CHEMWATCH

Bulletin Board

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ASIA PACIFIC

Cutting lead levels in paints: proposed amendments to group standards

2023-11-03

We'd like your feedback on our proposals to cut levels of lead in paints and graphic materials. You have until 26 January 2024.

- Submissions
- Evaluation
- Report
- Hearing or consideration
- Decision

We propose to amend a series of group standards to reduce the maximum allowable levels of lead in paint. The main aim of these proposals is to protect people's health and safety as lead is a highly toxic metal.

We are also proposing changes to reduce the risks from lead in graphic materials, especially those used by children (for example, finger paints, crayons, and felt-tip pens).

We will do this by amending the following sets of group standards:

- Surface Coatings and Colourants
- Aerosols
- Corrosion Inhibitors
- Graphic Materials.

The proposals

You'll find details and discussion of all proposals in the full Proposals document:

Read the Proposals document (PDF, 430KB)

Summary of the proposals

Our proposals:

- Limit lead in paints covered by the Surface Coatings and Colourants Group Standards and Aerosols Group Standards to 90 ppm.
- Add lead limits to the Corrosion Inhibitors Group Standards.
- Require evidence of compliance with lead levels where relevant.

- Update element migration (leaching) limits in graphic materials.
- Update references to the AS/NZS ISO 8124.3 standard to the most recent version. This standard covers lead leaching from toys.
- Amend group standards so all graphic materials marketed to children are only covered by the Graphic Materials Group Standard.
- Remove the notification requirement from the Graphic Materials Group Standard.
- Commencement is 6 months after notification in the Gazette.
- Products that don't meet the requirements of the amendments are to be disposed of 6 months after commencement.

Read More

NZ EPA, 03-11-23

https://www.epa.govt.nz/public-consultations/open-consultations/lead-in-paints/

EPA receives request to take first step in glyphosate reassessment process

2023-10-06

The Environmental Law Initiative (ELI) has applied to the Environmental Protection Authority (EPA) to decide whether there are grounds to reassess the herbicide glyphosate.

Establishing grounds is a specific legal requirement that must be met under the Hazardous Substances and New Organisms Act (HSNO) Act before an application can be made for a substance to be reassessed. A reassessment is a formal review of the rules controlling a substance that is already in use in New Zealand.

Glyphosate is the active ingredient in the weed killer Roundup, one of 89 mixtures containing glyphosate that are approved for use in Aotearoa New Zealand.

ELI says there is significant new information about the negative effects of the substance that warrants a reassessment.

Grounds for reassessment requests are non-notified processes. This means that the request is not publicly notified and there is no opportunity for submissions to be made.

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We have opted to release this information at this stage due to high public interest in glyphosate, and ELI's decision to publicly announce their request for grounds.

The process to establish grounds for reassessment

A decision-making committee will consider information from the applicant and our own research to decide whether there are grounds to reassess glyphosate.

Once a decision has been made, we will publish this on our website.

If the committee decides that grounds do exist, then a reassessment can be undertaken.

Anyone can apply for a formal reassessment, but only once grounds have been established.

Both the general public and people affected by a reassessment are given an opportunity to make a submission on the application.

Find out more about the hazardous substances reassessment process

Glyphosate use in Aotearoa New Zealand

Glyphosate was approved for use before the HSNO Act came into force in 1996. A number of glyphosate-containing substances were moved into the HSNO framework during a 'transfer' process in 2004.

At the time of this transfer, glyphosate-containing substances were assessed and assigned rules for use. They were also assigned hazard classifications.

Since then, there have been a number of applications under the HSNO Act seeking approval to import and manufacture glyphosate-containing substances.

These applications were assessed to determine whether the benefits of using the substance outweigh the adverse effects, in a process that looks at potential effects on the environment, public health, Māori culture, people and communities, and the economy.

Consideration by decision-makers also takes into account how the potential risks from substances can be managed.

We monitor international developments and continually review global research on hazardous substances, including glyphosate.

In 2021, we issued a call for information on glyphosate and received a total of 465 responses from members of the public, professional users, and suppliers of glyphosate, which has been helpful in understanding how glyphosate is used in New Zealand.

Read More

NZ EPA, 06-10-23

https://www.epa.govt.nz/news-and-alerts/latest-news/epa-receives-request-to-take-first-step-in-glyphosate-reassessment-process

China Imposes Export Control on Graphite and Related Products

2023-11-02

Exporters of regulated graphite and related products must apply for export license prior to custom clearance.

On October 20, 2023, China's Ministry of Commerce and the General Administration of Customs jointly published Announcement No.39 of 2023 to implement export controls on certain graphite and its products. It shall take effect from December 1, 2023.

Specifically, graphite and its products that meet the following characteristics will be officially managed as dual-use items:

Items	HS code (for reference)
High-purity (purity>99.9%), high-strength (flexural strength>30Mpa), high-density (density>1.73g/cm^3) artificial graphite materials and their products	3801100030 3801909010 6815190020
Natural flake graphite and its products (including spheroidized graphite, expanded graphite, etc.)	2504101000 2504109100 3801901000 3801909010 3824999940 6815190020

To export these items, it is required to apply in advance to Ministry of Commerce and obtain an export license for custom clearance.

In the meantime, temporary export controls on graphite-related items listed under Decision to Implement Temporary Export Control on Graphite Related Products (Announcement No. 50 of 2006 by the Ministry of Commerce, the State Commission of Science, Technology and Industry

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for National Defense, and the General Administration of Customs) are abolished.

Read More

Chemlinked, 02-11-23

https://chemical.chemlinked.com/news/chemical-news/china-to-restrict-export-of-graphite-and-related-products

India Further Delays Quality Control Orders for 6 Fatty Acids

2023-10-24

Once implemented, the QCOs shall mandate manufacturer of the 6 chemicals to apply for Grant of License by Bureau of Indian Standard to use the Standard Mark.

On October 20, 2023, India's Department of Chemicals and Petrochemicals (DCPC) issued a Notification on the gazette regarding the delayed implementation of Quality Control Orders (QCOs) for 6 types of fatty acids.

Originally planned to be implemented this month, new implementation date is set out for the 6 chemicals as follows:

Goods or Articles	Titile of Indian Standard	Implementation Date
Lauric Acid	IS 10931:1984 Lauric Acid — Specification	April 24, 2024
Acid Oil	IS 12029:1986 Acid Oil — Specification	April 24, 2024
Palm Fatty Acids	IS 12067:1987 Palm Fatty Acids —Specification	April 24, 2024
Rice Bran Fatty Acids	IS 12068:1987 Rice Bran Fatty Acids — Specification	April 24, 2024
Coconut Fatty Acids	IS 12069:1987 Coconut Fatty Acids — Specification	April 24, 2024
Hydrogenated Rice Bran Fatty Acids	IS	April 24, 2024

The Orders do not apply to chemicals for export only. The chemical products conforming to the requirements of the Orders shall bear the

Standard Mark under a license from the Bureau of Indian Standards. Any person who contravenes the provisions of the Orders shall be punished according to the Bureau of Indian Standards Act (BIS Act), 2016.

Read More

Chemlinked, 24-10-23

https://chemical.chemlinked.com/news/chemical-news/india-further-delays-quality-control-orders-for-6-fatty-acids

AMERICA

EPA Grants Tribal Petition to Protect Salmon from Lethal Chemical

2023-11-02

WASHINGTON (Nov. 2, 2023) – Today, in support of its mission to protect human health and the environment, the U.S. Environmental Protection Agency (EPA) is granting a petition from the Yurok Tribe, the Port Gamble S'Klallam Tribe, and the Puyallup Tribe of Indians to address the use of the chemical N-(1,3-Dimethylbutyl)-N'-phenyl-p-phenylenediamine (6PPD) in tires. The chemical 6PPD has been used in motor vehicle tires for more than six decades to make them more durable. It can also be found in other rubber products such as footwear, synthetic turf infill, and playgrounds.

6PPD reacts with ozone pollution in the air to form a byproduct called 6PPD-quinone, which may be present in stormwater runoff from parking lots and streets due to the presence of tire wear particles. Runoff may be washed into streams and other bodies of water during rain events. As a result, aquatic organisms can be exposed to 6PPD-quinone. Concentrations of 6PPD-quinone in stormwater in the Pacific Northwest were found to be lethal to coho salmon after only a few hours of exposure.

"Today, EPA is responding to our Tribal partners by taking action to protect the coho salmon, which are a key part of the Tribes' cultural identity and economic security," said **Assistant Administrator for the Office of Chemical Safety and Pollution Prevention Michal Freedhoff**."These salmon and other fish have suffered dramatic decreases in population over the years. Addressing 6PPD-quinone in the environment, and the use of its parent, 6PPD, is one way we can work to reverse this trend."

In August 2023, the Yurok Tribe, the Port Gamble S'Klallam Tribe, and the Puyallup Tribe of Indians submitted a petition under TSCA Section

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21 asking EPA to consider establishing regulations prohibiting the manufacturing, processing, use and distribution of 6PPD in tires.

Today, EPA is responding by granting this petition. EPA intends to publish an advanced notice of proposed rulemaking under Section 6 of the Toxic Substances Control Act (TSCA) by Fall 2024 in order to gather more information that could be used to inform a subsequent regulatory action.

For example, there are data showing that 6PPD-quinone is toxic to fish, with coho salmon being the most sensitive species studied to date. However, there are still uncertainties about the potential impacts of 6PPD-quinone on human health, as well as the potential for exposure from other sources of 6PPD-quinone.

EPA also plans to finalize a rule under Section 8(d) of TSCA to require manufacturers (including importers) of 6PPD to report lists and copies of unpublished health and safety studies to EPA by the end of 2024.

EPA's Work on 6PPD

It was EPA-funded research that first established the link between 6PPD-quinone and salmon deaths in the Puget Sound region in 2020. Since then, EPA has been engaged in ongoing efforts with other federal agencies, states, Tribes, industry, and other stakeholders to address information gaps and address concerns regarding the use of 6PPD and the risks of 6PPD-quinone.

EPA is continuing to fund research activities to expand its understanding of the impacts of 6PPD-quinone, and to fill data gaps. For example, the Office of Research and Development is continuing further investigation of 6PPD-quinone, including work on fate and transport, ecotoxicity, and green infrastructure solutions for stormwater contamination. The Office of Water is currently developing an analytical method for detection of 6PPD-quinone in surface and stormwater and is developing draft screening values for 6PPD-quinone and 6PPD to protect sensitive salmon and other aquatic life. The Agency is also coordinating with the National Science and Technology Council's Joint Subcommittee on Environment, Innovation and Public Health on potential cross-governmental research on human health effects.

To learn more about this effort, visit EPA's new 6PPD-quinone webpagedeveloped to keep the public and stakeholders updated as research progresses, alternatives to 6PPD are identified, and ways

to mitigate the effects of 6PPD-quinone on the environment are implemented.

Read More

US EPA, 02-11-23

https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/tsca-section-21#6ppd

FDA Proposes to Ban Food Additive, Continues Assessments of Additional Chemicals

2023-11-03

Today, the U.S. Food and Drug Administration proposed to revoke the regulation authorizing the use of brominated vegetable oil (BVO) in food. The agency concluded that the intended use of BVO in food is no longer considered safe after the results of studiesExternal Link Disclaimer conducted in collaboration with the National Institutes of Health (NIH) found the potential for adverse health effects in humans.

BVO is a vegetable oil that is modified with bromine. It is authorized by the FDA for use in small amounts to keep the citrus flavoring from separating and floating to the top of some beverages. In 1970, the FDA determined BVO was no longer "Generally Recognized as Safe" (GRAS) and began overseeing its use under our food additive regulations. Over the years many beverage makers reformulated their products to replace BVO with an alternative ingredient, and today, few beverages in the U.S. contain BVO.

The FDA prioritizes its review of chemicals in food based on risk, science, and regulatory authority. Although BVO has a long history of use in foods and was at one time considered GRAS, we have continued to study it to understand any potential health impacts. Recent toxicology studiesExternal Link Disclaimer conducted in collaboration with the NIH have now given us conclusive scientific evidence to support our proposal to remove the FDA's food additive authorization for BVO. The proposed action is an example of how the agency monitors emerging evidence and, as needed, conducts scientific research to investigate safety related questions, and takes regulatory action when the science does not support the continued safe use of additives in foods.

We recognize that California recently took steps to ban the use of four food ingredients, including BVO, in that state. The agency is continuously

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reviewing and reassessing the safety of a variety of chemicals in food to ensure the science and the law support their safe use in food, including all four ingredients that are part of the recent California law. In fact, the FDA is currently reviewing the color additive regulations authorizing the use of FD&C Red No. 3 in ingested drugs and foods (including dietary supplements) under the Delaney Clause of the Federal Food, Drug, and Cosmetic Act, which, in relevant part, prohibits the FDA from approving a color additive that is ingested if it causes cancer in animals or humans when ingested. A decision from the FDA is forthcoming.

Read More

FDA, 03-11-23

https://www.fda.gov/news-events/press-announcements/fda-proposes-ban-food-additive-continues-assessments-additional-chemicals

PFAS chemicals on your baby's diapers

2023-11-03

New testing finds evidence of "forever chemicals" in popular brands of both disposable and reusable cloth diapers.

There's nothing more important than making sure our babies are safe and healthy — and new testing from Mamavation has uncovered one more way to do that.

Partnering with EHN.org, the environmental wellness blog and community had 65 diapers and similar accessories from 40 different brands tested by a U.S. Environmental Protection Agency-certified lab and found levels of organic fluorine ranging from 10 parts per million (ppm) to 323 ppm. There were 15 detections — so 23% of the total products tested had evidence of PFAS.

Organic fluorine is a strong indicator of per- and polyfluoroalkyl substances, also known as PFAS or "forever chemicals"— which have been linked to health effects including reduced immune system function and vaccine response, developmental and learning problems for infants and children, certain cancers, lowered fertility, endocrine disruption and other impacts.

"The EPA has set new concentration lifetime limits for the most toxic PFAS compounds in water that are so low that they are currently impossible to detect at any given time," Terrence Collins, Teresa Heinz Professor of Green Chemistry & Director of the Institute for Green Sciences at Carnegie Mellon

University, told Mamavation. "We absolutely don't want babies exposed to products containing 10 ppm of extractable organic fluorine, which is massive compared to the water standards."

Read More

EHN, 03-11-23

https://www.ehn.org/non-toxic-diapers-2666123480.html

EPA to strengthen lead protections in drinking water after multiple crises, including Flint

2023-11-03

About four decades ago, when the Environmental Protection Agency was first trying to figure out what to do about lead in drinking water, Ronnie Levin quantified its damage: Roughly 40 million people drank water with dangerous levels of lead, degrading the intelligence of thousands of kids.

But new regulations were going to be costly and complicated. So, "instead of trying to deal with it substantively, they just tabled it," Levin, a former EPA researcher, said of some of her colleagues at the agency in the 1980s.

Levin's analysis then was leaked to the press, igniting a public outcry that pressured the EPA to act. And the rules it issued back then have stayed in place, with only modest changes, ever since.

Decades after officials banned lead in gasoline for new cars and stopped the sale of lead paint — huge steps toward eliminating significant sources of lead exposure to the public — there are still an estimated 500,000 U.S. children with levels of lead in their blood that are considered high, and experts say lead in drinking water is an important source.

Now the agency is aiming to further reduce lead levels in drinking water and tighten a rule that failed to prevent recent drinking water crises in cities like Flint, Michigan, and Newark, New Jersey. Although the specifics aren't public, the agency says it will propose requiring that utilities actively replace harmful lead pipes.

President Joe Biden has already called for eliminating the country's estimated 9.2 million lead pipes, lines that connect water mains under the street to homes and businesses and are responsible for most of the lead that seeps into drinking water.

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Read More

AP News, 03-11-23

https://apnews.com/article/epa-lead-water-pipe-announcement-flint-44b774f4a96567429b44badf9c89129a

EUROPE

New EU active substance approval decision

2023-11-03

Apply for product authorisation by the deadline to keep your products on the NI market

Following evaluation under the EU BPR, a decision has been taken to approve the following active substance/product type combination. This will affect NI:

- Reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate(CAS n/a EC n/a) in product types 2 and 4

Action for biocidal product suppliers

If you want to supply biocidal products containing this active substance in the relevant product types, you must apply for EU BPR product authorisationby 1 February 2025 to keep them on the NI market. New products must not be supplied in NI until product authorisation is granted.

Action for active substance suppliers

If you supply this active substance for use in biocidal products of the relevant product type, you may need to apply for technical equivalence. If you haven't demonstrated technical equivalence for your manufacturing source, EU BPR product authorisation cannot be granted for biocidal products containing your active substance.

Read More

HSE.gov.uk, 03-11-23

https://www.hse.gov.uk/

New EU redefinition of an active substance

2023-11-03

Active substance redefinition for biocidal products on the NI market

The below active substance was approved under EU BPR for product type 8 in 2016. The evaluation of product types 2 and 4 have recently been completed. The evaluation has concluded that, although the composition and reference specification were consistent with the product type 8 assessment and approval, the assigned name was not appropriate.

Therefore, a decision was made to redefine the active substance. New approvals were given for product types 2 and 4, product type 10 remains under review and the existing approval for product type 8 has been redefined as follows. This will affect NI:

Previous definition of the active substance as identified in Annex II of Delegated Regulation (EU) No. 1062/2014and approved in Implementing Regulation (EU) No. 2016/1093;

- Didecylmethylpoly(oxyethyl)ammonium propionate referred to with its chemical name 'poly(oxy-1,2-ethanediyl), α-[2-(didecylmethylammonio)ethyl]- ω-hydroxy-, propanoate (salt) (Bardap 26)' (CAS 94667-33-1 EC n/a) in product type 8

Expiry date 31 December 2027

New active substance identity as redefined in Implementing Regulation (EU) No. 2023/2088;

- Reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate (CAS n/a EC n/a) in product type 8

Expiry date 31 December 2027

Implementing Regulation (EU) No. 2016/1093 has been repealed.

Action for biocidal product suppliers

If you supply biocidal products containing this active substance for the relevant product type on the NI market, you will need to apply for a change to your authorisation. New products must not be supplied in NI until product authorisation is granted.

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Read More

HSE.gov.uk, 03-11-23

https://www.hse.gov.uk/

Glyphosate cancer findings of "extreme concern" as Europe weighs reauthorization of pesticide

2023-11-03

"We couldn't sit on this data."

This story was originally published in The New Lede, a journalism project of the Environmental Working Group, and is republished here with permission.

European researchers have found new evidence linking popular weed-killing products to cancer at levels currently considered safe.

The study focused on glyphosate, the active ingredient in Roundup herbicide and other brands, and is the latest in a series of studies examining the safety of the world's most widely used weed-killing chemical.

Notably, the work comes as the European Union is wrestling over whether or not to keep glyphosate products on the market after the current approval expires in December.

The research has not yet been peer reviewed, but was presented Wednesday at an international scientific conference.

Read More

EHN, 03-11-23

https://www.ehn.org/glyphosate-cancer-europe-2666077883.html

EU NSC Conducting Survey on Implementation of Nanosafety in Workplaces

2023-10-31

The European Union (EU) NanoSafety Cluster (NSC) announced on October 24, 2023, that it is conducting a survey on the implementation of nanosafety in workplaces. NSC states that the survey aims to gather insights on the current practices and challenges of implementing nanosafety in workplaces. According to NSC, responses will help shape

recommendations for future safety guidelines and protocols. NSC notes that participation will take approximately 15-20 minutes.

Read More

Nanoblog, 31-10-23

https://www.lawbc.com/eu-nsc-conducting-survey-on-implementation-of-nanosafety-in-workplaces/

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All comments submitted to the PFAS restriction proposal now online

2023-11-03

We have now published all 5 642 contributions received from the public to the proposal to restrict per- and polyfluoroalkyl substances (PFAS) in the EEA. They are compiled in 123 Word files that can be accessed through an index spreadsheet providing an overview of the feedback. We do not publish information that has been marked as confidential by the consultee.

The proposal, submitted to ECHA in January 2023, was prepared by five European countries. It is currently being evaluated by our scientific committees for Risk Assessment and for Socio-Economic Analysis. Read more on our topical page for PFAS.

Read More

ECHA, 03-11-23

https://echa.europa.eu/comments-submitted-to-date-on-restriction-report-on-pfas

IUCLID news

2023-10-30

The October 2023 service release is here

A new service release is available to be installed containing new features, improvements and fixes.

In this release there are no changes to the data format, making it fully compatible with the previous version released in May. It brings a series of new functionalities as well as fixes and improvements such as:

- Performance improvements of specific operations in IUCLID: for example, the export of files, the loading of the navigation tree, and the extraction of dossier content to a dataset. In addition, a new feature to export and import from a IUCLID drive can be activated by administrators of IUCLID servers.
- The finalisation of the updates required to support the preparation of Summary of Product Characteristics under the EU BPR in the future. This includes, for example, the access to the list of biocidal active substances from ECHA's repository, the creation of the SPC report for Single Products and Product Families, a set of validation rules to check

the completeness of the information. As part of this development we have technically enabled the possibility for the report generator to output files in .docx format, and is available for all IUCLID users. The IUCLID team can now start working on preparing report templates using this format.

You will find a full list of changes brought by this new version in the release notes. ECHA will host a webinar on the 21st of November to provide more information about the release and to answer questions.

ECHA Cloud Services users will see their IUCLID instances being upgraded automatically, starting as of today.

Note on patches that followed the May release: since the initial release of IUCLID 6 v7 on 27th of May, the IUCLID team has prepared and released a series of patches to address issues identified. You can find more information here. All the fixes included in these patches are also available in the latest version of IUCLID, they do not need to be installed separately. There is one specific issue that requires further work for users who have installed v7.0.1 or v7.0.2. Potentially affected users have been contacted individually, but please check the information under section 10.1.1.1 of the installation manual in case you have, at any point in time, updated your IUCLID database to v7.0.1 or v7.0.2.

Read More

ECHA, 30-10-23

https://iuclid6.echa.europa.eu/view-article/-/journal_content/title/the-october-2023-service-release-is-here

New version of ECETOC TRA Worker tool published

2023-10-27

ECETOC has recently updated its TRA Worker tool, by releasing the new version 3.2. You can find more information on the changes in ECETOC's technical report "TR 141 – Comparison of measured and modelled short-term inhalation and dermal exposure".

Some exposure estimates for workers have been modified. An overview of the changes and their impact on the exposure estimation can be found in table 5 of the report.

Registrants having already finalised the occupational exposure estimation based on previous versions of the ECETOC TRA tool are advised to look at the changes outlined in the report.

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If registrants conclude that these changes put into question the outcome of their assessment, they should consider updating it.

Chesar 3 does not enable to obtain those new estimates automatically. They can nevertheless be reported by using the "external tool functionality".

The exposure estimates from this new version of ECETOC TRA workers will be available in the future Chesar Platform, planned to be released in 2024.

Read More

ECHA, 27-10-23

https://chesar.echa.europa.eu/-/new-version-of-ecetoc-tra-worker-tool-published

Bright Spark

2023-11-10

https://www.google.com.au

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Hazard Alert

RDX

2023-11-10

USES [2,3]

RDX was widely used during World War II, often in explosive mixtures with TNT such as Torpex, Composition B, Cyclotols, and H6. RDX was used in one of the first plastic explosives. Outside military applications, RDX is also used in controlled demolition to raze structures.

EXPOSURE SOURCES & ROUTES OF EXPOSURE [3]

Exposure Sources

- Exposure typically only occurs in people who work with RDX and can potentially breathe RDX dust or get it on their skin.
- You can be exposed if you breathe RDX fumes from explosions or bombing ranges of burning RDX.
- You may be exposed to RDX by drinking contaminated water or by touching contaminated soil if you live near facilities that produce or use RDX. RDX has been found in water and soil near some ammunition plants, current or former military installations and storage areas.
- You may be exposed to RDX by ingesting agricultural crops grown in contaminated soils irrigated with contaminated water.

Routes of Exposure

- Inhalation – Minor route of exposure for general population. Predominant route of exposure for workers.
- Oral – Predominant route of exposure to for non-occupational exposure. Exposure can occur through ingestion of contaminated drinking water or consumption of agricultural products irrigated with contaminated water.
- Dermal – Skin contact may occur during manufacture of RDX.

HEALTH EFFECTS [4]

- The most sensitive target of toxicity is the nervous system. Seizures, convulsions, and tremors have been observed in humans and animals ingesting RDX.
- Some studies have found changes in serum chemistry parameters suggestive of impaired liver function; histological alterations have

RDX, which stands for Research Department explosive, is an explosive nitroamine widely used in military and industrial applications. It was developed as an explosive which was more powerful than TNT, and it saw wide use in World War II. RDX, also known as cyclonite, hexogen, and T4 has the chemical formula C3H6N6O6. Its chemical name is cyclotrimethylenetrinitramine. In its pure, synthesised state RDX is a white, crystalline solid. It is often used in mixtures with other explosives and plasticizers, phlegmatisers or desensitisers. RDX is stable in storage and is considered one of the most powerful and

not been found in the liver and the changes in clinical chemistry parameters were not considered biologically significant.
- Small decreases in erythrocyte and haemoglobin levels have been found in rodents, but this has not been consistently found longer-term studies.
- EPA has determined that RDX is a possible human carcinogen based on the presence of liver tumours in mice exposed to RDX in the diet for 1–2 years. However, a re-evaluation of this mouse study resulted in a re-classification of some of the hepatocellular adenomas as foci of cytoplasmic alterations.

SAFETY

First Aid Measures [5]

- **Inhalation:** Remove victim from area of exposure - avoid becoming a casualty. Remove contaminated clothing and loosen remaining clothing. Allow patient to assume most comfortable position and keep warm. Keep at rest until fully recovered. Seek medical advice if effects persist.
- **Skin Contact:** If skin or hair contact occurs, immediately remove any contaminated clothing and wash skin and hair thoroughly with running water. A component of this material can be absorbed through the skin with resultant toxic effects. Seek immediate medical assistance.
- **Eye Contact:** If in eyes, wash out immediately with water. In all cases of eye contamination, it is a sensible precaution to seek medical advice.
- **Ingestion:** Immediately rinse mouth with water. If swallowed, give a glass of water to drink. Get to a doctor or hospital quickly.
- **Medical attention and special treatment:** Treat symptomatically. Explosive material.

Workplace Controls & Practices [4]

Control measures include:

- Ensure ventilation is adequate and that air concentrations of components are controlled below quoted Exposure Standards.
- Natural ventilation should be adequate under normal use conditions.

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Personal Protective Equipment [5]

- It is recommended that to wear overalls, safety glasses and impervious gloves when handling RDX.
- Always wash hands before smoking, eating, drinking or using the toilet.

REGULATION

United States

OSHA: The United States Occupational Safety & Health Administration has set the following Permissible Exposure Limit (PEL)for RDX:

- Construction Industry: 29 CFR 1926.55 Appendix A -- 1.5 mg/m3 TWA; Skin
- Maritime: 29 CFR 1915.1000 Table Z-Shipyards -- 1.5 mg/m3 TWA; Skin

ACGIH: The American Conference of Governmental Industrial Hygienists has set a Threshold Limit Value (TLV) for RDX of 0.5 mg/m3 TWA; Skin; Appendix A4 - Not Classifiable as a Human Carcinogen

NIOSH: The National Institute for Occupational Safety and Health (has set a Recommended Exposure Limit (REL) for RDX of 1.5 mg/m3 TWA, 3 mg/m3 STEL; Skin

Australia

Safe Work Australia: Safe Work Australia has set a Time Weighted Average (TWA) concentration for RDX of 1.5mg/m3 for a 40-hour workweek.

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Researchers produce Mo-99 by electron accelerator with optimized target system

2023-11-08

Mo-99 is the mother nuclide of technetium-99m (Tc-99m), which is widely used in diagnostic nuclear imaging procedures. Currently, the majority of Mo-99 is produced from the nuclear reactors via fission of highly enriched uranium. Many efforts have been made to find alternatives. Production of Mo-99 via 100Mo(γ, n)99Mo reaction attracts a lot of attention due to its low level of co-produced impurities.

Researchers from the Institute of Modern Physics (IMP) of the Chinese Academy of Sciences (CAS), have investigated producing Mo-99 via 100Mo(γ, n)99Mo reaction.

In order to obtain a high yield of Mo-99, the researchers optimized the target system by means of Monte Carlo simulations before conducting irradiation experiments. In the experiments, the target system was irradiated at the terminal of the electron linear accelerator system at IMP. The bremsstrahlung was generated from the tantalum converter and Mo-99 was produced in the Mo-100 target.

The researchers analyzed the radioactivity of Mo-99 and radionuclidic purity of the Mo-99 product. The results showed that a manageable level of impurities was co-produced during irradiating the target system and high radionuclidic purity of Mo-99 product was achieved.

This study lays a sound foundation for producing medical isotope Mo-99 on a large scale with electron accelerators in China.

Phys Org, 08 November 2023

https://phys.org

Chinese researchers have developed a process for producing the medical isotope molybdenum-99 (Mo-99) using the electron accelerator system. The study was published in Applied Radiation and Isotopes.

Wasabi offers a memory-boosting kick to an aging brain

2023-11-06

But this Japanese condiment that packs a punch like few others has in recent times been the focus of studies into its positive impact on memory and cognitive function. Now, for the first time, it has been shown to improve short- and long-term memory, and bolster associative memory, in the brains of people aged 60-80 years.

In this study, the researchers performed a double-blinded randomized control trial on a cohort of 72 older adults for 12 weeks. Half took a daily

supplement made up of 100 mg of wasabi extract, while the control group received an inactive 100-mg cyclodextrin tablet.

The wasabi supplement contained 0.8 mg of 6-methylsulfinyl hexyl isothiocyanate (6-MSITC), the active ingredient that appears to hold the key to better memory function.

With previously studied anti-inflammatory and antioxidant qualities, 6-MSITC is present in cruciferous vegetables but is most concentrated in the underground rhizome of the wasabi plant (Eutrema japonicum). This part of the plant, of course, is used to make the earthy hot mustard-like paste that is an essential condiment for any sashimi and sushi spread.

Before and after the trial, the participants completed cognitive tests that included a focus on processing speed, attention, short-term memory, working memory, executive functions and visual-spatial abilities.

The results showed that those who took their nightly wasabi tablets had improved long- and short-term memory and did better on association tests, such as linking names to faces. The placebo cohort showed no differences in cognitive function.

The researchers believe 6-MSITC affects the brain's hippocampus region, which is a key component of memory function. They now hope to look at how this bioactive compound is affecting this area on a molecular level.

"These findings suggest that the 12 weeks' 6-MSITC intake selectively enhances working and episodic memory functions in healthy older adults," the researchers noted. "This study is the first to demonstrate that 6-MSITC has a benefit on memory functioning in healthy older adults."

The good news for those who don't enjoy the wasabi burn? When packaged up in a supplement, all the pain is happily bypassed.

The research was published in the journal Nutrients.

New Atlas, 06 November 2023

https://newatlas.com

Harnessing the Innate Power of a Cell To Remove Problem Proteins

2023-10-26

When targeting problem proteins involved in causing or spreading disease, a drug will often clog up a protein's active site so it can't function

Researchers who previously pioneered a new kind of protein degradation have mapped out how the process works.

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and wreak havoc. New strategies for dealing with these proteins can send these proteins to different types of cellular protein degradation machinery such as a cell's lysosomes, which act like a protein wood chipper.

In a new study published in Science on Oct. 20, Stanford chemists have uncovered how one of the pathways leading to this protein "wood chipper" works. In doing so, they have opened the door to new therapeutics for age-related disorders, autoimmune diseases, and treatment-resistant cancers. These findings may also improve therapeutics for lysosomal storage disorders, which are rare but often serious conditions mostly affecting babies and children.

"Understanding exactly how proteins are shuttled to lysosomes to be broken down can help us harness the innate power of a cell to get rid of proteins that cause the human body so much harm," said Carolyn Bertozzi, the Anne T. and Robert M. Bass Professor in the School of Humanities and Sciences and Baker Family Director of Sarafan ChEM-H. "The work done here is a clear look into a typically opaque intracellular process, and it's shining a light on a new world of possible drug discovery."

"The ability to understand the biology of this process means we can use inherent biology that already exists, and harness it to treat disease," said Steven Banik, assistant professor of chemistry in the School of Humanities and Sciences. "These insights offer a unique window into a new type of biology that we haven't really understood before."

Stopping proteins from going rogue

While proteins often do a body good, like help us digest our food or repair torn muscles, they can also be destructive. In cancer, for example, proteins can either become part of the tumor and/or allow for its unchecked growth, cause devastating diseases like Alzheimer's, and build up in the heart to affect how it pumps blood to the rest of the body.

To stop rogue proteins, drugs can be deployed to block a protein's active site and thus stop it from interacting with a cell, which was the standard of therapeutic research for decades. Then 20 years ago, proteolysis targeting chimeras (PROTACs) burst onto the scene, which can engage bad-acting proteins that are already inside a cell, and send them off to be broken down in the lysosome.

PROTACs are currently in clinical trials and have shown efficacy in treating cancer. But they can only target a protein if it is inside the cell, which is only 60% of the time. In 2020, Stanford ChEM-H researchers pioneered a

way to reach the other 40% of those proteins through lysosome targeting chimeras (LYTACs), which can identify and mark proteins that are hanging out around the cell, or on a cell's membrane, for destruction.

These findings kicked off a new class of research and therapeutics, but exactly how the process worked wasn't clear. Researchers also noticed that it was difficult to predict when LYTACs would be highly successful or fail to perform as anticipated.

New therapeutic targets

In this work, Green Ahn, then a Stanford graduate student and now a postdoctoral fellow at the University of Washington Institute for Protein Design, and lead author on the study, used a genetic CRISPR screen to identify and characterize the cellular components that modulate how LYTACs degrade proteins. Through this screening, the team identified a link between the level of neddylated cullin 3 (CUL3) – a protein that plays a housekeeping role in breaking down cellular proteins – and LYTAC efficacy. The exact tie isn't clear yet, but the more neddylated CUL3 present, the more effective LYTACs were.

Measuring the level of neddylated CUL3 could be a test given to determine which patients are more likely to respond to LYTAC therapy. This was a surprise finding, said Bertozzi, as no previous research pointed to this correlation before.

They also identified proteins that block LYTACs from doing their job. LYTACs work by binding to certain receptors on the outside of the cell, which they use to shuttle bad proteins into lysosomes for degradation. However, the researchers saw that proteins bearing mannose 6-phosphates (M6Ps), sugars that decorate proteins destined for lysosomes, will take a seat on those receptors, meaning LYTACs have nowhere to bind. By throwing a wrench into M6P biosynthesis, an increased fraction of unoccupied receptors resulted on the cell surface, which could be hijacked by LYTACs.

New biology, new pathways for treatment of disease

In addition to helping develop LYTACs into more effective therapeutics, these discoveries could also lead to new and more effective treatments for lysosome shortage disorders – genetic conditions where the body doesn't have enough or the right enzymes in lysosomes for them to work properly. This can cause toxic build ups of fat, sugars, and other harmful substances, which can lead to heart, brain, skin, and skeletal damage. One common

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treatment is enzyme replacement therapy, which utilizes similar pathways as LYTACs to travel to lysosomes where they can operate. Understanding how and why LYTACs work means that these enzymes could be delivered more effectively.

The researchers likened this work to an important discovery of how exactly the drug thalidomide works. It was originally prescribed in the 1950s for morning sickness to pregnant women, mostly in the United Kingdom, but was taken off the market in 1961 when it was linked to severe birth defects. However, in the 1990s, it was found to be an effective treatment for multiple myeloma. In 2010, researchers understood how: through degrading proteins, an observation which contributed substantially to the growing field of PROTAC research.

"LYTAC evolution is where the story of thalidomide and PROTACs was 15 years ago," Bertozzi said. "We're learning human biology that wasn't known before."

Technology Networks, 26 October 2023

https://technologynetworks.com

Research improves formable cellulose-based food packaging to replace single-use plastic

2023-11-07

The researchers are to present their findings at The Greener Manufacturing Show 2023 in Cologne, Germany, held November 8–9.

Typical commercial boards have between 3% and 6% extensibility and best commercial formable boards have 10%–18% extensibility. By utilizing foam forming technology, VTT has now obtained up to 30% extensibility. This enables brand owners to use rigid, cardboard-like packaging to serve consumers looking to buy more sustainable products.

This material improvement enables, for example, food brands producing cold cuts to increase cardboard-like package size from 75 grams up to 200–250 grams. By adjusting the tray forming process and tray dimensions even larger cardboard-like packages can be produced.

"Polypropylene film is one of the world's most used polymers—its extensibility is up to 300%. Our invention now offers a viable, sustainable alternative on the market," says Jarmo Kouko, Research Team Leader at VTT.

In a pilot-scale study to find alternative raw materials for rigid plastic packages, VTT Technical Research Center of Finland has obtained unprecedented maximum limits of its highly extensible formable cellulose-based webs used for rigid packaging applications. The results enable the manufacturing of a wide range of sustainable 3D packaging solutions that were previously unattainable.

"There's been a lot of great academic research around the world on how to eliminate plastics, but the challenge is that those seldom go beyond research. So, we're extremely excited and proud of the results we've produced in our pilot-scale study, which clearly shows the commercial potential of our rigid cellulose-based packaging.

"In industries that use huge amounts of plastic like the food packaging sector, we can find plenty of opportunities to reduce the use of fossil fuel based materials and replace them with sustainable ones that take us closer to carbon-neutral societies of the future and allow us to be more frugal with natural resources," he continues.

With the Single-use Plastics Directive and the European Commission's proposal for Packaging and Packaging Waste Regulation, plastic items like expanded polystyrene (EPS) food containers and cups have been banned in the European Union since 2021, and producers of single-use plastic products are expected to cover the costs of waste management for these products. Solutions like VTT's foam-formed cellulose-based packaging give suppliers a sustainable and affordable alternative to single-use plastic.

"The fact that VTT, together with gruppo x di x gruppo s.r.l. and Lappeenranta-Lahti University of Technology (LUT), were able to incorporate the product into existing product packaging lines with no changes in the process, making it affordable and easy for brands to adopt the product as a sustainable alternative to plastic packages can be a real game-changer," says Kristian Salminen, Lead, Bio-based Products at VTT.

The development work has been conducted as a part of a research program, where VTT in co-operation with 54 companies and Regional Council of Central Finland have up-scaled promising alternatives for plastic products.

Phys Org, 07 November 2023

https://phys.org

US proposes complete ban on trichloroethylene

2023-11-01

TCE is used in many manufacturing processes, from production of refrigerants and tyres to battery separators, Kornfeld explains. If implemented, the rule would require most uses of TCE to be ended within a year. 'They're phasing out TCE in pretty short order, except for some pretty narrow exemptions, and as a whole most TCE uses will be phased out within 10 years,' she says.

The US Environmental Protection Agency (EPA) has proposed a ban on all uses of trichloroethylene (TCE), a common industrial degreasing solvent considered to be a human carcinogen. The new rule, expected to be finalised sometime in 2024 after a stakeholder comment period, will broadly impact chemical companies, according to Lynn Kornfeld, a partner at the Denver, Colorado-headquartered law firm Holland & Hart.

'If you're a user of TCE in your processing, or have it in products, understanding where it is and understanding whether there are alternatives and starting to seek those now [is important], rather than being under the gun later,' warns Kornfeld.

Chemical companies should consider commenting on the EPA's proposed rule, during the 45-day comment period from 23 October . 'EPA is still seeking some input on how companies can implement this, and whether the existing chemical exposure levels are something that companies can comply with,' Kornfeld notes.

She points out that this regulatory approach by the EPA to TCE is similar to some of its recent rulemaking for chemicals like the widely used laboratory solvent dichloromethane (methylene chloride). Earlier this year, the agency proposed to ban most uses of dichloromethane under TSCA.

'Today, EPA is taking a major step to protect people from exposure to this cancer-causing chemical,' said Michal Freedhoff, who heads the EPA's Office of Chemical Safety and Pollution Prevention. 'Today's proposal to end these unsafe, unrestricted uses of TCE will prevent future contamination to land and drinking water and deliver the chemical safety protections this nation deserves,' she stated.

But the chemical industry in the US is pushing back. The American Chemistry Council (ACC) points out that TCE has several important uses in packaging and formulation, and as a solvent, where small amounts are used.

'If EPA decides to move forward with restrictions on consumer uses of TCE, it is important that it does not unnecessarily restrict valuable industrial uses,' cautions the ACC, which represents US chemical companies.

Chemistry World, 01 November 2023

https://chemistryworld.com

Psychedelic treatments are speeding towards approval — but no one knows how they work

2023-11-01

Most specialists expect the MDMA approval to go through on the weight of clinical evidence and popular support. Two large trials have shown that the drug can reduce the symptoms of PTSD when administered in controlled therapy sessions1,2. And it seems to do so more quickly than other treatments. But how MDMA and other psychedelics work is still

Psychedelic drugs have been undergoing a major makeover in psychiatry, earning mainstream acceptance that has eluded them for decades. In 2019, a variant of ketamine — an animal tranquillizer well known as a club drug — was approved by the US Food and Drug Administration (FDA) for treating post-traumatic stress disorder (PTSD). In May, Oregon opened its first treatment centre for administering psilocybin — the hallucinogenic compound found in magic mushrooms — following the state's decision to legalize it (psilocybin remains illegal at the federal level). And, after decades of effort, the Multidisci-

largely a mystery, both because the drugs have long been illegal and because psychiatric conditions are difficult to study in animals.

With the regulatory landscape shifting, legal psychedelic research is becoming easier — and potentially more profitable. Neuroscientists, psychiatrists, pharmacologists, biochemists and others are entering the field, bringing fresh ideas about what the drugs do at a cellular and molecular level and trying to unravel how these mechanisms might help to relieve symptoms of psychiatric conditions.

From a clinical perspective, understanding how the drugs work might not matter. "You don't need to know the mechanism of the drug to have a very effective therapy," says David Olson, a biochemist at the University of California, Davis. But, understanding more about psychedelics could lead to the development of proprietary drugs that are safer, less hallucinogenic and ultimately more effective. It could also affect the way psychedelics are administered in the clinic — helping providers to tailor treatments to each person.

Several key questions are driving the basic research that progresses in the background as MDMA and others march towards the market.

What is a psychedelic?

Indigenous cultures around the world have long used naturally occurring drugs such as psilocybin; peyote, which comes from a North American desert cactus; and ibogaine, extracted from the bark of a central-African shrub, to promote connectedness and open minds. Some evidence from the 1950s and 1960s suggested that these drugs and other synthetic compounds, such as ketamine or LSD, might have antidepressant effects3. But such research effectively ended in the late 1960s, when these substances were banned in most countries. The resurgence didn't begin until the early 2000s, when clinical trials testing ketamine and, later, MDMA showed that the compounds worked at least as well as conventional psychiatric drugs1,4.

From a pharmacological viewpoint, the word 'psychedelic' historically refers to hallucinogenic drugs, including psilocybin and LSD, that bind to a serotonin receptor called 5-HT2A found on the surfaces of neurons. Although that definition does not include ketamine or ibogaine, these drugs have often been lumped together with psychedelics in research papers and public discourse. Even tetrahydrocannabinol, the active ingredient in cannabis, is sometimes considered a psychedelic.

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This loose definition, combined with a lack of standardized reagents and protocols, can make it difficult for researchers to compare their work, says Bryan Roth, a pharmacologist at the University of North Carolina at Chapel Hill. "Much of what is being published is contradictory," he says. But differences in the definitions of these drugs are only the beginning.

How do these drugs work?

Considered as a broad group, psychedelics, including ketamine and MDMA, are "fabulously dirty", says Boris Heifets, an anaesthesiologist at Stanford University in California, meaning that they interact with many types of neuron and molecule across the brain. Even the classical psychedelics — such as LSD and psilocybin — interact with numerous receptors other than 5-HT2A. Studies differ on which are necessary for the drugs' proposed psychiatric benefits.

"Honestly this is going to be something that's going to be very difficult to unravel," Olson says. The way that ketamine, for instance, might combat symptoms of depression and PTSD is mysterious. The drug binds to and blocks the NMDA receptor, a channel on the surface of neurons that is deeply tied to forming new connections. Blocking it triggers a parade of molecular events that had not previously been linked to depression.

Some studies suggest that a breakdown product of ketamine that binds to an as yet-unidentified receptor could cause antidepressant effects5. But an October study published in Nature6 found that ketamine can become trapped in the NMDA receptor and suppress activity in certain brain regions for up to 24 hours, which could account for the duration of its effects.

All psychedelic drugs might have something in common, even if they don't use the serotonin receptor. In a paper published earlier this year7, neuroscientist Eero Castrén at the University of Helsinki and his team found evidence that psychedelics, including ketamine and psilocybin, all bind to the receptor for a brain signalling factor called brain-derived neurotrophic factor (BDNF), which is involved in neuron growth and brain rewiring. Conventional antidepressants, such as Prozac (fluoxetine), bind to the receptor, too, but the binding is up to 1,000 times stronger for psychedelics. That could explain why these drugs seem to improve symptoms in hours, whereas conventional antidepressants might take months, Castrén says.

Do psychedelics rewire the brain?

Although not everyone thinks that the BDNF receptor is the key, most scientists do think that psychedelic drugs promote brain plasticity, enabling the dendrites and axons that form neural circuits to diversify and make new connections. Plasticity could help a person with depression to see the world in a different way, or help a person with PTSD to disconnect their memories from a fear response.

But the nature of this plasticity and the brain regions involved are still hotly debated. "People talk about plasticity like there's an understood meaning everyone agrees upon," says Gerard Sanacora, a psychiatrist at Yale University in New Haven, Connecticut. "My concern is it's replacing the 'chemical imbalance' catchphrase", which was once broadly used to describe mental illness. "It's a huge black box."

Plasticity isn't necessarily a good thing either, says Lisa Monteggia, a neuroscientist at Vanderbilt University in Nashville, Tennessee. There are good reasons that the brain's wiring develops in the way it does and maintains connections between experiences and effects. Some conditions, including autism and schizophrenia, might sometimes result from too much plasticity in the brain. Furthermore, all kinds of drug, including cocaine and amphetamines, can induce some sort of plasticity, Monteggia says.

Her group has been studying whether ketamine induces a particular type of plasticity one that allows neurons to regulate how active they are in the face of a stimulus that would normally affect them in a certain way. Unlike the plasticity mechanisms that strengthen or weaken specific neuronal connections during learning and memory, this homeostatic plasticity allows neurons to fight against factors that try to change them. In doing this, ketamine might give the brain the tools it needs to maintain a healthy state. If this mechanism turns out to be true, Monteggia says, ketamine might serve as a "Rosetta Stone" for understanding how other psychedelics work.

Gül Dölen, a neuroscientist at Johns Hopkins University in Baltimore, Maryland, meanwhile, doesn't think psychedelics directly affect plasticity at all. Rather, she says, they might unlock something known as metaplasticity, making neurons more susceptible to a stimulus that induces plasticity — a hormone, for instance. This theory would put more importance on other factors — social interaction, for example, or reimagining a traumatic memory — in reshaping the neurons and forming new connections.

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In a paper published in June in Nature8, Dölen's group gave mice MDMA, ibogaine, LSD, ketamine or psilocybin while they were in the company of other mice. The treated mice became more willing to sleep in a compartment with others, and the effect lasted for weeks. Because adult mice don't tend to change their social behaviour, Dölen says the finding suggests that psychedelics reopened a 'critical period' in which young mice learn to associate sociality with good feelings.

The team also found that the treated animals' neurons started expressing a collection of genes involved in remodelling the protein network that exists outside cells, known as the extracellular matrix. This matrix acts as "grout" between neurons, Dölen says, and breaking it down frees dendrites and axons to form new connections.

What else might these drugs do?

Dölen says that psychedelics could be a "master key" that unlocks critical periods — making them more sensitive to particular stimuli. But much like plasticity, too much metaplasticity could be detrimental. Dölen says it would "melt the brain": breaking hard-earned neural circuits, causing seizures and amnesia, and destroying the ability to learn. That's why the stimulus connected to the drug experience — a social group for mice, for instance, or psychotherapy for humans — could be so important. That context might allow psychedelic therapies to circumvent the "melty brain problem", Dölen says.

The implications could extend beyond psychiatric conditions. Dölen's laboratory is currently testing whether psychedelics can open other critical periods in mice. Opening a critical period in the motor cortex, for instance, might lengthen the amount of time in which people who have had strokes can benefit from physical therapy. Psychedelics might help people to recover lost or impaired senses or even learn a new language, given the right conditions.

If context is essential, the hallucinogenic experience itself might be necessary to open critical periods. "The altered state invites all the different ways of thinking about things," says Rachel Yehuda, a psychiatrist at the Icahn School of Medicine at Mount Sinai in New York City. Her group is studying the use of MDMA and psilocybin in people with PTSD, which the researchers think helps people to open up about traumatic experiences and address them in ways they normally couldn't.

Yehuda's work has found that psychedelic treatment adds chemical markers to genes involved in psychiatric conditions9, although she is

quick to add that psychotherapy can cause the same kind of 'epigenetic changes'. "You do not have to ingest a drug to have a neurochemical change, we have neurochemical changes all the time," she says. The drug might simply enhance the therapy's ability to change a person's perspective permanently. "Clinically, we know there is more to the story than the way a compound is hitting a certain receptor," Yehuda says. "We don't have a full story and I don't think anyone does."

But others think that the direct effects of psychedelics on the brain are responsible for their efficacy. Olson's lab has found that chemical compounds derived from ibogaine and other drugs can increase neuroplasticity and decrease drug-seeking behaviour and depression in mice without causing hallucinations10. Inducing this kind of neuronal growth, he says, might be sufficient for some people, whereas others would benefit from psychotherapy or a transcendent experience. "These are questions that can only be answered in the clinic," he says.

Is it all a placebo effect?

Clinically testing a psychiatric drug against a placebo has always been hard — recipients want it to work, which can affect their level of depression. That's even worse when the drug creates an intense effect, making it unlikely that a study participant would mistake a placebo for the real thing. The FDA has approved a system for MDMA trials in which psychiatrists, who are not involved with administering therapy, evaluate the improvement in each person's symptoms without knowing who received the drug. The agency is therefore waiving its usual requirement to conceal treatment status from participants and the physicians administering the drugs during trials.

Heifets might have found a way to test the intensity of the placebo effect. In a small study11 posted on the preprint server medRxiv in June, his team tested ketamine in people undergoing surgery who were put under anaesthesia and unable to experience the drug's dissociative effects. People coming out of surgery often experience heightened symptoms of depression. But the researchers found that regardless of whether a patient received ketamine or a placebo, their symptoms improved if they thought they might be getting the drug.

Although Heifets isn't entirely sure why the placebo worked as well as ketamine, he suspects that the expectation of receiving the drug itself might have improved their mood. That's not necessarily a bad thing or "just a placebo effect", he says. After all, if a person's symptoms improve, it suggests that something is changing in their brain. "What our data

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strongly suggest is that non-drug factors are powerful mediators," Heifets says. "It forces a bit of reconsideration of what 'placebo' means."

Sanacora agrees: the expectation of receiving a drug could be one of many factors — both psychological and biochemical — that contribute towards psychedelics' overall effectiveness. "We'd be very naive to not realize that expectations play a large role," he says.

The real test will come with drugs that are similar to psychedelics but don't induce strong effects, including hallucinations. Olson's team and his start-up company, Delix Therapeutics in Boston, Massachusetts, are among those developing spin-off drugs that target the same brain pathways as psychedelics and cause plasticity without the trip. Several of these drugs, derivatives of ibogaine, LSD or other psychedelics, are now in clinical trials to determine whether they can treat mental illnesses. If they have the same clinical benefits, Olson says, they could be useful for certain people, including those with psychiatric conditions that can be triggered by an emotional experience. They could also avoid some side effects, such as heart conditions linked to drugs such as MDMA.

From a more practical standpoint, pharmaceutical companies can't patent a drug such as LSD, but they could patent a derivative with the same mechanism of action. A new drug with a known mechanism would be easier to regulate as well — agencies such as the FDA still worry about the potential for abuse with party drugs such as ketamine and MDMA.

Wherever the psychedelic business ends up, these mind-expanding drugs might broaden researchers' thinking about concepts such as neuroplasticity, psychology and the wiring of the brain. "What excites me most about psychedelics is they're incredibly useful tools for understanding the basic biology of the brain," Olson says.

Nature, 01 November 2023

https://nature.com

Secrets of the purple smoke of first high explosive created by alchemists revealed

2023-11-07

Fulminating gold is not actually a chemical fulminate, a compound containing the ion CNO-, such as mercury(II) fulminate or silver fulminate. Instead, it is a mixture of a number of different compounds with gold(III) compounds complexed with ammonia providing most of the explosive

The mystery behind why the world's first high explosive, fulminating gold, produces a purple smoke when it detonates has been solved, finally resolving a 400-year-old alchemical puzzle.

punch. Its name comes from its explosive nature, from the Latin fulmen, or lightning. It was first mentioned by alchemists in the 16th century, and described by the German alchemist Sebald Schwaertzer, purportedly in 1585, to create 'a beautiful, purple-coloured Aurum Fulminans' within four days.

Over time, fulminating gold became the subject of several myths, including that the explosion was only directed downward, attracting the interest of Europe's scientists. Major figures of the 17th and 18th century – including Robert Hooke, Carl Wilhelm Scheele and Antoine Lavoisier – all studied it, and it even temporarily blinded Jöns Jakob Berzelius when he dropped a breaker containing a sample in 1809, resulting in glass shards in his eye and permanent, purple-coloured scars on his hand. However, while the chemistry of the fulminating gold recipe has been understood for centuries, one question has lingered: why does its detonation produce purple smoke?

Now, Simon Hall's team at the University of Bristol has discovered the answer. The most common explanation for the purple smoke is that it contains gold nanoparticles. These metal nanoparticles are able to host an unusual phenomenon as a result of their size: wave-like oscillations in their electron clouds. These quasiparticles, known as surface plasmons, can interact with incoming light absorbing some wavelengths and reflecting others that have a longer wavelength than the oscillations in the electron cloud. However, this had never been confirmed experimentally. To do so, the team created fulminating gold, then detonated 5mg samples on aluminium foil by heating it; they then captured the smoke using copper meshes, and investigated what they had caught using transmission electron microscopy.

Sure enough, the team discovered the smoke contained spherical gold nanoparticles ranging in size from 30nm to 300nm, confirming the theory that the gold was playing a role in the mysterious smoke. The particles' presence also explains many of the other mysteries of the explosive, including why Berzelius' scars were purple (the wavelength of violet light is about 400nm), and how the explosive was used by alchemists to coat objects in a purple patina.

'The work confirms the long-held assumption that the purple fumes of fulminating gold contain elemental gold in the form of nanoparticles,' confirms Curt Wentrup, an organic chemist at the University of Queensland, who has researched the topic in the past.

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However, he adds, there is still one final mystery about fulminating gold: who discovered it? Although Schwaertzer's Chyrosopoeia Schwaertzeriana claimed it was written about in 1585, it was only published in 1718. Instead, Wentrup adds, the real originator was an alchemist (probably a German salt maker called Johann Thölde) writing under the pseudonym of a monk called Basil Valentine, who published the recipe in 1599 in his Twelve Keys of Basil Valentine. Schwaertzer, Wentrup adds, 'clearly refers to Basil Valentine' in his work – something not possible if he had really published his book 14 years earlier.

Chemistry World, 07 November 2023

https://chemistryworld.com

Anti-Anxiety Drug May Improve Brain Cancer Therapy

2023-10-27

A new research study shows that cerebro-spinal fluid reduces current treatment efficacy in brain cancer and identifies new therapeutic opportunities.

Cerebrospinal fluid, the clear colourless liquid that protects the brain, also may be a factor that makes brain cancers resistant to treatment, Australian researchers led by Associate Professor Cedric Bardy at the South Austraila Health and Medical Research Institute (SAHMRI) and Flinders University reveal in the journal Science Advances.

Reporting how this occurs, the study in high-profile journal Science Advances shows that a decades-old anti-anxiety drug can improve the effectiveness of chemo-radiotherapy towards glioblastoma, or GBM, the most common and lethal brain cancer.

Brain cancers kill more children and adults under 40 than any other cancer. They are resistant to therapies that kill cancers elsewhere in the body. The study team speculates that unique brain features might contribute to this.

The collaborative Australian team of neurobiologists, neurosurgeons and oncologists tested the effect of the precious resource of human cerebrospinal fluid on the growth of tumour cells collected from 25 local patients with glioblastoma.

Among their findings, the tumour cells quickly changed their identity and became more resistant to radiation and the drug temozolomide, which are mainstays of glioblastoma therapy.

Associate Professor Cedric Bardy says, "Glioblastoma kills so many people who are otherwise fit, healthy and young, within months. This is a horrible disease, and the treatments available are just not effective enough despite serious side effects.

"This study helps us understand the limitations of the current chemotherapies and provides new hope for repurposing a class of drugs that could be added to the standard of care. We are working hard now to try this on patients in a clinical trial."

Investigating the molecular basis for these changes, the team found glioblastoma cells exposed to cerebrospinal fluid were more resistant to ferroptosis, a form of therapy-induced cell death.

Importantly, they showed that trifluoperazine, an anti-anxiety drug used since the 1950s, could re-sensitise glioblastoma cells to both therapies. In contrast, trifluoperazine was found not to harm healthy brain cells. The researchers concluded that combining trifluoperazine with standard care may improve GBM patient survival.

Technology Networks, 27 October 2023

https://technologynetworks.com

Newer rheumatoid arthritis drugs work well in the real world

2023-11-05

Now, researchers in Japan have taken an important step in changing that, using extensive patient data to show that JAK inhibitors are as effective a first-line treatment as existing medications, even though they're still largely considered a back-up plan if others fail.

"Real-world patients have different characteristics compared with the patients recruited in randomized controlled trials," the researchers note in the study. "Therefore, it is important to investigate the effectiveness and safety of JAK inhibitors in real-world settings."

Analyzing the data of 622 patients from the ANSWER cohort study, the scientists evaluated four JAK inhibitors; baricitinib (BAR) known in the US as Olumiant, tofacitinib (TOF) known as Xeljianz, and upadacitinib (UPA) known as Rinvoq. They also assessed peficitinib (PEF), or Smyraf, which is predominantly available in Japan and Southeast Asia.

"We found that most patients have success with these medications, and the efficacy and safety of each of these JAK inhibitors was not significantly different in the treatment of rheumatoid arthritis," says lead author Dr Shinya Hayashi, a arheumatology specialist at Kobe University. "These medications offer options when biologic disease-modifying antirheumatic drugs (DMARDS) have failed."

They've been approved for the US market since 2012, but Janus kinase (JAK) inhibitors are still the new kid on the block in terms of rheumatoid arthritis treatment. As such, the real-world evidence on this class of drugs is scarce compared to established treatments.

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JAK inhibitors interrupt signals that cause inflammation. With rheumatoid arthritis, the body makes too many proteins called cytokines, which play a key role in inflammation. When these cytokines attach to immune cell receptors, the message is given to make even more of the proteins. JAK inhibitors block this messaging pathway, which calms the immune system response and, in turn, relieves painful arthritis inflammation.

JAK inhibitors are also effective for treating skin conditions such as eczema and vitiligo, and there are now around a dozen different types approved for use in the US.

Traditionally, the first treatment for rheumatoid arthritis is usually injections of methotrexate, a DMARD. Then, if the drugs don't do the trick, or they come with too many side effects, a patient may then be switched to an orally administered JAK inhibitor. The patients in the study had received the JAK inhibitor following poor responses to DMARDs.

But because they're a newer class of medication, much like glucagon-like peptide 1 (GLP-1) agonists for weight loss, they are often considered a 'when all else fails' plan B. Doctors generally prescribe DMARD biologics first, because there's more long-standing research available on these.

The researchers, assessing the data with various pain-indicator surveys, found that around 90% of the 622 patients were still taking their JAK inhibitors six months after beginning them.

Overall, about one-third of patients saw their arthritis enter remission within the six months, with more than 80% experiencing 'low disease activity,' in which symptoms were largely controlled.

The hesitancy in JAK inhibitors uptake has been due to concerns about real-world efficacy beyond controlled trials – which this study lays to rest – and potential side effects.

While the researchers say the study has its limitations, such as six months being a short time frame for long-term side effects, and a lack of studies comparing all classes of drugs, the four JAK inhibitors performed similarly to each other, and their effectiveness proved to be on par with existing DMARDs. A previous clinical study, showed they had comparable efficacy to TNF inhibitors, another type of DMARD.

Around 1.3 million Americans have rheumatoid arthritis, a chronic autoimmune condition that can greatly diminish quality of life and prove stubborn to treat.

The study was published in the journal Rheumatology.

New Atlas, 05 November 2023

https://newatlas.com

Scientists may have detected exotic nitrogen-9 isotope

2023-11-02

Researchers are interested in nuclei with large imbalances in the number of protons and neutrons that they contain. These proton- or neutron-rich nuclei tend to have exotic physical properties and offer scientists a way to study extreme examples of nuclear structure.

In an experiment at the National Superconducting Cyclotron Laboratory at Michigan State University, the US–China team fired an intense beam of oxygen-16 atoms at a beryllium target. From the products of this event, the team isolated a secondary beam of oxygen-13 atoms that were fired at a second beryllium target. Among the products formed during this event, the team detected a signal that seems likely to correspond to nitrogen-9 nuclei.

If confirmed, nitrogen-9 would be the first nuclide that decays by releasing five protons and an alpha particle. Boron-7, fluorine-13, sodium-17 and potassium-31 are currently the only known three-proton emitters, while carbon-8 and magnesium-18 are the only two nuclei that decay by the emission of four protons.

The team are now planning follow up experiments to provide further evidence for the finding.

Chemistry World, 02 November 2023

https://chemistryworld.com

An exotic nitrogen isotope featuring seven protons and just two neutrons may have been created by a research team from China and the US. The nitrogen-9 nucleus would be the first known example that decays by releasing five protons.

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Fleeting phenomenon of water autoionisation pinned down by neural network simulations

2023-11-08

'The autoionisation of water has been a subject of extensive study since Arrhenius first proposed it in 1884,' comments Gabriel Merino at Cinvestav-Mérida, Mexico, who wasn't involved in the study. During the reaction, water molecules dissociate to form hydronium and hydroxide ions, but finding out exactly how that happens hasn't been easy. 'Accurate modelling of this process has posed a challenge,' notes Merino. He believes that the results obtained by Liu and his colleagues are an important step in the right direction. 'The essence of their achievement is accomplishing both time efficiency and high accuracy – made possible through well-tempered machine learning-assisted metadynamics – which allows the generation of nanosecond-scale free energy landscapes that result in the precise reproduction of two fundamental chemistry constants: the equilibrium constant and the autoionisation constant of water.'

The team reported values of pKw=14.14 and kD=1.369 x 10-3s-1 for these two constants, respectively, both very close to experimental results. Liu points out that this is the first time that such close agreement between experimental data and modelling has been achieved and explains that this was possible because the new approach enables the characterisation of critical intermediate and transition states involved in the process. 'Due to the limited number of molecular dynamics trajectories, previous studies lacked sufficient statistical sampling to mimic the complex ionisation pathway,' he says, adding that the huge stability difference between water and the dissociated ions makes it impossible to obtain suitable data from conventional ab initio calculations.

'To overcome this computational bottleneck, a machine learning technique was employed to replace the time-consuming DFT calculations,' says Liu. He mentions that with the help of metadynamics, such large stability differences between reactants and products can be reduced by iteratively 'filling' the potential energy of the system, enabling frequent samplings throughout the whole reaction.

After analysing their results, the scientists concluded that the triple-proton transfer that initiates water autoionisation is a concerted process because they only observed one transition state located on the dissociation free-energy surface. 'However, a strong asynchronous character was also confirmed, where the transfer of the third proton is obviously delayed,'

Scientists in China have combined molecular dynamics with machine learning to carry out precise nanosecond-scale simulations of water ionisation,1 shedding light on a process that has been known for over a century but was tricky to understand because the events involved are so rare and hard to follow. 'The extremely scarce probability of observing water ionisation under natural conditions obstructs direct experimental probing and poses a great challenge to the theoretical community for characterising the free-energy profile and revealing the reaction mechanism,' says Ling Liu from Nanjing University,

notes Liu. 'This finding resolves disputes on whether water ionisation proceeds through double- or triple-proton transfer.'

Liu adds that water ionisation occurs through what he and his team call a dual presolvation mechanism, which starts with a pair of hypercoordinated and undercoordinated waters bridged by a water molecule. 'This invokes an enhanced local electric field on the migrating protons and introduces a push–pull effect to promote water dissociation,' he says.

Merino believes that the new results could have a significant impact in chemistry because the methodology 'can be applied to a wide range of phenomena involving water and dissociation processes'.

Chemistry World, 08 November 2023

https://chemistryworld.com

Could the Next Successful Antiviral Come From Willow Tree Bark?

2023-11-08

From a seasonal cold to a stomach bug, nobody likes catching a virus — and epidemics can be devastating. We need safe, sustainable antiviral options to treat the outbreaks of the future. Scientists in Finland have now shown that an extract of willow bark — a plant which has already provided several medicines, including the precursor to modern aspirin — has a broad-spectrum antiviral effect in cell sample experiments.

The extract worked both on enveloped coronaviruses, which cause colds as well as Covid-19, and non-enveloped enteroviruses, which cause infections such as flu and meningitis. There are no clinically approved drugs which work against enteroviruses directly, so this extract could be a future game-changer.

"We need broadly acting and efficient tools to combat the virus load in our everyday life," said Prof Varpu Marjomäki of the University of Jyväskylä, senior author of the study in Frontiers in Microbiology. "Vaccinations are important, but they cannot deal with many of the newly emerging serotypes early enough to be effective on their own."

Medicines from nature

The scientists had previously tested willow bark extract on enteroviruses, and found it was highly successful: in this new study, they expanded the

Scientists have found that specially processed samples of willow bark extract have an antiviral effect which isn't seen in already known medical compounds from willow bark, such as salicylic acid, the precursor to modern aspirin. The extract worked against two common types of virus with very different structures, enteroviruses and coronaviruses, suggesting the potential for a new broad-spectrum antiviral to help us fight viruses that are otherwise hard to treat.

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remit of their research to look at additional kinds of virus and to try to understand the mechanism of the extract's action.

To make the extract, they harvested commercially grown willow branches. The bark was cut into pieces, frozen, ground, and then extracted using hot water. This produced the extract samples which the scientists tested against enteroviruses — strains of Coxsackievirus A and B — and coronaviruses — a seasonal coronavirus and Covid-19.

The scientists used a cytopathic effect inhibition assay to see how long the extract took to act on infected cells and how well it inhibited viral activity. The extract did not harm the cells themselves and efficiently protected cells from infection. A binding assay carried out on the Covid-19 samples further showed that although this virus could enter cells even if treated with the extract, it couldn't reproduce once it was inside.

Catching viruses out

The authors had previously found that the extract was effective against enteroviruses, which meant it could act against two differently-structured types of virus, enveloped and non-enveloped. However, the mechanism of action appeared to be very different, because treated enteroviruses couldn't enter cells.

The scientists then experimented with the timing of addition of the extract to see if the extract attacked particular stages of the virus life cycle. They found that the extract seemed to act on the surface of the virus, rather than any given stage of its replication cycle.

They also examined the treated virus under the microscope to understand the effects of the extract better. Both viruses clustered together instead of spreading out, but the enveloped coronaviruses appeared to have been broken down, while the non-enveloped enteroviruses appeared to have been locked down, prevented from releasing their genome and reproducing.

"The extracts acted through distinct mechanisms against different viruses," said Marjomäki. "But the extracts were equally effective in inhibiting the enveloped as well as non-enveloped viruses."

Future treatment for colds and flu?

The authors also tested existing medical compounds derived from willow bark, as well as commercially prepared salixin extract and salixin powder. Of these, only the salixin extract showed antiviral activity, suggesting

that the success of the scientists' willow bark extract could result from the interactions of different bioactive compounds.

The scientists fractionated their extract to understand its chemical composition, but didn't get clear answers as to which of the many effective compounds might be primarily responsible for the antiviral effect. Further research will be needed to understand the bioactive compounds involved, their chemical structure, and how they work, potentially leading to revolutionary new antiviral treatments.

"We are presently continuing fractionations and bioactive molecule identification from willow bark extracts," said Marjomäki. "This will give us a number of identified pure molecules which we can study in further detail. Also, we will study a larger number of viruses with purified components. Purified components will give us better opportunities to study their mechanisms of action."

Technology Networks, 08 November 2023

https://technologynetworks.com

Fructose Might Be the Primary Driver of Obesity

2023-11-06

Commonly known as "fruit sugar," fructose is a simple, monosaccharide sugar found in many plants. But the compound that sweetens your watermelon, apples, and oranges can mess with your cells' energy metabolism, Richard Johnson, a professor of medicine at the University of Colorado, and his co-authors Laura G. Sánchez-Lozada and Miguel A. Lanaspa explain in a paper published October 17 in the journal Obesity.

"We suggest that obesity is not a disease of energy excess but rather a disease of energy crisis," they wrote.

The fructose hypothesis

As studies in rodents have elucidated, fructose uniquely suppresses the function of mitochondria compared to other nutrients. When these cellular powerhouses are slowed, the cells get stuck in a low-energy state, triggering hunger and thirst. Eating nutrients including fats and protein eventually restores cellular energy levels, but not before we've eaten more calories than we need. This excess gets stored as fat.

Numerous hypotheses attempt to explain obesity's meteoric rise over the past few decades. There's the energy balance hypothesis, which states that weight gain is due to consuming more calories than the amount expended. There's the carbohydrate-insulin hypothesis, which argues that excess consumption of carbohydrates stimulates an insulin response that drives cells to accumulate fat. Then there's the protein-leverage hypothesis, which suggests that we don't eat enough protein, driving incessant hunger. Now, researchers have put forth a new hypothesis that places the blame on a sugar

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In the long term, frequent fructose exposure can damage mitochondria and reduce the amount of mitochondria in cells, the researchers say, locking people in a low-energy state which drives chronic overeating.

High-fructose corn syrup in processed foods is a common source of fructose, but many other sugars such as honey and cane sugar also contain the compound. Due to our body's metabolism, refined carbohydrates, salty foods, and alcohol (particularly beer) also generate fructose. As already mentioned, fruits contain fructose, but Johnson and his colleagues say that they are still quite healthy to eat. The amount of fructose inside whole fruits is far less than what is inside juices or candy. Moreover, the fibers present counteract fructose's negative metabolic effects.

Obesity's "theory of everything"

Like physicists attempting to combine general relativity and quantum mechanics with a "theory of everything," the researchers behind the fructose-survival hypothesis say that it unifies the other obesity-explaining hypotheses rather than competes with them. Fructose's energy-reducing effect underlies all of them.

With food in abundance, the metabolic changes driven by fructose result in obesity and poor health today, but they would have aided our survival in the deep past, when food was scarcer. For example, finding a fruit tree would likely have been a rare, fortuitous event for our ancestors. It would have been in their interest to eat as much as possible before the fruits fell off and rotted or were eaten by another animal. These calories could then be stored as fat to provide energy when food was not as plentiful.

But in much of the world today, food scarcity is not a problem, and fructose can be found in a great many of the things we eat, particularly those that are processed. So what can be done?

In a book published last year, Johnson recommended avoiding soft drinks, fruit juices, and other super sugary foods, watching salt intake, and limiting red meat and alcohol consumption, among other basic dietary tips. He also urged regular exercise as it stimulates mitochondrial activity and growth.

Johnson's ultimate goal is to bring a drug that inhibits fructose metabolism to market. He's working on formulating and testing one now, and hopes that his efforts will bear fruit in the next five years or so.

Real Clear Science, 6 November 2023

https://realclearscience.com

Consensus definition of sustainable chemistry sets a clear direction for science, governments and investors

2023-11-09

25 years ago, John Warner and Paul Anastas published their 12 principles of green chemistry. These principles were widely adopted as the field's guiding framework and have helped green chemistry evolve into a major chemistry subdiscipline. By contrast, the field of sustainable chemistry has no such framework and is under-developed in comparison, despite having a great deal of overlap.

Moreover, recent legislative efforts by both the European Commission and the US Government require criteria that can be used to determine whether a chemical process is sustainable. The US Sustainable Chemistry Research and Development Act, 2021, for example, mandates the US Office of Science and Technology Policy to define sustainable chemistry.

Joel Tickner from the University of Massachusetts Lowell in the US, who put the working group behind the definition together, says groups other than chemical researchers will benefit from the definition. A key example is investors, who are increasingly conscious of the impacts of climate change and need some way to determine which companies are working in a sustainable way. Similarly, governments who want to incentivise more sustainable practices through tax benefits need criteria to determine who qualifies. 'It's important to find a measurable way to evaluate progress and to avoid greenwashing,' explains Tickner.

The working group comprised 20 individuals from academia, industry, government, the investment community and the not-for-profit sector. While the majority were from North America or Europe, the working group accounted for bias arising from this by forming a subcommittee with a specific mandate to consider and incorporate other perspectives. This subcommittee was particularly focused on environmental justice, such as people from certain ethnic groups or economic demographics being disproportionately exposed to harmful substances released into the environment by the chemical industry because of where they live.

Sustainable chemistry should be defined as 'the development and application of chemicals, chemical processes, and products that benefit current and future generations without harmful impacts to humans or ecosystems.' That's the outcome of a working group tasked with developing a robust and actionable definition. They've also come up with a set of criteria to accompany the definition that considers social equality, safety and transparency, among other things.

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To arrive at a satisfactory definition, the working group had to make compromises. For example, Tickner says in an early draft 'we had the word "eliminate" a lot, and a lot of the industry people said "eliminating hazards is just not going to happen, you can't fully get rid of hazards.' So, we changed some of the language to soften it, but then made it clear that this is where we'd like to go. We understand that we're probably never going to get there, but unless you have that north star, you're never going to aim for it.'

'The definition has resulted from a considered and detailed process – it strikes me as as reasonable a working definition as any to go with right now,' comments Helen Sneddon, an expert in green chemistry from the University of York in the UK. However, she says it's important that the definition enables action: 'There is value in having [a definition] to align different groups – and save time. Ultimately, we want to be making a difference not revisiting definitions to make sure everyone is on the same page each time different stakeholders meet.'

Tickner echoes this sentiment and accepts that the new definition is only a starting point. The next step will be to develop metrics that can be used to measure companies and processes by criteria laid out alongside the definition, thereby allowing it to be put to practical use.

Chemistry World, 09 November 2023

https://chemistryworld.com

Ketamine Clinics Misleading Consumers About Side Effects, Suggests Study

2023-11-07

The review was published in a research letter in JAMA Network Open.

Dr. Michael DiStefano, a study co-author and assistant professor in the Department of Clinical Pharmacy at the University of Colorado Anschutz Medical Campus, said that the marketing materials used by direct-to-consumer advertisers may create "unrealistic expectations" for potential clients.

Ketamine: legal but unapproved

Ketamine has been used as an anesthetic drug in human and animal medicine for decades. It has been swept up in the search for rapid-acting antidepressant molecules and a variant of the compound, Janssen's drug Spravato®, has been approved by the US Food and Drug Administration

An analysis of Maryland ketamine advertisers has suggested that their websites and marketing materials are awash with false and misleading claims about the drug's addictiveness, side effects and approval status.

(FDA) for treatment-resistant depression. Generic ketamine has also been the subject of numerous clinical trials as an antidepressant but is importantly not approved by the FDA for any psychiatric use. Instead, the drug is used off-label by physicians for this purpose, alongside a long list of other conditions, including everything from chronic pain, to opioid withdrawal and even Lyme disease.

DiStefano's study reviewed the websites of 17 ketamine advertisers across 26 locations in Maryland. The providers offered a battery of potential ketamine procedures, including infusions, intramuscular injections and oral or intranasal administrations of the drug. Of these 17, 10 failed to mention that the ketamine treatment they offer is an off-label procedure. "[Patients] will also likely spend a substantial amount out-of-pocket to access these treatments, as off-label or experimental treatments are not often covered by insurance," says DiStefano. These bills could potentially be vast: the cost per infusion varied from $360 to $2500 at some clinics.

One clinic even falsely claimed that their ketamine treatment was FDA-approved.

Addictiveness overlooked

The team also looked at the list of side effects and risks disclosed by the ketamine providers in their promotional materials. Outside of the clinic or operating room, ketamine has a second life as a party drug and is addictive. DiStefano's analysis showed that 7 of 17 providers failed to mention the drug's potential for misuse or addiction in their promotional materials, while 9 didn't warn consumers that there would be a risk from driving after taking the drug. A trio of providers even falsely stated that ketamine was non-addictive on their website.

The high cost of these treatments means abuse at the clinics themselves is unlikely, but that same financial barrier means patients could potentially be driven to take the drug illicitly, although there is limited evidence of this happening in practice. This isn't the only risk, says DiStefano, "There are concerns other than addiction, such as effects on cognition, from repeated dosing with ketamine. More research is needed to understand these potential long-term effects."

The authors note that as the clinics and advertisers featured in the study don't manufacture, pack or distribute the ketamine they administer, an FDA loophole leaves them outside the agency's regulatory remit. This is an oversight that should be rectified as soon as possible, says DiStefano:

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"The FDA's regulatory authority could be clarified or updated to apply to consumer advertising by any business entity that sells prescription drugs."

Technology Networks, 7 November 2023

https://technologynetworks.com

"Superatomic" material beats silicon for fastest semiconductor ever

2023-11-31

Semiconductors are the beating heart of electronic devices, and silicon reigns supreme. These materials form the basis of transistors and integrated circuits, which themselves lay the foundation for smartphones to supercomputers and everything in between.

Now, scientists at Columbia University have found a new semiconductor material that seems to outperform all the rest. Known as Re6Se8Cl2, the material is made up of a mix of rhenium, selenium and chlorine, the atoms of which cluster together and behave like one big atom – a "superatom." And this is where it gets its speed.

In any material, the atomic structure gives off tiny vibrations that travel as quantum particles called phonons, which can scatter energy-carrying particles like electrons or excitons. This energy is quickly lost as heat, and managing it is a constant hurdle in designing electronic chips and systems.

But Re6Se8Cl2 has a neat little trick up its sleeve. Its excitons don't scatter when they're hit by phonons but actually bind to them, creating another form of quasiparticle called acoustic exciton-polarons. These can still carry energy, but travel much more slowly than regular excitons – and counterintuitively, this ultimately leads to faster speeds than in silicon.

The team compares it to the old story of the tortoise and the hare. Electrons can travel very quickly through silicon, but they tend to bounce all over the place, which isn't the most efficient travel path. The polarons in Re6Se8Cl2, on the other hand, are slower and aren't affected by other phonons, so they move farther and more consistently over time.

In effect, the team found that the polarons in Re6Se8Cl2 moved about twice as fast as electrons in silicon. Taking into account that they can be controlled by light instead of electricity, the team estimates that theoretical electronic devices made using the material could end up six orders of magnitude faster than existing ones.

Scientists have found that a "superatomic" material is the fastest and most efficient semiconductor ever. Taking advantage of a tortoise-and-hare mechanism, the new material can transport energy much faster than silicon.

"In terms of energy transport, Re6Se8Cl2 is the best semiconductor that we know of, at least so far," said Milan Delor, an author of the study.

Unfortunately, don't expect blistering-fast processors using the material in your computer any time soon – the team says it's unlikely this particular concoction will ever make it to market. Rhenium is just too rare and expensive for consumer goods. But having proved the concept, the researchers believe similar, hopefully cheaper materials might exhibit the same behavior.

"We can now start to predict what other materials might be capable of this behavior that we just haven't considered before," said Delor. "There is a whole family of superatomic and other 2D semiconductor materials out there with properties favorable for acoustic polaron formation."

The research was published in the journal Science.

New Atlas, 31 October 2023

https://newatlas.com

New antifungal molecule kills fungi without toxicity in human cells, mice

2023-11-08

Amphotericin B, a naturally occurring small molecule produced by bacteria, is a drug used as a last resort to treat fungal infections. While AmB excels at killing fungi, it is reserved as a last line of defense because it also is toxic to the human patient—particularly the kidneys.

"Fungal infections are a public health crisis that is only getting worse. And they have the potential, unfortunately, of breaking out and having an exponential impact, kind of like COVID-19 did. So let's take one of the powerful tools that nature developed to combat fungi and turn it into a powerful ally," said research leader Dr. Martin D. Burke, an Illinois professor of chemistry, a professor in the Carle Illinois College of Medicine and also a medical doctor.

"This work is a demonstration that, by going deep into the fundamental science, you can take a billion-year head start from nature and turn it into something that hopefully is going to have a big impact on human health," Burke said.

Burke's group has spent years exploring AmB in hopes of making a derivative that can kill fungi without harm to humans.

A new antifungal molecule, devised by tweaking the structure of prominent antifungal drug Amphotericin B, has the potential to harness the drug's power against fungal infections while doing away with its toxicity, researchers at the University of Illinois Urbana-Champaign and collaborators at the University of Wisconsin-Madison report in the journal Nature.

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In previous studies, they developed and leveraged a building block-based approach to molecular synthesis and teamed up with a group specializing in molecular imaging tools called solid-state nuclear magnetic resonance, led by professor Chad Rienstra at the University of Wisconsin-Madison. Together, the teams uncovered the mechanism of the drug: AmB kills fungi by acting like a sponge to extract ergosterol from fungal cells.

In the new work, Burke's group worked again with Rienstra's group to find that AmB similarly kills human kidney cells by extracting cholesterol, the most common sterol in people. The researchers also resolved the atomic-level structure of AmB sponges when bound to both ergosterol and to cholesterol.

"The atomic resolution models were really the key to zoom in and identify these very subtle differences in binding interactions between AmB and each of these sterols," said Illinois graduate student Corinne Soutar, a co-first author of the paper.

"Using this structural information along with functional and computational studies, we achieved a significant breakthrough in understanding how AmB functions as a potent fungicidal drug," Rienstra said. "This provided the insights to modify AmB and tune its binding properties, reducing its interaction with cholesterol and thereby reducing the toxicity."

Armed with the information from the NMR studies, the Illinois team began synthesizing and testing derivatives with slight changes to the region that binds to ergosterol and cholesterol, while also boosting the kinetics of the ergosterol-removing process to maintain efficacy.

Enabled by collaborators and facilities at the Carl R. Woese Institute of Genomic Biology and U. of I. veterinary clinical medicine professor Dr. Timothy Fan, the researchers tested the most promising derivatives—first with in vitro assays, quickly assessing the efficacy in killing fungi; then moving to cell cultures and eventually live mice, assessing toxicity.

One molecule, dubbed AM-2-19, stood out from the rest.

"This molecule is kidney-sparing, it is resistance evasive and it has broad spectrum efficacy," said postdoctoral researcher Arun Maji, a co-first author of the paper. "We tested this molecule against over 500 different clinically relevant pathogen species in four different locations. And this molecule completely surprised us by either mimicking or surpassing the efficacy of current clinically available antifungal drugs."

The researchers tested AM-2-19 in human blood and kidney cells to screen for toxicity. They also tested AM-2-19 in mouse models of three common, stubborn fungal infections and saw high efficacy.

"During my medical rotations, we called AmB 'ampho-terrible,' because of how hard it was on patients," Burke said. "Decoupling the efficacy from the toxicity turns 'ampho-terrible' into 'ampho-terrific.' We are very excited about the potential we are seeing, although clinical study is needed to see if this potential translates to people."

As a first step toward clinical application, AM-2-19 has been licensed to Sfunga Therapeutics and recently entered Phase 1 clinical trials.

Phys Org, 08 November 2023

https://phys.org

"Super Melanin" Can Heal and Protect the Skin From Sun Damage

2023-11-02

In a new study, the scientists show that their synthetic melanin, mimicking the natural melanin in human skin, can be applied topically to injured skin, where it accelerates wound healing. These effects occur both in the skin itself and systemically in the body.

When applied in a cream, the synthetic melanin can protect skin from sun exposure and heals skin injured by sun damage or chemical burns, the scientists said. The technology works by scavenging free radicals, which are produced by injured skin such as a sunburn. Left unchecked, free radical activity damages cells and ultimately may result in skin aging and skin cancer.

Melanin in humans and animals provides pigmentation to the skin, eyes and hair. The substance protects your cells from sun damage with increased pigmentation in response to sunlight — a process commonly referred to as tanning. That same pigment in your skin also naturally scavenges free radicals in response to damaging environmental pollution from industrial sources and automobile exhaust fumes.

"People don't think of their everyday life as an injury to their skin," said co-corresponding author Dr. Kurt Lu, the Eugene and Gloria Bauer Professor of Dermatology at Northwestern University Feinberg School of Medicine and a Northwestern Medicine dermatologist. "If you walk barefaced every day in the sun, you suffer a low-grade, constant bombardment of

Imagine a skin cream that heals damage occurring throughout the day when your skin is exposed to sunlight or environmental toxins. That's the potential of a synthetic, biomimetic melanin developed by scientists at Northwestern University.

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ultraviolet light. This is worsened during peak mid-day hours and the summer season. We know sun-exposed skin ages versus skin protected by clothing, which doesn't show age nearly as much."

The skin also ages due to chronological aging and external environmental factors, including environmental pollution.

"All those insults to the skin lead to free radicals which cause inflammation and break down the collagen," Lu said. "That's one of the reasons older skin looks very different from younger skin."

When the scientists created the synthetic melanin engineered nanoparticles, they modified the melanin structure to have higher free radical scavenging capacity.

"The synthetic melanin is capable of scavenging more radicals per gram compared to human melanin," said co-corresponding author Nathan Gianneschi, the Jacob and Rosaline Cohn Professor of Chemistry, Materials Science & Engineering, Biomedical Engineering and Pharmacology at Northwestern. "It's like super melanin. It's biocompatible, degradable,nontoxic and clear when rubbed onto the skin. In our studies, it acts as an efficient sponge, removing damaging factors and protecting the skin."

Once applied to the skin, the melanin sits on the surface and is not absorbed into the layers below.

"The synthetic melanin stabilizes and sets the skin on a healing pathway, which we see in both the top layers and throughout the body," Gianneschi said.

Pivoting to a new theory

The scientists, who have been studying melanin for nearly 10 years, first tested their synthetic melanin as a sunscreen.

"It protected the skin and skin cells from damage," Gianneschi said. "Next, we wondered if the synthetic melanin, which functions primarily to soak up radicals, could be applied topically after a skin injury and have a healing effect on the skin? It turns out to work exactly that way."

Lu envisions the synthetic melanin cream being used as a sunscreen booster for added protection and as an enhancer in moisturizer to promote skin repair.

"You could put it on before you go out in the sun and after you have been in the sun," Lu said. "In both cases, we showed reduction in skin damage and inflammation. You are protecting the skin and repairing it simultaneously. It's continuous repair."

The cream could also potentially be used for blisters and open sores, Lu said.

Topical cream quiets immune system

Gianneschi and Lu discovered that the synthetic melanin cream, by soaking up the free radicals after an injury, quieted the immune system. The stratum corneum, the outer layer of mature skin cells, communicates with the epidermis below. It is the surface layer, receiving signals from the body and from the outside world. By calming the destructive inflammation at that surface, the body can begin healing instead of becoming even more inflamed.

"The epidermis and the upper layers are in communication with the entire body," Lu said. "This means that stabilizing those upper layers can lead to a process of active healing."

How the experiment worked

The scientists used a chemical to create a blistering reaction to a human skin tissue sample in a dish. The blistering appeared as a separation of the upper layers of the skin from each other.

"It was very inflamed, like a poison ivy reaction," Lu said.

They waited a few hours, then applied their topical melanin cream to the injured skin. Within the first few days, the cream facilitated an immune response by initially helping the skin's own radical scavenging enzymes to recover, then by halting the production of inflammatory proteins. This initiated a cascade of responses in which they observed greatly increased rates of healing. This included the preservation of healthy skin layers underneath. In samples that did not have the melanin cream treatment, the blistering persisted.

"The treatment has the effect of setting the skin on a cycle of healing and repair, orchestrated by the immune system," Lu said.

Melanin could protect people from toxins including nerve gas

Gianneschi and Lu are studying melanin as part of research programs funded by the U.S. Department of Defense (DOD) and the National

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Institutes of Health (NIH). This has included looking at melanin as a dye for clothing that would also act as an absorbent for toxins in the environment, particularly nerve gas. They showed they could dye a military uniform black with the melanin, and that it would absorb the nerve gas.

Melanin also absorbs heavy metals and toxins. "Although it can act this way naturally, we have engineered it to optimize absorption of these toxic molecules with our synthetic version," Gianneschi said.

The scientists are pursuing clinical translation and trials testing for efficacy of the synthetic melanin cream. In an initial step, the scientists recently completed a trial showing that the synthetic melanins are non-irritating to human skin.

Given their observation that melanin protects biologic tissue from high energy radiation, they surmise that this could be an effective treatment for skin burns from radiation exposure.

The promising work may well provide treatment options for cancer patients in the future, undergoing radiation therapy.

Technology Networks, 02 November 2023

https://technologynetworks.com

Study finds a thyroxine derivative enhances brain drug delivery

2023-11-08

In the study, prodrugs were used to transport anti-inflammatory drugs into the brain, where they were efficiently delivered into glial cells. Glial cells support neurons and are known to be activated in many brain diseases to produce mediators that maintain inflammation. Hence, in order to have an impact on chronic inflammation in the brain, it is crucial to deliver anti-inflammatory drugs into precisely the right cell types. The concept is completely new, even on a global scale.

Researchers at the University of Eastern Finland School of Pharmacy have long been attempting to enhance brain drug delivery by using the L-type amino acid transporter 1, i.e., the LAT1 protein and prodrugs that utilize it, amino acid derivatives. However, the OATP1C1 transporter protein used in the new study was found to be far more effective at transporting thyroxine derivatives than LAT1.

A new study from the University of Eastern Finland shows that the delivery of drugs into the brain, and especially into glial cells, can be enhanced with prodrugs that temporarily incorporate thyroxine or a thyroxine-like For the first time ever, researchers used the organic anion-transporting polypeptide 1C1 (OATP1C1) to enhance drug delivery into the brain.

The study employed computational molecular modeling to create protein models that were used to design and synthesize new prodrugs.

Drug transport mechanisms remain surprisingly poorly understood

"A surprising observation from our study was that increasing the molecular size of drugs enhanced their delivery into the brain and into glial cells. Up until now, it has been thought that a large molecular size isn't exactly helpful in brain drug delivery," says Research Group Director, Associate Professor Kristiina Huttunen of the University of Eastern Finland.

"This study highlights how poorly we still understand drug transport mechanisms in our system. This is also a major reason why many new drugs, especially those intended to affect the central nervous system, unfortunately never make it to the market. The more we know about these transport mechanisms, the better we can take their effects into account when seeking to influence the distribution of drugs in our body. This should also be taken into account very early on in drug development."molecule. The transporter protein OATP1C1, which is found in the brain, can be utilized in the delivery of such prodrugs. The results were published in Journal of Medicinal Chemistry.

Phys Org, 08 November 2023

https://phys.org

Is Spermidine a Legitimate Anti-Aging Compound?

2023-11-03

As you might have surmised, spermidine is definitely not a mixture of male reproductive cells and a sugary red cocktail ingredient (though it was originally isolated from semen). Rather, it is a polyamine compound found mostly in protein-making ribosomes inside cells. In the body, it controls various metabolic processes necessary for proper cell function.

Autophagy

One of the things spermidine does is promote autophagy. Derived from Greek meaning "self eating," this is the process whereby a cell disassembles damaged or degraded components and recycles them into new, better functioning parts. As shown below, a cell initiates autophagy by forming a vesicle and shoving whatever it wants to recycle inside of it. The vesicle, called an autophagosome, then merges with a lysosome, which is acidic and contains degradative enzymes. Following the merger, the contents inside are broken down and recycled.

Spermidine is having a moment. The compound, which sounds like a portmanteau of "sperm" and "grenadine," has exploded in popularity over the past few years, as indicated by Google search volume. Supplement sellers market it as an anti-aging molecule and peddle it in powder and pill form.

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Spermidine sellers tout autophagy as the molecule's anti-aging "secret sauce," so to speak, except they euphemistically label it "cellular renewal." This slick salesmanship is not entirely unfounded. Numerous studies in model organisms show that spermidine supplementation extends animals' lifespans, slows cardiovascular decline, protects against certain neurological disorders, and boosts liver function.

In humans, observational studies indicate that spermidine concentrations in tissues decline with age. They also suggest that people who eat diets rich in spermidine tend to live longer than people whose diets are lacking the compound. Spermidine is found in foods like wheat germ, fermented soy, soybeans, aged cheese, mushrooms, peas, nuts, apples, pears, and broccoli. Ingested spermidine is quickly absorbed from the gut and distributed throughout the body with little to no degradation.

So then does taking the stuff in supplement form slow aging and grant other health benefits? Frank Madeo, a professor of biochemistry at the University of Graz, has performed much of the research on spermidine in model organisms and has been building toward randomized clinical trials in humans for more than a decade.

Spermidine in clinical trials

The first of these was just published last year. Madeo and more than a dozen colleagues recruited 100 older adults between the ages of 60 and 90 and gave half of them a daily spermidine supplement and the other half a placebo. Over the next 12 months, the researchers monitored changes in subjects' cognitive abilities and various physiological markers. When the trial ended, they found no benefits of spermidine over placebo.

As Madeo and his co-authors noted in their concluding remarks, it's possible that the dose wasn't high enough. But it's just as likely, if not more so, that spermidine simply isn't the "anti-aging" compound that researchers hoped it would be. The annals of science are littered with drugs that looked promising in animal trials but didn't pan out in humans.

Spermidine is widely available and generally safe to consume at recommended doses, so it's likely that additional human clinical trials will arrive in the future. Is it possible that these studies will have more glowing results than the first trial? Certainly. But like the spermidine supplements available on Amazon, you probably shouldn't put your money on it.

Real Clear Science, 03 November 2023

https://realclearscience.com

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