soil chemists, and plant geneticists — who have long worked to reduce heavy metals in the food supply — continue to look for potential solutions, from new land management practices to nano-sized fertilizers to genetic engineering. Not all of these technologies are available yet; however, even when they are, eliminating heavy metals entirely won't be easy.

Read More

Undark, 15-05-23

<https://undark.org/2023/05/15/the-daunting-task-of-cutting-heavy-metals-from-baby-food/>

### End plastic pollution: towards an international legally binding instrument

2023-03-07

Noting with concern that the high and rapidly increasing levels of plastic pollution represent a serious environmental problem at a global scale, negatively impacting the environmental, social and economic dimensions of sustainable development, Recognizing that plastic pollution includes microplastics, Noting with concern the specific impact of plastic pollution on the marine environment, Noting that plastic pollution, in marine and other environments, can be of a transboundary nature and needs to be tackled, together with its impacts, through a full-life-cycle approach, taking into account national circumstances and capabilities, Reaffirming General Assembly resolution 70/1 of 25 September 2015, by which the General Assembly adopted the 2030 Agenda for Sustainable Development, Reaffirming also the principles of the Rio Declaration on Environment and Development, adopted in Rio de Janeiro, Brazil, in 1992, Stressing the urgent need to strengthen the science-policy interface at all levels, improve understanding of the global impact of plastic pollution on the environment, and promote effective and progressive action at the local, regional and global levels, recognizing the important role played by plastics in society, Recalling United Nations Environment Assembly resolutions 1/6, 2/11, 3/7, 4/6, 4/7 and 4/9\* and affirming the urgent need to strengthen global coordination, cooperation and governance to take

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## REACH Update

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### EFPIA and ECHA publish more data to help developing alternative methods to animal tests

2023-05-17

Additional information about the hazard properties of 75 substances from 370 tests has recently been published as IUCLID datasets. This more than doubles the amount of data that was made initially available for the scientific community developing alternative test methods when the joint initiative kicked off a year ago.

Helsinki, 17 May 2023 – A pilot project led by the European Federation of Pharmaceutical Industries and Associations (EFPIA), and supported by ECHA, has made an updated set of archived data from unpublished chemical tests available on the IUCLID website. The database contains now altogether information about the hazard properties of 94 substances from 517 tests. This follows the project's initial delivery of data one year ago.

This data can help, for example, to develop predictive computational testing models, read across and other alternative test methods with the objective to decrease the reliance on animal testing. The following table gives an overview of the number and type of studies by endpoint groups.

[Read More](#)

ECHA, 17-05-23

<https://echa.europa.eu/-/efpia-and-echa-publish-more-data-to-help-developing-alternative-methods-to-animal-tests>

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## Janet's Corner

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### FanTheories

2023-05-26



HOW TO ANNOY SCIENTISTS: REFER TO ALL HYPOTHESES AS "FAN THEORIES"

<https://xkcd.com/2683/>



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## Hazard Alert

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### Acetic Acid

2023-05-26

#### USES [4,5]

Acetic acid is the main ingredient in vinegar; the condiment contains between 3-9% acetic acid. The acid is also used as a food additive (aka E260), for flavour and as an acidity regulator. It is used to make polyvinyl and cellulose acetate. Large quantities of the acid are used to make ink for dyes, pharmaceuticals, photographic chemicals, rubber and plastics. It is also used in some household cleaning products.

#### ROUTES OF EXPOSURE [6]

Routes of exposure include inhalation and skin/eye contact.

#### HEALTH EFFECTS

Acetic acid poisoning affects a range of systems, including the integumentary and respiratory systems.

#### Acute Effects [7]

Severity of symptoms depend on the level and type of exposure.

Inhalation of the acid may result in irritation of the respiratory tract, resulting in coughing, mucous membrane damage and choking. It could also cause dizziness, headaches, weakness, nausea and pulmonary oedema. It may cause transient loss of voice. Ingestion of the acid may result in burns on the mucous membranes of the throat, mouth and oesophagus. It may also cause nausea, vomiting, diarrhoea, shock (including clammy skin and shallow breathing), convulsions or a coma. Skin and eye contact could result in pain and burns, which may heal at a slow pace. Direct eye contact with the acid may result in lachrymation, burns and photophobia. Severe burns could result in permanent damage, but milder burns tend to heal quickly.

#### Chronic Effects [7]

Chronic exposure to acetic acid is toxic to multiple body systems. Long term exposure to the acid can result in erosion of the teeth, ulcerative changes in the mouth, bronchial irritation (including a cough and frequent bouts of bronchial pneumonia), and gastrointestinal disturbances. Chronic exposure to the acid can also result in systemic breathing problems,

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blackening of the skin and teeth, nausea, vomiting, diarrhoea, and chronic respiratory inflammation.

#### SAFETY

##### First Aid Measures [7]

**Ingestion:** DO NOT induce vomiting. Move patient into recovery position. If the person is conscious (and not showing any signs of drowsiness), then you can give them water to rinse their mouth. Contact a medical professional immediately.

**Skin contact:** Remove all contaminated clothing, footwear and accessories. Do not re-wear clothing until it has been thoroughly decontaminated. Immediately rinse affected areas with plenty of soap and water. Contact a doctor immediately.

**Eye contact:** Flush eyes (including under the eyelids), with fresh running water for at least 15 minutes. Removal of contact lenses should only be done by skilled personnel. Contact a medical professional immediately.

**Inhalation:** If the person inhales fumes, combustion products or aerosols, remove them from the contaminated site. Prostheses, such as false teeth, should be removed prior to first aid procedures, as they may block airways. Perform CPR if you are qualified and if the patient is unconscious and not breathing. Use a one-way valve and mask if possible. Immediately contact a medical professional.

**General:** Never administer anything by mouth to an unconscious, exposed person.

##### Exposure Controls/Personal Protection [7]

**Engineering controls:** Emergency eyewash fountains and quick-drench areas should be accessible in the immediate area of the potential exposure. Ensure there is adequate ventilation.

**Personal protection:** Safety glasses with side shields or chemical goggles, protective and dustproof clothing, gloves (do not wear polyethylene gloves; wear elbow length PVC gloves), a P.V.C apron and an appropriate mask or dusk respirator. Do not wear contact lenses as they could absorb chemicals in the air. Wear impervious shoes. Other protection could overalls. For specifications regarding other PPE, follow the guidelines set in your jurisdiction.

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### REGULATION [6]

#### United States:

The National Institute for Occupational Safety and Health (NIOSH) has set a Time Weighted Average (TWA) concentration limit for acetic acid of 10ppm.

#### Australia [7]

Australia Exposure Standards have set a TWA for acetic acid of 10ppm.

### REFERENCES

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<https://www.cdc.gov/niosh/npg/npgd0002.html>

# Bulletin Board

## Gossip

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### Some Doctors Still Aren't Cool with Medical Cannabis

2023-05-22

"We still have a real separation between the medicinal use of cannabis and mainstream health care, and that creates risks and problems," says Daniel Kruger, a research investigator at the University of Michigan Institute for Social Research. "We need to have better integration to promote health, both for individuals and society."

Kruger and colleagues surveyed more than 1,500 Michigan physicians in a university-affiliated health care system. The doctors answered a series of questions via an anonymous online survey, recording their responses on a five-option scale. Their findings appear in the journal Cannabis and Cannabinoid Research.

The study was created in response to rapidly changing conditions surrounding the legalization and use of medical cannabis throughout the United States.

"Most Americans have lived under cannabis prohibition for most of their lives, and we've seen a very rapid transition from cannabis being something that's considered illegal and a substance of abuse to millions of Americans having access to cannabis legally and millions of Americans using cannabis to treat all sorts of different health or medical conditions," Kruger says.

The widespread use has created conflict between patients and doctors, particularly when it comes to information about how and when medical cannabis should be used, Kruger says. While information is plentiful on the internet, among family connections, and even from those legally selling medical and recreational cannabis, doctors often have little formal training or educational background concerning the drug.

There have also been very few formal studies on its effects and use cases, which often results in doctors deciding not to authorize medical cannabis use for their patients, he says.

Only about a third of physicians in the study had recommended medical cannabis to a patient and just 10% had signed an authorization form. Kruger believes a lack of education on the drug and its effects is a significant contributing factor to those rates.

"Most doctors and other health professionals were trained in the 'prohibition era,' the war on drugs, and so on," he says. "They got the

**Although cannabis is legal in Michigan, doctors in the state are hesitant to authorize their patients to use it, a study finds.**

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same kind of messages, many of which people consider to be false about cannabis being a gateway drug and having no benefits.”

Under those circumstances, many physicians default to federal guidelines that still classify medical cannabis as a Schedule 1 controlled substance, which in turn leads to people using cannabis medicinally on their own, with limited or nonexistent guidance from their doctors.

But that could be changing. Kruger believes the study could precede a shift in how doctors think about and recommend medical cannabis.

“Most, if not all, of the previous surveys of physicians have basically been attitude surveys,” he says. “Generally, they found that people overall did not support it. But this is the first study to actually go in depth and get into the actual specific behaviors of doctors and patients and the patient/physician interaction.”

The study was funded the University of Michigan Medical School. Additional coauthors are from the University at Michigan and the University at Buffalo.

Futurity, 22 May 2023

<https://futurity.org>

### Patients are Split on Getting Health Care from Artificial Intelligence

2023-05-22

Artificial intelligence-powered medical treatment options are on the rise and have the potential to improve diagnostic accuracy.

The findings in PLOS Digital Health, however, show that most patients aren't convinced the diagnoses provided by AI are as trustworthy as those delivered by human medical professionals.

“While many patients appear resistant to the use of AI, accuracy of information, nudges, and a listening patient experience may help increase acceptance,” says Marvin J. Slepian, professor of medicine at the University of Arizona College of Medicine-Tucson, of the study's other primary finding: that a human touch can help clinical practices use AI to their advantage and earn patients' trust.

**About 52% of participants in a new study would choose a human doctor rather than AI for diagnosis and treatment.**

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“To ensure that the benefits of AI are secured in clinical practice, future research on best methods of physician incorporation and patient decision making is required.”

For the study, the researchers placed participants into scenarios as mock patients and asked whether they would prefer to have an AI system or a physical doctor for diagnosis and treatment, and under what circumstances.

In the first phase, the researchers conducted structured interviews with actual patients, testing their reactions to current and future AI technologies. In the second phase of the study, the researchers polled 2,472 participants across diverse ethnic, racial, and socioeconomic groups using a blinded, randomized survey that tested eight variables.

Overall, participants were almost evenly split, with more than 52% choosing human doctors as a preference versus approximately 47% choosing an AI diagnostic method. If study participants were prompted that their primary care physicians felt AI was superior and helpful as an adjunct to diagnosis or otherwise nudged to consider AI as good, the acceptance of AI by study participants on re-questioning increased. This signaled the significance of the human physician in guiding a patient's decision.

Disease severity—leukemia versus sleep apnea—did not affect participants' trust in AI. Compared to white participants, Black participants selected AI less often and Native Americans selected it more often. Older participants were less likely to choose AI, as were those who self-identified as politically conservative or viewed religion as important.

The racial, ethnic, and social disparities identified suggest that differing groups will warrant specific sensitivity and attention as to informing them as to the value and utility of AI to enhance diagnoses.

“I really feel this study has the import for national reach. It will guide many future studies and clinical translational decisions even now,” Slepian says. “The onus will be on physicians and others in health care to ensure that information that resides in AI systems is accurate, and to continue to maintain and enhance the accuracy of AI systems as they will play an increasing role in the future of health care.”

Additional coauthors are from the University of Texas at Arlington, the James E. Rogers College of Law, the University of Utah, and the University of Arizona.

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The National Institutes of Health funded the study.

Futurity, 22 May 2023

<https://futura.org>

### New Antibiotic May Soon Treat Scary 'Abc' Pneumonia

2023-05-22

The findings have led a unanimous expert committee to recommend that the Food and Drug Administration (FDA) approve the new drug, which could be available this summer to combat the often-fatal pneumonia strain known as carbapenem-resistant *Acinetobacter baumannii*-calcoaceticus complex (ABC), typically acquired in hospitals.

"Antibiotic-resistant infections are a serious and persistent problem at healthcare facilities, and the [Centers for Disease Control] ranks ABC at the highest level on its threat list," says Keith Kaye, chief of the Division of Allergy, Immunology, and Infectious Disease at Robert Wood Johnson Medical School and first author of the trial report in *The Lancet Infectious Diseases*.

"An estimated 8,500 hospital-acquired cases killed 700 patients and cost \$280 million in 2019, so we greatly needed a breakthrough treatment like sulbactam-durlobactam."

The trial gave imipenem-cilastatin to 181 patients with laboratory-confirmed ABC and then randomized them to additional treatment with either sulbactam-durlobactam or the best existing treatment, an antibiotic called colistin. Mortality due to multiple causes after 28 days was 12 of 63 (19%) in the sulbactam-durlobactam group and 20 of 62 (32%) in the colistin group.

The trial was large enough to prove that sulbactam-durlobactam prevents at least as many fatalities as colistin, but not large enough to prove its superiority in this trial will persist in real-world use, though it may.

The trial results do prove that sulbactam-durlobactam beats colistin in one crucial respect: tolerability. Kidney injury, serious adverse events, and all treatment-related adverse events were significantly lower for patients who received sulbactam-durlobactam than for patients who received colistin.

Another advantage of the novel antibiotic is dosing. All patients receive the same injectable dose of sulbactam-durlobactam. Doses of colistin in the study, on the other hand, varied with patient weight, so it's

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considerably easier for providers to prescribe or administer the wrong amount.

As its name implies, sulbactam-durlobactam combines two drugs. Sulbactam has been approved for use since 1986, but durlobactam is new and has yet to win approval. That could change soon, however. The FDA's Antimicrobial Drugs Advisory Committee reviewed advance results of the new trial, along with earlier studies, and recommended on April 17 that the FDA approve the new combination for ABC treatment.

FDA officials are free to reject such recommendations but almost always follow recommendations from advisory committees, which comprise independent experts on particular classes of disease and medication.

"If all moves quickly, infected patients could begin receiving sulbactam-durlobactam as part of normal clinical care the second half of this year," Kaye says. "Unfortunately, sulbactam-durlobactam isn't the sort of wide-spectrum antibiotic that could prove effective in treating a wide variety of antibiotic-resistant infections, but it's very good at treating this particularly dangerous one, and that's a significant win."

Futurity, 22 May 2023

<https://futura.org>

### Illegal, occasionally deadly, and not much fun. What is the frog toxin Kambô and why do people use it?

2023-05-16

In the past decade, Kambô use has also been on the rise in neo-shamanic or complementary medicine in Western countries. Many users say they experience positive after-effects, but bad outcomes ranging from prolonged vomiting to seizures and even death have also been reported.

In Brazil, it's illegal to sell or market Kambô. In Australia, where two deaths after Kambô rituals have led to coronial inquests, it was listed by the Therapeutic Goods Administration in 2021 as a Schedule 10 poison: "a substance of such danger to health as to warrant prohibition of sale, supply and use".

Despite government bans and several fatalities, Kambô use in Western countries still seems to be going strong. So what does Kambô do, and what do users get out of it?

**Kambô is an oozy substance harvested from the defensive skin secretions of the Amazonian giant monkey tree frog. In the traditional medicine of some indigenous peoples of the Amazon, Kambô is applied to superficial burns on the skin of participants to produce an intense purging effect.**

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### The Kambô ritual

Kambô comes from the giant monkey tree frog (*Phyllomedusa bicolor*) which lives in the Upper Amazon rainforest. The frogs are captured and their limbs are tied with thread to four vertical twigs, to enable harvesting of their secretions by gentle scraping. The frogs are then released, physically unharmed.

The clear mucus-like secretion is typically spread onto bamboo sticks and air-dried for storage and transport. The Kambô is then prepared by reconstituting with water before application.

Kambô contains a range of biologically active molecules that most likely provide the frogs with defences against predators.

To harvest Kambô, the defensive secretions of the frog are scraped off before the frog is released, unharmed. Shutterstock

In the ritual, superficial burns are first made on the recipient's skin, then Kambô is applied to the burns using a short length of rainforest vine. Next, the thick red sap of the "dragon's blood" tree (*Croton lechleri*) is applied to the burns as an antiseptic.

Traditionally, among the indigenous Amazonian tribes that use Kambô, there is virtually no ceremony involved. It plays more of a role in their traditional medicine and hunting practices than in informing their cosmology.

In Kambô rituals catering to Westerners, the practice is often carried out in a ceremony involving songs, musical instruments, burning of incense, and prayers.

Traditionally, three to five small burns are made with a smouldering stick on the upper arm or lower leg of the recipient.

In Western neo-shamanic practice, however, Kambô is often applied to a larger number of burns. The burns may be located elsewhere on the body, including the neck, upper back, chest, and the Yogic chakra locations.

### What Kambô does to the body?

Following introduction via the small burns, the active ingredients of the Kambô pass rapidly into the body. They move through the lymphatic system – essentially the body's drainage system, running parallel to the blood circulatory system – and thence into the bloodstream.

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As a result, participants experience a short, intense purgative experience. The physiological effects are complex, rapid and sometimes paradoxical.

Typically, the first symptoms reported are an initial rush of heat and redness of the face. Nausea and vomiting are often experienced within several minutes, accompanied by general malaise, racing heart, dizziness and swelling of the face, and sometimes an urge to defecate.

A photo of a person's shoulder with four dark dots on a patch of reddened skin.

Kambô is typically applied to superficial burns, which are then covered with an antiseptic sap. Shutterstock

Further effects include the feeling of a lump in the throat or difficulty swallowing, abdominal pain, nausea, vomiting, diarrhoea, runny nose and tears, swollen lips, eyelids or face, and occasionally a swollen tongue or throat.

These physiological effects are generally expected, and indeed sought, by those performing and undergoing the Kambô ritual.

Aside from the range of physiological effects discussed above, Kambô is not regarded as exerting any direct psychedelic or hallucinogenic effects. Nor is it known to be used by anyone for this purpose.

### What can go wrong?

The duration of the physical effects is usually 15–30 minutes. However, individual responses vary considerably and, on occasion, the symptoms may last several hours.

Kambô has caused harm in only a very limited number of documented cases, although the documented harms have included death. A handful of case reports describe incidents of hepatitis, psychosis, prolonged vomiting, hyponatremia (low blood sodium), seizure, rupture of the oesophagus and cardiac arrest.

Those extreme consequences are particularly few relative to the presumably large number of administrations globally, in both the traditional indigenous and the recent Western contexts.

Accurate figures about usage are impossible to obtain, but one academic source notes over 6,000 members of various closed Facebook groups devoted to Kambô, and the International Association of Kambô Practitioners' Facebook page has over 2,500 followers.

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**What are the perceived benefits of Kambô?**

Despite the documented harms, the great majority of users of Kambô anecdotally report positive physical, emotional and spiritual after-effects.

In Western societies, including Australia, the use of Kambô for healing or wellness has risen rapidly in recent years. The rise has coincided with the emergence of a subculture that questions the merits of the Western medical model and embraces alternative modes of health and medicine.

However, there is limited evidence of the directly measurable health benefits of Kambô in the peer-reviewed academic literature. The putative benefits claimed by the Kambô community largely remain to be substantiated by clinical research.

The actual or potential health benefits conferred by Kambô treatment can be difficult to distinguish from the anticipated or perceived benefits related to psychological effects. These psychological effects in turn may relate to the belief or faith systems that may be involved.

One important aspect of the Kambô experience is purging, particularly by way of vomiting but also defecation.

Many advocates see purging as representing a means of personal transformation through cleansing or detoxification. Purging may also be thought to expel various harmful, negative or generally undesirable aspects of both an emotional and a spiritual nature.

Participants may also feel a benefit from the overall "ordeal" or "challenge". In this regard, significant parallels may be drawn between the purging elicited by Kambô and that associated with the psychoactive brew ayahuasca.

To understand what people gain from Kambô, we may need to move into the domain of philosophical speculation. However, the concepts of personal transformation and spiritual growth are very real to many adherents, and their role in Kambô's perceived benefits should not be discounted.

theconversation, 16 May 2023

<https://theconversation.com>

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**The WHO says we shouldn't bother with artificial sweeteners for weight loss or health. Is sugar better?**

2023-05-18

Artificial sweeteners are either natural compounds or synthesised compounds that taste sweet like sugar – and are up to 400 times sweeter by weight – but provide no or negligible energy. As a comparison, sugar has 17kj (or four calories) per gram, so one teaspoon of sugar would have 85 kilojoules.

Several types of artificial sweeteners are used in Australia. Some are synthetic, others are extracted from foods such as monk fruit and the stevia plant.

So, what do the new WHO guidelines mean for people who have switched to artificial sweeteners for health reasons? Should they just go back to sugar?

**Promoted for weight loss**

As a practising clinical dietitian in the 1990s, I remember when artificial sweeteners began to appear in processed foods. They were promoted as a way of substituting sugar into food products that may lead to weight loss.

A can of sugar-sweetened soft drink contains on average about 500kj. Theoretically, the substitution of one sugar-sweetened can of soft drink with an artificially sweetened can of soft drink every day would reduce your weight by about 1kg per month.

But research over the past few decades shows this doesn't hold up.

**What's the new advice based on?**

The WHO has based its recommendation on a systematic review it has conducted. Its objective was to provide evidence-based guidance on the use of artificial sweeteners in weight management and for disease prevention.

Weight management is important, given obesity increases the risk of diseases such as diabetes and certain types of cancer, which are the leading cause of death globally.

The WHO's systematic review included data from different types of studies, which give us different information:

**This week, the World Health Organization (WHO) advised that "non-sugar sweeteners should not be used as a means of achieving weight control or reducing the risk of noncommunicable diseases" such as diabetes and heart disease.**

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- 50 were randomised controlled trials (when scientists intervene and make changes – in this case to the diet – while keeping everything else constant, to see the impact of that change)
- 97 were prospective cohort studies (when scientists observe a risk factor in a large group of people over a period of time to see how it impacts an outcome – without intervening or make any changes)
- 47 were case-control studies (another type of observational study that follows and compares two groups of otherwise matched people, aside from the risk factor of interest).

Randomised controlled trials provide us with causal data, allowing us to say the intervention led to the change we saw.

Prospective cohort and case-control only give us associations or links. We can't prove the risk factors led to a change in the outcomes – in this case, weight – because other risk factors that scientists haven't considered could be responsible. But they give great clues about what might be happening, particularly if we can't do a trial because it's unethical or unsafe to give or withhold specific treatments.

The WHO's systematic review looked at body fatness, non-communicable diseases and death.

For body fatness, the randomised controlled trials showed those consuming more artificial sweeteners had slightly lower weight – an average of 0.71kg – than those consuming less or no artificial sweeteners.

But the cohort studies found higher intakes of artificial sweeteners were associated with a higher BMI, or body mass index (0.14 kg/m<sup>2</sup>) and a 76% increased likelihood of having obesity.

The prospective cohort studies showed for higher intakes of artificial sweetened beverages there was a 23% increase in the risk of type 2 diabetes. If artificial sweeteners were consumed as a tabletop item (that the consumer added to foods and drinks) there was a 34% increase in the risk of diabetes.

In people with diabetes, artificial sweeteners did not improve or worsen any clinical indicators used to monitor their diabetes such as fasting blood sugar or insulin levels.

Higher intakes of artificial sweeteners were associated with an increased risk of type 2 diabetes, cardiovascular disease and death in the long-term prospective observational studies that followed participants for an average of 13 years.

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But artificial sweeteners were not associated with differences in overall cancer rates or premature death from cancer.

Overall, while the randomised controlled trials suggested slightly more weight loss in people who used artificial sweeteners, the observational studies found this group tended to have an increased risk of obesity and poorer health outcomes.

### Does the review have any shortcomings?

The WHO's advice has led to some criticism because the randomised controlled trials did show some weight loss benefit to using artificial sweeteners, albeit small.

However, the WHO clearly states its advice is based on the multiple research designs, not just randomised controlled trials.

Additionally, the WHO assessed the quality of the studies in the review to be of "low or very low certainty".

### Are they unsafe?

This advice is not suggesting artificial sweeteners are unsafe or should be banned. The WHO's scientific review was not about chemical or safety issues.

### So, are we better off having sugar instead?

The answer is no.

In 2015, the WHO released guidelines on added sugar intake to reduce the risk of excess weight and obesity. Added sugars are found in processed and ultra-processed foods and drinks such as soft drinks, fruit drinks, sports drinks, chocolate and confectionery, flavoured yoghurt and muesli bars.

It recommended people consume no more 10% of total energy intake, which is about 50 grams (ten teaspoons), of sugar per day for an average adult who needs 8,700kj a day.

The WHO's recommendation is in line with the Australian Dietary Guidelines, which recommends no more than three serves of discretionary foods per day, if you need the extra energy. However it's best to get extra energy from the core food groups (grains, vegetable, fruit, dairy and protein group) rather than discretionary foods.

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**So, what do I drink now?**

So, if artificial and sugar in drinks are not advised for weight loss, what can you drink?

Some options include water, kombucha with no added sugar, tea or coffee. Soda and mineral water flavoured with a small amount of your favourite fruit juice are good substitutes.

Milk is also a good option, particularly if you're not currently meeting your calcium requirements.

theconversation, 18 May 2023

<https://theconversation.com/>

**Machine intelligence for designing molecules and reaction pathways**

2023-05-23

Many research groups are making significant progress in using artificial intelligence (AI) and machine learning methods to design feasible molecular structures with desired properties, but progress in putting the design concepts into practice has been slow. The greatest impediment has been the technical difficulties in finding chemical reactions that can make the designed molecules with efficiencies and costs that could be practicable for real-world uses.

"Our novel machine learning algorithm and associated software system can design molecules with any desired properties and suggest synthetic routes for making them from an extensive list of commercially available compounds," says statistical mathematician Ryo Yoshida, leader of the research group.

The process uses a statistical approach called Bayesian inference, which works with a vast set of data about different options for starting materials and reaction pathways. The possible starting materials are all combinations of the millions of compounds that can be readily purchased. The computer algorithm assesses the huge range of feasible reactions and reaction networks to discover a synthetic route towards a compound with the properties it has been instructed to aim for. Expert chemists can then review the results to test and refine what the AI proposes. AI makes the suggestions while humans decide which is best.

**Researchers in Japan have developed a machine learning process that simultaneously designs new molecules and suggests the chemical reactions needed to make them. The team at the Institute of Statistical Mathematics (ISM) in Tokyo published their results in the journal Science and Technology of Advanced Materials: Methods.**

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"In a case study for designing drug-like molecules, the method showed overwhelming performance," says Yoshida. It also designed routes towards industrially useful lubricant molecules.

"We hope that our work will accelerate the process of data-driven discovery of a wide range of new materials," Yoshida concludes. In support of this aim, the ISM team has made the software implementing their machine learning system available to all researchers on the GitHub website.

The current success focused only on the design of small molecules. The team now plan to investigate adapting the procedure to design polymers. Many of the most important industrial and biological compounds are polymers, but it has proved difficult to make new versions proposed by machine learning due to challenges in finding reactions to build the designs. The simultaneous design and reaction discovery options offered by this new technology might break through that barrier.

Phys.org, 23 May 2023

<https://phys.org>

**Fluorine-based novel drug synthesis at lightning speed**

2023-05-22

The research team led by Professor Dong-Pyo Kim and Jeong-Un Joo (Department of Chemical Engineering at POSTECH), and Professor Heejin Kim and Hyune-Jea Lee (currently, a researcher at Samsung Advanced Institute of Technology) from the Department of Chemistry at Korea University has successfully developed a new method for synthesizing trifluoromethyl intermediate (-CF<sub>3</sub>) from fluoroform (CHF<sub>3</sub>).

It involves the use of a special reactor capable of achieving an ultra-fast mixing between gas and liquid. This method offers promising prospects for the synthesis of novel fluorine-based new drugs. The research was published in Nature Communications.

Fluorine is not found in its pure form naturally, but instead exists solely in the form of various chemical compounds. Sodium fluoride, a compound containing fluorine, is used as an ingredient in toothpaste due to its ability to coat teeth and prevent cavities.

Recent studies have highlighted the potential of synthetic drug molecules containing fluorine as they possess high permeability into cell membranes of diseased tissues and exhibit strong binding affinity against proteins.

**How short is one second? The duration of a second can be defined as one 86,400th of a 24-hour day. A bullet train traveling at 300 km per hour can cover a distance of 83 meters in one second. On average, an individual's blink lasts for 0.3 seconds, allowing for three blinks to occur within one second. A joint team of researchers from POSTECH has proposed a synthesis method for fluorine-based compound via a rapid mixing reaction between a gaseous component and liquid that takes less than a single second.**



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Consequently, there is growing interest in the development of drugs containing fluorine.

There are several approaches to synthesizing trifluoromethyl, but the most cost-effective method involves substituting a hydrogen atom from fluoroform, a simple precursor, with another element or functional group. However, gaseous fluoroform is volatile, which makes it difficult to mix with liquids and exhibits low reactivity. Moreover, it decomposes instantly, requiring the addition of a substance that can react with it. Unfortunately, this process can result in unintended chemical reactions that lead to a low yield of trifluoromethyl.

To address the challenge of synthesizing trifluoromethyl from fluoroform, the research team developed a novel gas-liquid reactor with a zigzag-shaped channel and highly permeable non-porous membranes sandwiched between upper and lower channels. This configuration allowed for the swirling and mixing of superbase, a liquid utilized for dehydrogenation, and gaseous fluoroform within the reactor.

By breaking fluoroform bubbles into smaller pieces to increase the contact area between gas and liquid, the team was able to effectively produce trifluoromethyl anion (CF<sub>3</sub><sup>-</sup>). Unlike traditional approaches, they produced a fluoride intermediate effectively without requiring stabilizers or additives.

The research team synthesized a fluorine-based compound by immediately adding a compound that will react with the fluoride anion intermediate. The entire process, which involved the generation of a fluorine anion intermediate from fluoroform took place within a second. The team maximized the formation of a trifluoromethyl anion, which is known to be short-lived, and rapidly facilitated the subsequent reaction before the intermediate decomposed.

This method allowed for improved yield of fluoride-based compounds and introduced a robust technique for the synthesis of fluorine-based drugs.

The research findings have significant implications for industrial applications in the economically efficient synthesis of fluoride compounds, making them more practical as well contributing significantly to studies on several unstable intermediates.

Phys.org, 22 May 2023

<https://phys.org>

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### Using an organic catalyst to make chlorine more energy efficiently

2023-05-18

Thomas Turek, with Clausthal University of Technology, has published a News and Views piece in the same journal issue outlining the work done by the team in China.

Chlorine (a yellowish-green gas at room temperature) is widely used to disinfect water, such as in swimming pools. But it is also used in a wide variety of other applications such as making plastics and bleaching paper. Unfortunately, the process for producing chlorine uses a lot of energy and also emits a lot of carbon dioxide—it involves electrolysis of sodium chloride solutions that generate both chlorine and sodium hydroxide—both of which are used in manufacturing applications.

For that reason, scientists have been looking for more efficient and cleaner ways to make the material. One such approach has involved the use of organic (instead of metal) catalysts because they tend to be less expensive, less toxic and they are generally easier to obtain.

After searching for possibilities, the team found an organic molecule in the amide group RCON-H that enabled the creation of chlorine by helping chloride ions in salt water combine in ways that led to the production of chlorine on a positive electrode. They also found that adding CO<sub>2</sub> gave rise to the intermediate, carbamic acid, which enhanced efficiency of the catalyst exponentially; this was because it binds to the amide nitrogen and in so doing created a radical species.

They also found that after the reaction, it was relatively easy to separate the CO<sub>2</sub> from the chlorine because of the differences in physical properties. Testing showed that the process was able to achieve a density of 10 kA m<sup>-2</sup> and had a selectivity of 99.6% with an overpotential of just 89 mV.

The team concludes by noting that future processes using the new catalyst would use far less energy than the conventional approach and they would be much cleaner—many would not release any harmful by-products at all. They also suggest that their new approach could pave the way in general for a cleaner approach to producing chlorine.

Phys.org, 18 May 2023

<https://phys.org>

**A team of chemists from Tsinghua University and Guangxi Normal University, both in China, has found an organic catalyst that can be used to make chlorine more energy efficiently. In their paper published in the journal Nature, the group describes how they searched for and found an organo-catalyst with an amide functional group that could be used to enable a chlorine evolution reaction.**

**Chemical engineers at Monash University have developed an industrial process to produce acetic acid that uses the excess carbon dioxide (CO<sub>2</sub>) in the atmosphere and has a potential to create negative carbon emissions.**

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**Vinegar could be secret ingredient in fight against climate crisis**

2023-05-22

Acetic acid is an important chemical used in several industrial processes and is an ingredient in household vinegar, vinyl paints and some glues. Worldwide industrial demand for acetic acid is estimated to be 6.5 million tons per year.

This world-first research, published in Nature Communications, shows that acetic acid can be made from captured CO<sub>2</sub> using an economical solid catalyst to replace the liquid rhodium or iridium based catalysts currently used.

Liquid catalysts require additional separation and purification processes. Using a solid catalyst made from a production method that doesn't require further processing also reduces emissions.

Lead researcher Associate Professor Akshat Tanksale said the research could be a widely adopted practice for industry. "CO<sub>2</sub> is over abundant in the atmosphere, and the main cause of global warming and climate change. Even if we stopped all the industrial emissions today, we would continue to see negative impacts of global warming for at least a thousand years as nature slowly balances the excess CO<sub>2</sub>," Prof. Tanksale said.

"There is an urgent need to actively remove CO<sub>2</sub> from the atmosphere and convert it into products that do not release the captured CO<sub>2</sub> back into the atmosphere. Our team is focused on creating a novel industrially relevant method, which can be applied at the large scale required to encourage negative emissions."

The research team first created a class of material called the metal organic framework (MOF) which is a highly crystalline substance made of repeating units of iron atoms connected with organic bridges.

They then heated the MOF in a controlled environment to break those bridges, allowing iron atoms to come together and form particles of a few nanometers in size.

These iron nanoparticles are embedded in a porous carbon layer, making them highly active while remaining stable in the harsh reaction conditions. This is the first time an iron based catalyst has been reported for making acetic acid.

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From an industrial point of view, the new process will be more efficient and cost effective. From an environmental perspective, the research offers an opportunity to significantly improve current manufacturing processes that pollute the environment.

This means a solution to slow down or potentially reverse climate change while providing economic benefits to the industry from the sales of acetic acid products.

The researchers are currently in the process of developing the process for commercialization in collaboration with their industry partners as part of the Australian Research Council (ARC) Research Hub for Carbon Utilization and Recycling.

Phys.org, 22 May 2023

<https://phys.org>

**Chemists synthesize natural pharmaceutical product waixenicin A from coral**

2023-05-17

Soft corals are a rich source of bioactive natural products. The genus *Xenia* produces the so-called *Xenia* diterpenoids, which are characterized by their structural complexity and diverse biological activities. Due to their promising activities, pharmaceutical companies are also showing increasing interest in them—some *Xenia* diterpenoids feature anti-inflammatory and anti-cancer properties, for instance. The first representatives of these substances were isolated as early as 1977, however, they have only been studied to a limited extent.

The biggest challenge is the low availability of natural sources. Many marine organisms, including corals, are largely impossible to cultivate. Large-scale extraction of *Xenia* diterpenoids from corals in nature would represent an enormous impairment of their sensitive ecosystem. Several attempts to produce the complex molecular structures in the laboratory have failed, and to date only a handful syntheses of structurally simplified modifications have been described in the literature.

**Inhibition of ion channel**

In 2014, the group of Thomas Magauer started their research on the synthesis of waixenicin A. The goal was to develop a flexible synthetic strategy to this natural product and to explore its mode of action as well as potential for drug development.

**Chemists led by Thomas Magauer at the University of Innsbruck succeeded in synthesizing the natural product waixenicin A for the first time. This molecule is found in soft corals and is of great interest to the pharmaceutical industry due to its potential medical applications. The study is published in the Journal of the American Chemical Society.**

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Waixenicin A is a unique member of the Xenia diterpenoids and was first isolated from the Hawaiian octocoral *Anthelia edmondsoni* at Harvard Medical School in 1984. Initial testing in 2011 revealed that waixenicin A is a selective and highly potent inhibitor of the TRPM7 ion channel. Ion channels play an essential role in various biological processes, including neural signaling and the perception of a wide variety of sensations such as heat, taste, and pain.

### Earlier work on herbicides leads to success

Magauer's group finally succeeded in synthesizing waixenicin A in the laboratory in April 2023. The synthesis was very challenging due to the special properties of the natural product but was finally accomplished with the help of an efficient synthetic strategy that Magauer's group had established during previous work in the area of herbicides.

Despite early progress and a significant breakthrough in 2017, the desired bicyclic scaffold was not accessible in the laboratory. The presence of several labile functional groups as well as a strained nine-membered ring prevented the successful synthesis for several years.

Eventually, a solution based on an earlier study on the synthesis of the herbicide Cornexistin was developed. The use of an intramolecular ring closure enabled efficient assembly of the desired molecular scaffold. Sequential functionalization of a key bicyclic intermediate allowed selective incorporation of the side chain and completed the first synthesis of waixenicin A. Further diversification of the key intermediate provided access to two additional Xenia diterpenoids: 9-Deacetoxy-14,15-deepoxyxeniculine and Xeniafaraunol A. Particularly intriguing was the conversion to Xeniafaraunol A, which could be performed in only one step. The significance of this step for the biosynthesis and the biological activity is yet unexplored, so exciting research questions are guaranteed.

The Magauer group is currently optimizing the developed route and is working on the synthesis of a unique substance library. In collaboration with Susanna Zierler's group, the latter will be investigated for its inhibitory effect on the TRPM ion channel. Additional binding studies will provide important insights into the mode of action of this fascinating family of natural products.

Phys.org, 17 May 2023

<https://phys.org>

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## Curiosities

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### swallowed Capsule Grabs Info About Gut Health

2023-03-18

Most of the process of digestion takes place in our small intestine, where enzymes break down food so it can be absorbed through the gut wall.

"The small intestine has so far only been accessible in sedated people who have fasted, and that's not very helpful," says professor Oliver Fiehn, director of the West Coast Metabolomics Center at the University of California, Davis. Metabolomics is the study of the metabolome, the small molecules involved in metabolism in cells, tissues, and organs.

As a result, most studies of gut metabolism and the gut microbiome are based on stool samples, but stool samples are really sampling the lower colon, not the small intestine.

"Measuring gut metabolites in stool is like studying an elephant by examining its tail," says Dari Shalon of Envivo Bio, inventor of the CapScan device, and coauthor of two papers on the findings. "Most metabolites are made, transformed, and utilized higher up in the intestines and don't even make it into the stool. CapScan gives us a fuller picture of the gut metabolome and its interactions with the gut microbiome for the first time."

The capsule is swallowed and collects a small volume of biofluids and microorganisms on the way from the upper intestine to the colon until it is recovered in stool. By using a pH-sensitive coating on the capsule, the researchers could choose which area of the intestinal tract to sample.

"This capsule and reports are the first of their kind," says Fiehn, a senior author of a Nature Metabolism paper and co-corresponding author of a Nature paper on the findings. "All other studies on human gut microbiota focused on stool as a surrogate for colon metabolism. However, of course, the fact is that 90% of human digestion happens in the upper intestine, not the colon."

The researchers were able to look at the variation in upper intestinal contents during normal daily digestion in 15 healthy people.

They used a "multiomics" approach to analyze the samples for bacteria, viruses, host proteins, and metabolites from food. They found that the upper intestine and stool differed in all these areas, sometimes dramatically, and identified nearly 2,000 metabolites. The team also found associations between diet, including fruit and alcohol, and metabolites.

**A specially designed capsule can voyage through the digestive system, collecting new data about digestion and microorganisms.**

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Two individuals who had taken antibiotics in the previous six months showed large variations in levels of bioactive fatty acid esters of hydroxy fatty acids, or FAFHAs, and sulfonolipids, metabolites that are thought to be associated with preventing inflammation and diabetes. A species of bacteria named *Blautia* was identified as most involved in fatty acid metabolism.

“Overall, this device can help elucidate the roles of the gut microbiome and metabolome in human physiology and disease,” Fiehn says.

Additional authors of the *Nature Metabolism* paper are from UC Davis, Stanford University School of Medicine, and Silicon Valley Neurogastroenterology and Motility Center. Additional authors of the *Nature* paper also include those from Max-Planck Institute of Biochemistry, Martinsried, Germany; Stanford University; Chan Zuckerberg Biohub, San Francisco; and Penn State.

The work had support in part from the National Science Foundation, the National Institutes of Health, and the Bill and Melinda Gates Foundation.

Futurity, 18 May 2023

<https://futura.org>

### sunlight Gets Recyclable Powder to Disinfect Water

2023-05-22

At least 2 billion people worldwide routinely drink water contaminated with disease-causing microbes.

The discovery of this ultrafast disinfectant could be a significant advance for nearly 30% of the world’s population with no access to safe drinking water, the researchers say.

“Waterborne diseases are responsible for 2 million deaths annually, the majority in children under the age of 5,” says study co-lead author Tong Wu, a former postdoctoral scholar of materials science and engineering in the Stanford School of Engineering.

“We believe that our novel technology will facilitate revolutionary changes in water disinfection and inspire more innovations in this exciting interdisciplinary field.”

Conventional water-treatment technologies include chemicals, which can produce toxic byproducts, and ultraviolet light, which takes a relatively long time to disinfect and requires a source of electricity.

**A low-cost recyclable powder can kill thousands of water bacteria per second when exposed to ordinary sunlight, researchers report.**

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The new disinfectant is a harmless metallic powder that works by absorbing both UV and high-energy visible light from the sun. The powder consists of nano-size flakes of aluminum oxide, molybdenum sulfide, copper, and iron oxide.

“We only used a tiny amount of these materials,” says senior author Yi Cui, professor of materials science and engineering and of energy science and engineering in the Stanford Doerr School of Sustainability. “The materials are low cost and fairly abundant. The key innovation is that, when immersed in water, they all function together.”

After absorbing photons from the sunlight, the molybdenum sulfide/copper catalyst performs like a semiconductor/metal junction, enabling the photons to dislodge electrons. The freed electrons then react with the surrounding water, generating hydrogen peroxide and hydroxyl radicals—one of the most biologically destructive forms of oxygen. The newly formed chemicals quickly kill the bacteria by seriously damaging their cell membranes.

For the study, the team used a 200 milliliter [6.8 ounce] beaker of room-temperature water contaminated with about 1 million *E. coli* bacteria per mL [.03 oz.].

“We stirred the powder into the contaminated water,” says co-lead author Bofei Liu, a former materials science and engineering postdoc. “Then we carried out the disinfection test on the Stanford campus in real sunlight, and within 60 seconds no live bacteria were detected.”

The powdery nanoflakes can move around quickly, make physical contact with a lot of bacteria and kill them fast, he says.

The chemical byproducts generated by sunlight also dissipate quickly.

“The lifetime of hydrogen peroxide and hydroxy radicals is very short,” Cui says. “If they don’t immediately find bacteria to oxidize, the chemicals break down into water and oxygen and are discarded within seconds. So you can drink the water right away.”

The nontoxic powder is also recyclable. Iron oxide enables the nanoflakes to be removed from water with an ordinary magnet. In the study, the researchers used magnetism to collect the same powder 30 times to treat 30 different samples of contaminated water.

“For hikers and backpackers, I could envision carrying a tiny amount of powder and a small magnet,” Cui says. “During the day you put the powder

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in water, shake it up a little bit under sunlight and within a minute you have drinkable water. You use the magnet to take out the particles for later use.”

The powder might also be useful in wastewater treatment plants that currently use UV lamps to disinfect treated water, he adds.

“During the day the plant can use visible sunlight, which would work much faster than UV and would probably save energy,” Cui says. “The nanoflakes are fairly easy to make and can be rapidly scaled up by the ton.”

The study focused on *E. coli*, which can cause severe gastrointestinal illness and can even be life-threatening. The US Environmental Protection Agency has set the maximum contaminant-level goal for *E. coli* in drinking water at zero. The researchers plan to test the new powder on other waterborne pathogens, including viruses, protozoa, and parasites that also cause serious diseases and death.

The study appears in *Nature Water*. The US Department of Energy funded the work.

Futurity, 18 May 2023

<https://futurity.org>

### Microplastics Mess with Seabirds’ Guts

2023-05-18

That increases the presence of pathogens and antibiotic-resistant microbes, while decreasing the beneficial bacteria found in the intestines, the researchers report.

Scientists have worried about the potential harms of microplastics for years. These small plastic particles less than 5 mm in length have been found everywhere because of plastic pollution—from the Earth’s deep oceans to remote regions in Antarctica, and even the seafood we eat.

“Our findings reflect the circumstances of animals in the wild. Since humans also uptake microplastics from the environment and through food, this study should act as a warning for us,” the authors say.

“The gut microbiome encompasses all the microbes in the gastrointestinal tract, which help control the digestion of food, immune system, central nervous system, and other bodily processes. It’s a key indicator of health and well-being,” says Julia Baak, a PhD candidate in the natural resource

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sciences department at McGill University and a coauthor of the study in *Nature Ecology & Evolution*.

To gain a better understanding of how species are affected by diets chronically contaminated with microplastics, the scientists examined the gut microbiome of two seabird species, the northern fulmar (*Fulmarus glacialis*) and the Cory’s shearwater (*Calonectris borealis*) that live mainly on the high seas and feed on marine mollusks, crustaceans, and fish.

“Until now there was little research on whether the amounts of microplastics present in the natural environment have a negative impact on the gut microbial health of affected species,” says Gloria Fackelmann, who conducted the study as part of her doctoral thesis at the Institute of Evolutionary Ecology and Conservation Genomics at Ulm University in Germany.

In studying the seabirds, the researchers discovered that microplastic ingestion changed the microbial communities throughout the gastrointestinal tract of both seabird species.

“The more microplastics found in the gut, the fewer commensal bacteria could be detected. Commensal bacteria supply their host with essential nutrients and help defend the host against opportunistic pathogens. Disturbances can impair many health-related processes and may lead to diseases in the host,” says Fackelmann.

Most studies exploring the impact of microplastics on the microbiome are done in labs using very high concentrations of microplastics, the researchers say.

“By studying animals in the wild, our research shows that changes in the microbiome can occur at lower concentrations that are already present in the natural environment,” Fackelmann says.

Futurity, 18 May 2023

<https://futurity.org>

**A research group has developed a prototype calcium (Ca) metal rechargeable battery capable of 500 cycles of repeated charge-discharge—the benchmark for practical use.**

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### Researchers develop calcium rechargeable battery with long cycle life

2023-05-23

The breakthrough was reported in the journal *Advanced Science* on May 19, 2023.

With the use of electric vehicles and grid-scale energy storage systems on the rise, the need to explore alternatives to lithium-ion batteries (LIBs) has never been greater. One such replacement is Ca metal batteries. As the fifth most abundant element in the Earth's crust, calcium is widely available and inexpensive and has higher energy density potential than LIBs. Its properties are also thought to help accelerate ion transport and diffusion in electrolytes and cathode materials, giving it an edge over other LIB-alternatives such as magnesium and zinc.

But many hurdles remain in the way of Ca metal batteries' commercial viability. The lack of an efficient electrolyte and the absence of cathode materials with sufficient Ca<sup>2+</sup> storage capabilities have proved to be the main stumbling blocks.

In 2021, some members of the current research group provided a solution to the former problem when they realized a new fluorine-free calcium (Ca) electrolyte based on a hydrogen (monocarborane) cluster. The electrolyte demonstrated markedly improved electrochemical performances such as high conductivity and high electrochemical stabilities.

"For our current research, we tested the long-term operation of a Ca metal battery with a copper sulfide (CuS) nanoparticle/carbon composite cathode and a hydride-based electrolyte," says Kazuaki Kisu, assistant professor at Tohoku University's Institute for Materials Research (IMR).

Also, a natural mineral, CuS has favorable electrochemical properties. Its layered structure enables it to store a variety of cations, including lithium, sodium and magnesium. It has a large theoretical capacity of 560 mAh g<sup>-1</sup>—two to three times higher than present cathode materials for lithium-ion batteries.

Through nanoparticulation and compositing with carbon materials, Kisu and his colleagues were able to create a cathode capable of storing large amounts of calcium ions. When employed with the hydride-type electrolyte, they produce a battery with a highly stable cycling performance. The prototype battery maintained 92% capacity retention over 500 cycles based on the capacity of the 10th cycle.

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The group is confident that their breakthrough will help advance research into cathode materials for Ca-based batteries. "Our study confirms the feasibility of Ca metal anodes for long-term operations, and we are hopeful the results will expedite the development of Ca metal batteries," says Kisu.

TecheXplore, 23 May 2023

<https://techxplore.com>

### Edible CBD coating keeps fruit fresher for longer

2023-05-21

We're all familiar with that disappointment of bringing home a punnet of strawberries only to find that the ones on the bottom are already mushy and moldy. In recent years researchers have investigated edible coatings that give fruit and other spoilable foods a longer shelf life without affecting their nutritional value or taste, using materials made from spider silk, shrimp shells, eggs, pectin, or milk proteins – and now scientists have added CBD to the list.

CBD is a non-hallucinogenic compound in cannabis, and it's increasingly finding use in treating anxiety, epilepsy, pain and other problems. Among its potential benefits, recent studies have found signs of antimicrobial activity, so scientists at Thammasat University and Chulabhorn Research Institute in Thailand set out to investigate whether CBD could be used to preserve fruit for longer.

The team combined CBD with biodegradable polymers already used in drug delivery to make nanoparticles measuring 400 nanometers wide. These were then mixed with water and a food additive called sodium alginate. Next, the researchers dipped strawberries into the resulting solution, followed by a second bath in ascorbic acid and calcium chloride, which turned the coating into a gel.

To test the coating's preservation abilities, the team placed treated and untreated strawberries into open plastic containers and kept them at fridge temperatures for several weeks. And sure enough, the CBD-treated berries decayed far less over 15 days than the naked ones, keeping their color for longer. Higher amounts of CBD also seemed to perform better than lower amounts.

**It may be delicious and healthy, but fruit is frustratingly fickle too, often going bad quickly in the fridge. Now, researchers in Thailand have developed an invisible, edible coating made with cannabidiol (CBD) that can preserve fruit for much longer.**

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With further study, this new coating could be useful in reducing food waste and could be applied to other fruit as well as different types of food prone to spoilage.

NewAtlas, 21 May 2023

<https://newatlas.com>

### Plastic-eating fungi thriving in man-made 'plastisphere' may help tackle global waste

2023-05-17

~ A new study published in the *Journal of Hazardous Materials* by researchers at the Royal Botanic Gardens, Kew, and partners has identified a diverse microbiome of plastic-degrading fungi and bacteria in the coastal salt marshes of Jiangsu, China.

The international team of scientists counted a total of 184 fungal and 55 bacterial strains capable of breaking down polycaprolactone (PCL), a biodegradable polyester commonly used in the production of various polyurethanes. Of these, bacterial strains within the genera *Jonesia* and *Streptomyces* have the potential to further degrade other petroleum-based polymers—natural or synthetic chains of molecules bound together.

The plastic-degrading microorganisms were sampled in May 2021 from Dafeng in eastern China, a UNESCO-protected site near the Yellow Sea Coast. The sampling confirmed the presence of a terrestrial plastisphere, a term that is relatively new to terrestrial ecology as past studies have primarily focused on marine environments. The microbiome of this "man-made ecological niche" of coastal plastic debris was further found to be distinct from the surrounding soil.

Scientists are increasingly looking at microorganisms, such as fungi and bacteria, to help tackle some of the most pressing challenges of the modern age, including the rising tide of plastic pollution. According to the United Nations Environment Program (UNEP), 400 million tons of plastic waste is produced annually, with a steep increase in levels of plastic pollution since the 1970s. Researchers are, however, hopeful that answers to this problem could be found in the plastisphere.

Past research has already recognized the potential of microorganisms to tackle plastic waste; a 2017 study led by researchers from China and Pakistan identified a strain of the fungus *Aspergillus tubingensis* that was

~ A new study published in the *Journal of Hazardous Materials* by researchers at the Royal Botanic Gardens, Kew, and partners has identified a diverse microbiome of plastic-degrading fungi and bacteria in the coastal salt marshes of Jiangsu, China.

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breaking down plastic at a landfill in Islamabad, Pakistan. To date, 436 species of fungi and bacteria have been found to degrade plastic and Kew scientists and partners believe their latest findings could lead to the development of efficient enzymes designed to biologically degrade plastic waste.

The Research arrives ahead of World Environment Day 2023 on June 5, the theme of which is finding solutions to the plastic waste crisis under the campaign of #BeatPlasticPollution.

Dr. Irina Druzhinina, Senior Research Leader in Fungal Diversity and Systematics at RBG Kew, says, "Microbiologists across the board feel responsible for finding solutions to the ecologically friendly treatment of plastic waste because bacteria and fungi will be the first organisms to learn how to deal with this new material. We have no doubt that microbes will figure out ways to effectively degrade plastic, but this may take thousands of years if we leave nature to run its course. That is why our task is to utilize the knowledge we already possess of microbial biology, to speed up and direct the evolution of microbes and their individual genes to do the job now."

Because of their longevity and hydrophobic surface, plastics in aquatic ecosystems have created a 'microbial reef' of sorts for fungi and bacteria to attach to. And in the case of certain biodegradable plastics, they can provide microbes with a source of carbon to metabolize—a food source. At Dafeng, the researchers collected 50 samples of plastic waste from seven different types of petroleum-based polymers: polyethylene terephthalate (PET), expanded polystyrene (EPS), polyethylene (PE), polyurethane (PU), polyamide (PA), polypropylene (PP), and polyvinyl chloride (PVC).

Among the samples, the researchers identified 14 genera of fungi, including the plant pathogens *Fusarium* and *Neocosmospora*. Plant-pathogenic fungi draw their nutrients from plants but do so in a way that harms their host. The study's findings indicate these fungi may be better at degrading PCL plastics and other synthetic polymers than saprotrophic fungi—fungi that feed on dead plant and animal remains.

Dr. Druzhinina adds, "The ecological niche of the Dafeng salt marshes is precisely why we chose to investigate the microbial communities present in the plastic waste there, and so far our findings have proven to be both exciting and promising."

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In the wild, fungi play a key role in breaking down organic matter and moving it through the carbon cycle. Over millions of years, the ability to break down many complex and naturally occurring polymers, such as cellulose, has evolved. In fact, the enzymes secreted by fungi are extremely efficient at breaking down complex organic compounds, including carbohydrates and proteins.

Alongside the fungi at Dafeng, the research team recognized two genera of bacteria, *Streptomyces* and the recently discovered genus *Jonesia*, as promising candidates for plastic degradation. In particular, the species *Jonesia* cf. *Quinghaiensis* dominated the 55 sampled bacterial strains.

Xuesong Li, Master's Student at Nanjing Agricultural University, China, says, "The opportunity to work on a project with potentially impactful solutions to tackling rising levels of plastic pollution across the globe was an immediate draw, particularly as this was my first research project. There was some initial concern we might not gather enough data from a single sampling, but the results so far have been overwhelming, and we have had to restrain ourselves from isolating more and more cultures to study their characteristics. And though bacteria proved highly active in this regard, I personally favored working with fungi, as these organisms have vast potential for applications far beyond the degradation of plastic."

Despite the many exciting developments made in the field, the study's authors warn that our understanding of plastic-associated microorganisms is still in its infancy. Many questions about these ecological niches remain unanswered and the study's authors faced some limitations in precisely identifying the analyzed strains down to a species level.

Dr. Feng Cai, Sun Yat-sen University in Shenzhen, China, says, "What strikes me the most is the sheer power of microbial diversity, especially if you consider how challenging it is to detect them; they are microscopic in size, secretive in nature, and simple in appearance. However, when we shift our perspective and view them through a biochemical lens, we gain access to an abundant complexity that awaits our exploration. It is truly exhilarating to realize we have barely scratched the surface and have already discovered a wealth of potentially promising resources for future technologies. This realization fills me with an incredible sense of satisfaction, knowing that there are numerous discoveries still to be made and that our work can potentially lead to significant advancements in the field."

RBG Kew is home to one of the oldest and biggest fungaria in the world with more than 1.25 million specimens, but the kingdom of fungi remains

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one of the great big mysteries of the natural world. Estimates vary but there could be several million species yet to be discovered on top of the more than 144,000 species described to date, and scientists are positive that among them are new sources of food, medicine, and other beneficial compounds.

PhysOrg, 17 May 2023

<https://phys.org>

~2 plastics additives, insecticide face global ban

2023-05-12

The two plastics chemicals are the flame retardant Dechlorane Plus and the ultraviolet stabilizer UV-328. The targeted pesticide is methoxychlor. All three chemicals meet the criteria for inclusion in the treaty: they are persistent, bioaccumulative, and harmful to human health and the environment, the delegates found.

Environmental advocates welcome the decision to add the three chemicals to the Stockholm Convention, but they point out that exemptions will allow continued use of the plastics additives.

The agreement is an important step "toward protecting human health and the environment from three chemicals linked to serious health conditions and threats to biodiversity," Sara Brosché, a science advisor with the International Pollutants Elimination Network (IPEN), says in a statement. "But we are disappointed that financial interests caused unnecessary and dangerous exemptions that will lead to ongoing toxic exposures, especially for waste workers and communities in low- and middle-income countries where plastics and other materials containing these chemicals often end up."

During the Geneva meeting, IPEN released a study showing high levels of Dechlorane Plus in the blood of electronic-waste recyclers in Thailand. The flame retardant is widely used in electronics and automobiles. When such products are broken down for recycling, workers are exposed to high doses of the chemical, the study finds. Dechlorane Plus is associated with reproductive and neurodevelopmental disorders.

UV-328 protects polymers from breaking down under ultraviolet radiation. The chemical is linked to adverse liver and kidney effects in animal studies. UV-328 is the first nonhalogenated chemical to be added to the Stockholm Convention.

**Delegates from around the world have agreed to add two plastics additives and a pesticide to the Stockholm Convention on Persistent Organic Pollutants, an international treaty that lists toxic substances for global elimination. The agreement was reached during a 2-week meeting that wrapped up May 12 in Geneva, Switzerland.**



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Labeling of products that still contain the two plastics additives remains a sticking point. The convention's scientific review committee plans to evaluate options for identifying the substances in products and waste.

Negotiations on methoxychlor, an organochlorine pesticide, were much less contentious than those for the two plastics additives. Delegates agreed to add the insecticide to the Stockholm Convention without exemptions.

Methoxychlor was once used to combat numerous insects on crops, ornamentals, livestock, and pets. It is banned in the US and the European Union because of its toxicity, persistence, and ability to bioaccumulate.

The US has not ratified the Stockholm Convention, but it participates as an observer in meetings. The Geneva event was held together with meetings of the parties of the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal and the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. The three international treaties aim to improve management of chemicals and waste.

The Stockholm Convention is the only one of the three treaties that eliminate or restricts the production and use of chemicals. The Basel Convention focuses on identifying hazardous substances in waste. The Rotterdam Convention focuses on hazardous substances in international trade.

C&N, 12 May 2023

<https://cen.acs.org>

### Finger on the pulse of drug delivery: Preclinical study could pave the way for multiple drug doses in a single injection.

2023-05-18

One potential way to increase adherence is to reduce how often a person needs to take their medication. This can be achieved through a controlled-release system, where a single injection contains a drug that is continually released in the body over an extended period of time. Unfortunately, many controlled-release systems deliver a substantial portion of their cargo right after injection, which can result in inconsistent drug dosing—more drug is released initially (potentially resulting in toxicity) and less

**Pharmaceutical drugs can save lives, but taking these medications as prescribed—especially among those with chronic conditions—can be challenging, for a variety of different reasons. Improving medication adherence could reduce unfavorable health outcomes, hospitalizations, and preventable deaths, while simultaneously reducing health care costs by up to \$300B annually in the United States alone.**

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drug is released over time (potentially at too small a dose to be effective). A system that could release discrete doses at specific time points could revolutionize the way drugs are delivered, from multi-dose vaccinations to daily medications.

Responding to this challenge, researchers from Rice University have developed PULSED (for Particles Uniformly Liquified and Sealed to Encapsulate Drugs). Their method, recently reported in *Advanced Materials*, creates drug-filled microparticles that can be engineered to degrade and release their therapeutic cargo days or weeks after injection. By combining multiple microparticles with different degradation times into a single injection, the researchers could develop a drug formulation that delivers many doses over time.

"As a field, we are continually aiming to develop effective and efficient drug delivery systems that maximize therapeutic benefit and minimize side effects, which can ultimately improve medication adherence," said Luisa Russell, Ph.D., a program director in the Division of Discovery Science & Technology at the National Institute of Biomedical Imaging and Bioengineering (NIBIB). "With several doses combined into a single treatment, the controlled-release system described here could transform the therapeutic landscape, potentially negating the need for frequent drug administration, both at home and at the clinic."

The PULSED microparticles are composed of PLGA, or poly(lactic-co-glycolic acid), a commonly used polymer in a number of FDA-approved devices. PLGA is made up of repeating units of lactic acid and glycolic acid, two molecules that occur naturally in our bodies. By extending the overall length of the polymer, modifying the ratio of lactic acid to glycolic acid, and "capping" the end of the polymer with different molecules, researchers can dictate how long it takes PLGA to disintegrate (and thereby release its therapeutic payload).

"In our case, we can combine populations of microparticles with different PLGA compositions that each release their entire contents at one distinct time point," explained senior study author Kevin McHugh, Ph.D., an assistant professor at Rice University. "This allows us to achieve multiple release events at specific, predetermined times."

Here's how the drug-loaded microparticles are made: Heated, semiliquid PLGA is pressed into a mold and then cooled, solidifying in the shape of hollow cylinders with an opening at the top. The core of each microparticle is filled with therapeutic cargo, and then the top of the microparticles are heated, causing the PLGA to melt and flow over the

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opening to seal the drug inside. The initial particles that the researchers developed were 400 micrometers in diameter (for reference, the thickness of a dime is about 1350 micrometers).

As a first step, the researchers filled four different PLGA microparticle shells with dextran (a type of sugar) that was tagged with a fluorescent molecule, allowing them to easily visualize and measure cargo release. They incubated the microparticles in a body-temperature buffer to mimic real-life conditions and found that the microparticles released their contents at staggered intervals, ranging from roughly eight to 31 days, depending on the PLGA formulation. Importantly, the researchers found that each microparticle formulation released its cargo rapidly, emptying 75% of the dextran over a period of approximately one to three days. They had similar results when they repeated the experiments in mice.

“While we extended the microparticle degradation time to roughly five weeks in this study, we have only begun to tinker with PLGA compositions to further extend their degradation times and subsequent drug release,” said McHugh. “Based on our previous work with other systems, we are confident that by changing PLGA length and component ratios, we could extend release to six months and likely much longer.”

After the researchers optimized their microparticle fabrication process, they needed to ensure that a pharmaceutical drug was still viable once encased inside. Many drugs—especially biologic agents, which are developed using living components—are sensitive to heat, which the researchers use to seal their microparticles.

What’s more, the researchers wanted to be certain that long-term storage inside the human body—conditions that heat and acidify the microparticles—wouldn’t adversely affect the drug. They encapsulated bevacizumab (an FDA-approved antibody that is used to treat several types of cancer) into their microparticles along with different kinds of excipients (inactive drug stabilizers) and evaluated the drug’s activity. With the right combination of excipients, the microparticles released bioactive and viable bevacizumab, even after weeks under simulated body conditions.

Finally, the researchers wanted to push the envelope and further miniaturize their microparticles. While the original particles could easily flow through an 18-gauge needle, which is routinely used for things like blood collection, smaller needles are preferred for pediatric vaccinations and insulin administration, which typically range from 22 to 31 gauge. Using a smaller mold and the same fabrication method, the researchers

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were able to shrink the microparticles down to a diameter of 100 micrometers. The loading capacity of these tiny microparticles is 50-fold lower than the original microparticles, but they could potentially be used with even the smallest of commonly used needles, said McHugh. Future work will include evaluating the disintegration time and cargo release of these miniaturized particles.

“Routes of drug administration are often underappreciated in the field of pharmaceutical medicine,” McHugh said. “Our study, while still early in development, could reshape how routine vaccinations and recurring medications are delivered, ultimately improving medication adherence and human health.”

PhysOrg, 18 May 2023

<https://phys.org>

### Scientists uncover health benefits of melatonin supplement for cattle

2023-05-24

MSU faculty and students in the Department of Animal and Dairy Sciences and the Mississippi Agricultural and Forestry Experiment Station are making intriguing discoveries about the functions of melatonin in the bovine body and how this hormone can help support cattle health.

MSU Associate Professor Caleb Lemley has an extensive history of studying the use of melatonin as a supplement in cattle. He has been studying how the hormone affects blood flow between dam and fetus during gestation for nearly a decade.

“Over the years, we’ve looked at melatonin’s antioxidant benefits, which help alleviate oxidative stress in the animals and have implications on their cardiovascular health,” said Lemley.

“Summer heat is a major stressor for cattle, and in our research here at Mississippi State, we’ve found that melatonin can potentially be used to control the animal’s body temperature,” added Postdoctoral Associate Zully Contreras-Correa. “At night, when melatonin levels are highest, body temperature is lowest. Our recent research showed that melatonin supplementation during summertime reduced body temperature in pregnant cattle, so we hope to research it further in other livestock species.”

**Those needing extra sleep often reach for the bottle of melatonin, but Mississippi State scientists are discovering a host of other proven and potential health benefits for cattle who receive the supplement.**

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Because melatonin controls a body's circadian rhythm and responds to light, levels also fluctuate throughout the year, being naturally higher in the winter and lower in the summer.

"We just completed a study comparing melatonin supplements given to cattle living in Montana to our cattle at MSU over the winter months, and the differences were notable," said Lemley. "We saw a very limited response in the Montana cattle compared to the Mississippi cattle, so we believe these treatments may be more effective in the Southeast."

Doctoral students Riley Messman and Rebecca Swanson also are involved with melatonin research.

The scientists recently published a literature review in the journal *Biomolecules* titled "Melatonin in Health and Disease: A Perspective for Livestock Production." These scientists examined over 100 studies spanning six decades to show that this hormone—naturally produced in the brain—acts in ways that extend far beyond its basic function of regulating circadian rhythm.

One of the latest discoveries about melatonin is its effects on the microbiome, bacterial communities that live inside the body. In her graduate studies, Messman conducted research looking at its impact on the microbiome in the bovine vaginal tract.

"As melatonin levels fluctuate throughout the day and throughout the year, so do bacterial populations," said Messman. "So, melatonin is altering the microbiome and the immune system, which plays a role in pretty much every physiological process you could think of."

As part of her graduate work, Swanson has researched melatonin's role in skeletal muscle growth.

"Nutrient restriction naturally occurs in specific areas of the United States and at certain times of the year," she said. "Melatonin can help alleviate some of that nutrient restriction and promote the production of amino acids and more efficient muscle growth."

Because melatonin is considered a supplement and is not approved by the Food and Drug Administration, there has been a limited amount of research on its full effects and potential benefits. And while it's currently a legal supplement for show animals, food animals may not legally receive melatonin supplementation. Lemley emphasized it is unlikely that traces of the supplement would be present in the muscle tissue at the time of processing.

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"Melatonin has a rapid rate of clearance and will leave the body within a day," he said. "When you consider that and the low cost of supplementing the cattle at 25 cents a day, there are a lot of potential benefits for producers."

There is much yet to discover about the far-reaching ways that melatonin can support the health of cattle by simply manipulating the levels of this naturally present hormone through supplementation. MSU scientists will continue their work to further discoveries about its benefits.

PhysOrg, 24 May 2023

<https://phys.org>

### Fine particulate matter found to catalyze oxidative stress in the lungs

2023-05-17

In scientific literature, the total production of reactive oxygen species (ROS) such as H<sub>2</sub>O<sub>2</sub> is commonly used as proxy for the toxicity of air pollutants and their ability to induce oxidative stress and inflammation. The research team led by Thomas Berkemeier from the MPIC in Mainz found that ROS concentrations in the epithelial lining fluid (ELF) of the human respiratory tract may be primarily determined by the release of endogenous H<sub>2</sub>O<sub>2</sub> and the inhalation of ambient gas-phase H<sub>2</sub>O<sub>2</sub>, while the chemical production of H<sub>2</sub>O<sub>2</sub> through inhaled PM<sub>2.5</sub> is less important.

"Based on our simulations, we think that the overall concentrations of these reactive species in the lungs are large anyway, and not directly dependent on levels of air pollution," says Dr. Thomas Berkemeier, head of the Chemical Kinetics & Reaction Mechanisms group at the MPIC. They used a computer model to understand the relevant physical, chemical, and biological processes, and quantify the health effects of different types of air pollutants.

"Our new model simulates the chemical reactions that happen in the respiratory tract. For the first time, we included production, diffusion, and removal of hydrogen peroxide from cells and the blood stream into our computer model. This was quite challenging, because it is not so easy to put these processes in biological tissues into equations," explains Thomas Berkemeier.

#### New research directions

**A new study conducted by a team of scientists from the Max Planck Institute for Chemistry (MPIC) reveals that the adverse health effects of fine particulate matter (PM<sub>2.5</sub>) are attributable to the conversion of peroxides into more reactive species such as the hydroxyl radical (OH) rather than the direct chemical production of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) as previously thought.**

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## Curiosities

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“The findings of this study suggest that the current paradigms for assessing the differential toxicity of individual PM<sub>2.5</sub> components need to be critically reassessed,” says Prof. Dr. Ulrich Pöschl, Head of the Multiphase Chemistry Department at the MPIC. The study proposed that the chemical production of superoxide and H<sub>2</sub>O<sub>2</sub> in a cell-free assay may not be a suitable metric for assessing the differential toxicity of individual PM<sub>2.5</sub> components, and some acellular oxidative potential assays may not capture the actual deleterious effects of PM<sub>2.5</sub>.

### Fine particulates might act through Fenton chemistry

However, the production of hydroxyl radicals (OH) was strongly correlated with Fenton chemistry of PM<sub>2.5</sub> in the model calculations. “The model simulations suggest that PM<sub>2.5</sub> mostly acts by conversion of peroxides into highly reactive OH radicals. Thus, PM<sub>2.5</sub> is not so much the fuel, but rather the catalyst of the chemical reactions that cause damage to cells and tissues,” says Berkemeier explaining the role of inhaled particles in the model.

Additionally, PM<sub>2.5</sub> may stimulate the production of superoxide from endogenous sources, which further contributes to the adverse health effects of air pollution.

The study underscores the importance of continued research to better understand the chemical mechanisms underlying the health effects of air pollution and to develop effective strategies to mitigate these effects. The authors believe that this study will contribute significantly to this important research effort. Their findings are published in *Environmental Science: Atmospheres*.

Air pollution is a major health risk that affects millions of people worldwide, but the underlying chemical mechanisms are not yet fully understood. Fine particulate matter (PM<sub>2.5</sub>) typically contains chemical components that can trigger oxidation reactions. When inhaled and deposited in the human respiratory tract, they can induce and sustain radical reaction cycles that produce reactive oxygen species (ROS) in the epithelial lining fluid (ELF) that covers the airways and alveoli in human lungs.

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Numerous studies have shown that excess concentrations of ROS like hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and hydroxyl radicals (OH) can cause oxidative stress injuring cells and tissues in the respiratory tract.

PhysOrg, 17 May 2023

<https://phys.org>

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## Technical Notes

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