

Bulletin Board

Contents

AUG. 02, 2024

(click on page numbers for links)

REGULATORY UPDATE

ASIA PACIFIC

APVMA clarifies the recalls process for agvet chemicals.....	4
Safe Work Australia has published a new WHS profile of electricians to help illustrate the nature of risks they most frequently encounter while performing their duties.....	5
Drinking water scarcity hits even capital of Kashmir	5
Sri Lanka Strengthens Quality Controls on Imported Goods.....	6

AMERICA

NC commission delays advancing limits on forever-chemical water pollution — again	7
Southern Oregon residents worry state isn't monitoring water quality closely enough after arsenic scare	8
From Emerging Compounds to Forever Chemicals - Navigating Evolving Regulation of and Responsibility for PFAS in the Environment	9
'Truly frightening': Pesticides increasingly laced with forever chemicals...10	

EUROPE

Update of the scientific opinion on tetrabromobisphenol A (TBBPA) and its derivatives in food.....	12
--	----

INTERNATIONAL

Scientists make concerning chemical discovery thanks to English otters: 'They have the potential to cause toxic effects'	13
--	----

REACH UPDATE

Current Testing Proposals.....	14
--------------------------------	----

JANET'S CORNER

Appendix.....	15
---------------	----

HAZARD ALERT

Boron	16
-------------	----

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*** While Chemwatch has taken all efforts to ensure the accuracy of information in this publication, it is not intended to be comprehensive or to render advice. Websites rendered are subject to change.**

Bulletin Board

Contents

AUG. 02, 2024

GOSSIP

Weight-loss power of oats naturally mimics popular obesity drugs	23
Chemical and transportation industries could get a boost with new catalyst coating	26
Glassy gel is hard as plastic and stretches 7 times its length	27
New Shingles Vaccine May Cut Risk of Dementia.....	28
'Miracle' filter turns store-bought LEDs into spintronic devices.....	30
Valuable "super-black" material derived from plasma-treated wood.....	32
Researchers develop an energy efficient, reusable, and versatile catalytic system using abundant cobalt	33
Breakthrough in plant disease: New enzyme could lead to anti-bacterial pesticides.....	35
Does honey ever go bad?	37

CURIOSITIES

PFAS Can End Up in Breast Milk, and Rice and Red Meat May Be Prime Sources	40
100% of toxic "forever chemicals" break down overnight in new reaction	42
A Band-Aid for the heart? New 3D printing method makes this, and much more, possible.....	43
Vegan Diet Appears to Slow Aging in 8-Week-Long Study.....	46
Breakthrough in plant disease: New enzyme could lead to anti-bacterial pesticides.....	48
Weight-loss drugmakers bet billions on boosting supplies	50
Hydrogel can preserve medications for weeks outside of a fridge.....	54
Health-threat 'forever chemicals' removed from water with 3D-printed ceramic ink.....	55
Drugs and vaccines could be freed from cold chains by hydrogel	56
The next generation of RNA chips	58

TECHNICAL NOTES

(Note: Open your Web Browser and click on Heading to link to section) ...	61
CHEMICAL EFFECTS	61
ENVIRONMENTAL RESEARCH	61
PHARMACEUTICAL/TOXICOLOGY	61
OCCUPATIONAL.....	61

Bulletin Board

Regulatory Update

AUG. 02, 2024

ASIA PACIFIC

APVMA clarifies the recalls process for agvet chemicals

2024-07-19

The Australian Pesticides and Veterinary Medicines Authority (APVMA) regulates agvet chemicals used in the management of pests and diseases in plants and animals, up to and including the point of retail sale. For an agvet chemical product to be legally manufactured, imported, supplied, sold or used in Australia, it must be registered by the APVMA – unless exempt by the Agvet Code. Management after the point of sale, including use of agvet chemicals, is regulated by state and territory authorities.

Both the APVMA and the product holder (the individual or company who holds the registration for the product, also referred to as 'the holder' and defined under Part 1, section 3 of the Agvet Code) are responsible for different parts of the recall process.

When recalls are necessary

Australians expect that the agvet chemical products they buy are safe and effective and that product holders will take appropriate actions to protect the health and safety of consumers. Recalls of an agvet chemical product may be initiated to mitigate potential risks to safety (such as incorrect labelling or packaging failures), concerns that the product may not work as intended, or because of a potential risk to trade. This can be undertaken as a voluntary recall (where a supplier voluntarily recalls a product from the market). Alternatively, the APVMA can compel a supplier to recall the product (known as a compulsory recall).

Product holders are responsible for limiting the risk to public safety as quickly as possible by removing the product from sale, contacting consumers, and providing advice to anyone in possession of the recalled product. The holder of the product registration or active constituent approval is responsible for the recall, regardless of where the recalled product currently is in the supply chain – manufacturer, importer, distributor or retailer.

Read More

APVMA, 19-07-24

<https://www.apvma.gov.au/>

Bulletin Board

Regulatory Update

AUG. 02, 2024

Safe Work Australia has published a new WHS profile of electricians to help illustrate the nature of risks they most frequently encounter while performing their duties.

2024-07-22

Using Safe Work Australia's Beta Occupational Hazards Dataset and National Dataset for Compensation-based Statistics, alongside ABS Census data, this profile highlights how electricians have a significantly higher level of exposure to job hazards and body positioning hazards compared to all other occupations.

Key insights from the profile include:

- Over the last 10 years, 'body stressing' has consistently been the most common type of work-related injury or illness for electricians (an average of 35.1% of all serious claims during the period).
- The frequency of serious claims for electricians that experienced 'electrocution, shock from electric current' is approximately 6 times greater than the average across all occupations.
- Installing electrical equipment may involve working on rooftops, ladders or elevated structures, making 'falls from a height' another risk that disproportionately affects electricians.
- Tragically, these hazards have led to fatal injuries. Over the past 10 years, 44 Electricians died from traumatic injuries at work. Of these, 23 (or 52%) were a result of electrocution, and a further 9 resulted from falls from a height.

These insights can help persons conducting a business or undertaking (PCBUs) and workers better understand and manage the risks of electrical work.

Read More

Safe Work Australia, 22-07-24

View the profile on the Our Data. Your Stories website.

Drinking water scarcity hits even capital of Kashmir

2024-07-20

Srinagar, July 20 (NVI): - Drinking water scarcity, mostly found in dry and plain areas, has ironically hit Kashmir which is renowned for umpteen

Bulletin Board

Regulatory Update

AUG. 02, 2024

water bodies like rivers and streams, flowing directly from the ice-capped mountains enveloping the valley.

Srinagar, the capital of the 'Paradise on Earth', is facing a shortage of drinking water to an extent that the authorities have had to issue an appeal to the general masses to use the essential commodity judiciously.

The government attributes the scarcity of drinking water to the "continuous dry spell and heat wave" and have urged the public in Kashmir to use water judiciously.

"Due to increase in temperature in Kashmir Valley the consumption/ drawls of water supply have increased considerably, which has resulted in shortage of water supply in some parts of Srinagar City especially in tail end areas. As such, general public is appealed to use the drinking water judiciously and avoid wastages/misuse of water by using it in Lawns, Kitchen-Gardens, washing of vehicles etc." said a public message issued by Executive Engineer, Water Works Division, Srinagar.

It added that, "the consumers using direct online boosters are appealed to stop this practice immediately for equitable distribution of water supply in their respective areas. This is an offence under Jammu & Kashmir Water Resources Regulation and Management Act 2010 and the department shall be forced to take action against all such offenders."

Read More

NVI, 20-07-24

<https://newsvibesofindia.com/drinking-water-scarcity-hits-even-capital-of-kashmir/>

Sri Lanka Strengthens Quality Controls on Imported Goods

2024-06-24

Sri Lanka issued the updated version of the Standardization and Quality Control Regulations, which primarily outlines the applicable Sri Lankan Standard for imported goods and the requirements for supporting documents demonstrating adherence to these standards.

On May 17, 2024, the Ministry of Finance, Economic Stabilization and National Policies of Sri Lanka introduced the Standardization and Quality Control Regulations under the Imports and Exports (Control) Act, No.1 of 1969, aiming to enhance quality control and standardization of imported

Bulletin Board

Regulatory Update

AUG. 02, 2024

goods, including cosmetics. Comprising 13 Articles and 2 Schedules, this new regulation primarily outlines the applicable standards in Sri Lanka for imported goods and the requirements for supporting documents demonstrating adherence to these standards. It replaces the previous Imports and Exports Control (Standardization and Quality Control) Regulations 2017 released on March 29, 2018, and its subsequent amendments.

Read More

Chemlinked, 18-06-24

<https://cosmetic.chemlinked.com/news/cosmetic-news/sri-lanka-strengthens-quality-controls-on-imported-goods>

AMERICA

NC commission delays advancing limits on forever-chemical water pollution — again

2024-07-19

Republican-appointed leaders of the Environmental Management Commission have twice declined to advance proposed rules that would restrict industry's release of some "forever" chemical pollution into drinking water supplies across North Carolina.

The N.C. Department of Environmental Quality wants to regulate eight specific chemicals that are found in drinking water in North Carolina, compounds understood well enough to determine their safe exposure levels.

That could both reduce people's exposure to per- and polyfluoroalkyl pollution and lower communities' expanding cost to clean up drinking water, DEQ officials say.

The department is seeking two different regulations. Surface water rules would aim to protect drinking water supplies and wildlife by setting limits on chemicals released into rivers, creeks and other above-ground water. Groundwater rules would largely impact how much existing contamination companies will need to clean up.

Approving the surface water rule alone would cost companies and public utilities about \$9.5 billion over the next 36 years, according to a

Bulletin Board

Regulatory Update

AUG. 02, 2024

fiscal analysis approved recently by the N.C. Office of State Budget and Management.

Read More

The Herald Sun, 19-07-24

<https://ca.news.yahoo.com/nc-commission-delays-advancing-limits-093000150.html>

Southern Oregon residents worry state isn't monitoring water quality closely enough after arsenic scare

2024-07-22

A Jackson County resident had questions after she learned about elevated arsenic levels in her drinking water. Her concerns reveal gaps in water regulation throughout the state.

Teresa Blazer has lived at Rogue Meadows for nine years. It's a tidy mobile home park in the town of Shady Cove, just off the Rogue River where her retired husband regularly catches his daily limit of Chinook and coho salmon.

In February, by chance, Blazer found out she had been drinking dangerous levels of arsenic. She was asking a neighbor in a nearby park that shares well water about a boil notice she had received after a water line broke. The neighbor, instead, brought to her attention a different letter from park management that revealed their well water had above the federal legal limit of arsenic.

"They had received this notice in January about high arsenic. And I was like, 'Well, our park never received that. I wonder why?'" says Blazer from her home, which today has stacks of printouts from the Oregon Health Authority's website displayed on a table.

Read More

OPB, 22-07-24

<https://www.opb.org/article/2024/07/20/southern-oregon-arsenic-drinking-water/>

Bulletin Board

Regulatory Update

AUG. 02, 2024

From Emerging Compounds to Forever Chemicals - Navigating Evolving Regulation of and Responsibility for PFAS in the Environment

2024-07-19

Per- and polyfluoroalkyl substances (PFAS) have become a focal point of regulatory scrutiny nationwide due to their persistent environmental presence and potential health risks.

For businesses, navigating the evolving landscape of PFAS regulation is crucial—these substances are widely used in various industrial and consumer applications, from firefighting foams to non-stick cookware. Understanding the legal implications of PFAS regulation, including stringent reporting requirements, potential liability, and compliance strategies, is essential to mitigate risks and ensure sustainable operations. This article summarizes current PFAS regulations, examines the regulations' impact on businesses, and offers practical guidance for legal compliance and proactive risk management.

Understanding PFAS

PFAS encompass thousands of individual compounds, including well-known substances like perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS). PFAS are human-made chemicals in use since the 1940s to repel oil and water and resist heat. Such characteristics make them useful in commercial and consumer products such as food packaging, water- and stain-repellent fabrics, breathable clothing, cosmetics, and car wax as well as industrial and manufacturing processes such as metal plating and semiconductor manufacturing. These properties make PFAS exceptionally durable and effective in various applications, but they also contribute to their persistence in the environment, earning them the nickname "forever chemicals."

Despite their utility, PFAS have raised health and environmental concerns. Due to their widespread use and persistence, PFAS accumulate in the environment and in human and animal tissues. Certain PFAS exposure over a prolonged period has been linked to cancer and other illnesses. The persistence and bioaccumulation potential of PFAS caught the attention of the United States Environmental Protection Agency (EPA) in the mid-2000s. The EPA then launched into developing comprehensive regulatory measures to control the use of PFAS and mitigate their impact.

Federal and State Regulatory Approaches to PFAS

Bulletin Board

Regulatory Update

AUG. 02, 2024

The EPA began a PFOA stewardship program in 2006 as it worked to develop health advisory limits. In recent years, the EPA has intensified its efforts to regulate PFAS. Central to this regulatory evolution is the EPA's PFAS Strategic Roadmap, unveiled in October 2021, which outlines an ongoing comprehensive approach to tackling PFAS contamination. The Roadmap marked a pivotal shift in the EPA towards stricter oversight and enforcement aimed at researching toxicity levels, restricting and reducing exposure, and mitigating the risks associated with PFAS manufacturing and use. Following the publication of the PFAS Strategic Roadmap, EPA announced health advisory limits for four kinds of PFAS, warning that the compounds are more toxic than previously thought. Over the last two years, it reduced the health advisory limits for PFOS and PFOA and added health advisories for two chemicals considered replacements for PFOA and PFOS, one group familiar to North Carolinians known as GenX chemicals and the other known as perfluorobutane sulfonate (PFBS). The North Carolina Department of Environmental Quality (NCDEQ) released its own Action Strategy for PFAS in June 2022 after investigating GenX in the Cape Fear River, which affected the drinking water of residents in the greater Wilmington and Fayetteville areas.

Recently, the EPA has folded PFAS regulation into several existing federal environmental statutes, discussed below. By this action, the EPA seeks to increase knowledge of and protections against the risks of PFAS in the environment.

[Read More](#)

National Law Review, 19-07-24

<https://natlawreview.com/article/emerging-compounds-forever-chemicals-navigating-evolving-regulation-and>

'Truly frightening': Pesticides increasingly laced with forever chemicals

2024-07-24

Toxic "forever chemicals" are increasingly being used in US pesticides, threatening human health as they contaminate waterways and are sprayed on staple foods, a study said Wednesday.

Per- and polyfluoroalkyl substances (PFAS) have come under increasing scrutiny in recent years, but environmental regulations against them have mainly paid attention to sources such as industrial facilities, landfills and consumer products like certain cookware and paints.

Bulletin Board

Regulatory Update

AUG. 02, 2024

New research published in the peer-reviewed journal *Environmental Health Perspectives* says that pesticides used on crops including corn, wheat, spinach, apples and strawberries—and other sources such as insect sprays and pet flea treatment—can now be added to the list.

“The more we look, the more we find it,” co-author Alexis Temkin, a toxicologist at the nonprofit Environmental Working Group, told AFP.

“And it just emphasizes the importance of cutting down on sources and really regulating these chemicals.”

Research suggests that high levels of exposure to forever chemicals weakens human immune systems, making them less responsive to vaccines and more susceptible to infections.

There is also emerging evidence they may reduce fertility, lead to growth delays in children, and interfere in the body’s natural hormones.

For the new paper, the authors trawled public databases and carried out freedom of information requests to obtain information on both “active” and “inert” ingredients in pesticides.

Active ingredients are those that target pests, while those that are called inert are everything else. The latter are not required to be disclosed on the label even though they can increase the efficacy and persistence of the toxic active ingredient, and can be toxic themselves.

The researchers uncovered a concerning trend: 14 percent of all US pesticide active ingredients are PFAS, including nearly one-third of active ingredients approved in the past decade.

Eight approved inert ingredients in pesticides were PFAS, including the non-stick chemical known by the brand name Teflon.

Read More

Phys.org, 24-07-24

<https://phys.org/news/2024-07-pesticides-laced-chemicals.html>

Bulletin Board

Regulatory Update

AUG. 02, 2024

EUROPE

Update of the scientific opinion on tetrabromobisphenol A (TBBPA) and its derivatives in food

2024-07-15

The European Commission asked EFSA to update its 2011 risk assessment on tetrabromobisphenol A (TBBPA) and five derivatives in food.

Neurotoxicity and carcinogenicity were considered as the critical effects of TBBPA in rodent studies. The available evidence indicates that the carcinogenicity of TBBPA occurs via non-genotoxic mechanisms. Taking into account the new data, the CONTAM Panel considered it appropriate to set a tolerable daily intake (TDI). Based on decreased interest in social interaction in male mice, a lowest observed adverse effect level (LOAEL) of 0.2 mg/kg body weight (bw) per day was identified and selected as the reference point for the risk characterisation. Applying the default uncertainty factor of 100 for inter- and intraspecies variability, and a factor of 3 to extrapolate from the LOAEL to NOAEL, a TDI for TBBPA of 0.7 µg/kg bw per day was established. Around 2100 analytical results for TBBPA in food were used to estimate dietary exposure for the European population. The most important contributors to the chronic dietary LB exposure to TBBPA were fish and seafood, meat and meat products and milk and dairy products. The exposure estimates to TBBPA were all below the TDI, including those estimated for breastfed and formula-fed infants. Accounting for the uncertainties affecting the assessment, the CONTAM Panel concluded with 90%–95% certainty that the current dietary exposure to TBBPA does not raise a health concern for any of the population groups considered. There were insufficient data on the toxicity of any of the TBBPA derivatives to derive reference points, or to allow a comparison with TBBPA that would support assignment to an assessment group for the purposes of combined risk assessment.

Read More

EFSA, 15-07-24

<https://www.efsa.europa.eu/en/efsajournal/pub/8859>

Bulletin Board

Regulatory Update

AUG. 02, 2024

INTERNATIONAL

Scientists make concerning chemical discovery thanks to English otters: 'They have the potential to cause toxic effects'

2024-07-21

Researchers in England found PFAS compounds in the bodies of dead otters, raising more concerns about the environmental impacts of these toxic chemicals. PFAS — perfluoroalkyl and polyfluoroalkyl substances — are known as “forever chemicals” because they can take thousands of years to break down.

What happened?

Phys.org posted a report on a new study from Cardiff University's Otter Project that analyzed PFAS concentrations in the bodies of dead otters found near a factory that previously used these chemicals. In the paper, the scientists revealed that 33 types of PFAS compounds were found in the bodies of 20 otters between 2015 and 2019.

What's more, almost all of the otters also had PFAS replacement chemicals in their bodies, albeit at lower concentrations than the PFAS; these structurally similar compounds were introduced by manufacturers after regulations on some PFAS, such as PFOA and PFOS, were enacted.

One of the compounds discovered isn't even produced in the U.K., and the scientists believe it could have been introduced to the environment through products imported from China.

Read More

The Cool Down, 21-07-24

<https://www.thecooldown.com/outdoors/otter-pfas-chemicals-waterproofing-fabric/>

Bulletin Board

REACH Update

AUG. 02, 2024

Current Testing Proposals

2024-07-22

Here you can find the substances and hazard endpoints for which ECHA is currently inviting third parties to submit scientifically valid information and studies.

Please also note the following:

The link under 'View dossier'

Specific grounds for the testing proposal

Read-across/category approach proposed

Read More

ECHA, 22-07-24

<https://echa.europa.eu/information-on-chemicals/testing-proposals/current>

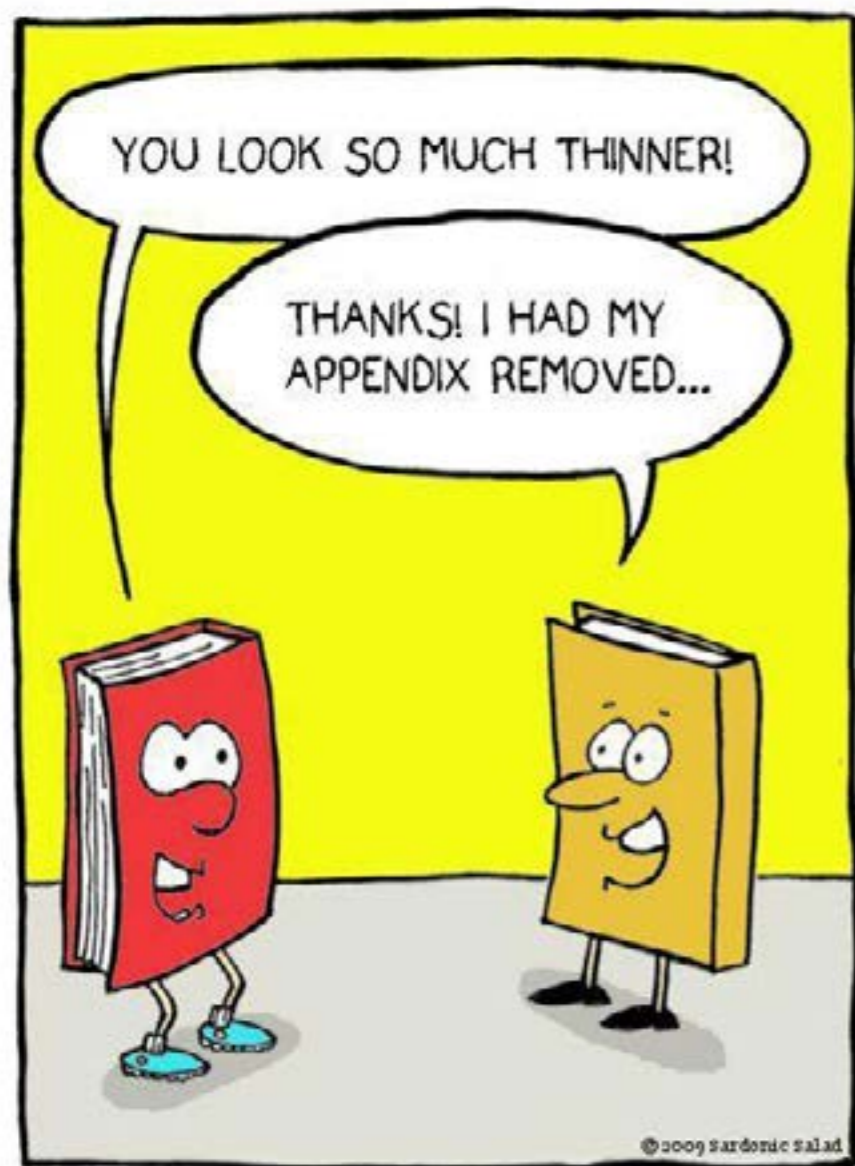
Bulletin Board

Janet's Corner

AUG. 02, 2024

Appendix

2024-08-02



<https://www.pinterest.com.au/pin/596445544377689140/>

Bulletin Board

Hazard Alert

AUG. 02, 2024

Boron

2024-08-02

It is a non-metallic element and the only non-metal of the group 13 of the periodic table. Boron is electron-deficient, possessing a vacant p-orbital. It has several forms, the most common of which is amorphous boron, a dark powder, unreactive to oxygen, water, acids and alkalis. It reacts with metals to form borides. At standard temperatures boron is a poor electrical conductor but is a good conductor at high temperatures. [2] Boron is found in the environment primarily combined with oxygen in compounds called borates. Common borate compounds include boric acid, sodium tetraborates (also referred to as borax) and boron oxide. [1,2]

USES [2,3]

Boron is used in special-purpose alloys, in cementation of iron, as oxygen scavenger for copper and other metals, as fibres and filaments in composites with metals or ceramics, as semiconductor, for nuclear reactors, as a shield for nuclear radiation and in instruments used for detecting neutrons. Boron is used in pyrotechnic flares (distinctive green colour), for rockets (as an igniter), in boron-coated tungsten wires and in high temperature brazing alloys.

Borates are used mostly to produce glass. They are also used in fire retardants, leather tanning industries, cosmetics, photographic materials, soaps and cleaners, adhesives and for high-energy fuel. Some pesticides used for cockroach control and some wood preservatives also contain borates.

Borax is used in soldering metals, as a cleansing flux in welding, in the manufacture of glazes and enamels (e.g. for covering steel of refrigerators and washing machines), in tanning, in cleaning compounds, to artificially age wood, as a preservative against wood fungus (either alone or with other antiseptics), and in fireproofing fabrics. It is also used for curing and preserving skins, in cockroach control and as a water softener in washing powders.

Boric acid is used for weatherproofing and fireproofing fabrics, as a preservative, in the manufacture of cements, crockery, porcelain, enamels, glass, borates, leather, carpets, hats, soaps, and artificial gems, and in nickel-plating baths. It is also used in the manufacture of cosmetics, in ointments and eye washes, as a mild antiseptic, in printing and dyeing, in photography, for impregnating wicks, for hardening steel, in welding flux,

Boron is a chemical element with symbol B and atomic number 5.

Bulletin Board

Hazard Alert

AUG. 02, 2024

copper brazing, as an insecticide for cockroaches and carpet beetles, and in fungus control for citrus fruits.

Boron oxide is used in metallurgy, in the analysis of silicon dioxide in silicates, in blowpipe analysis, for the production of boron, in heat-resistant glassware, as a fire-resistant additive for paints, in electronics and as an herbicide.

Boron carbide is used as an abrasive, in the manufacture of hard and chemical-resistant ceramics or wear-resistant tools, in the refractory industry, in light weight cermets, in armour tiles, in radiation protection and shielding, in the nuclear industry in control rods in nuclear reactors (high capture cross-section to absorb thermal neutrons), as raw material for producing other boron containing materials (e.g. titanium boride), and in solid fuel (propellant for ducted rockets).

Boron nitride is used as a refractory material, laboratory reagent, and abrasive. Boron trichloride is used in the manufacture and purification of metal alloys, in bonding of iron and steel, in soldering fluxes, and in the manufacture of electrical resistors. It is also used to extinguish magnesium fires in heat resisting furnaces.

Boron trifluoride is widely used to promote various organic reactions. Boron filaments are high-strength, lightweight materials that are used in fibre optics research and for advanced aerospace structures.

EXPOSURE SOURCES & ROUTES OF EXPOSURE [3]

Exposure Sources

- **Industry sources:** Boron can be released from industries that use boron and boron compounds, e.g. leather tanning, cement works, and glass works.
- **Diffuse sources:** Boron can be released from household use of consumer products containing borates such as cosmetics, washing powders, or pesticides, and sub-threshold facilities.
- **Natural sources:** Boron is not an abundant element. The element boron does not occur in nature and boron is mostly found combined with oxygen in compounds called borates. Common borate compounds include boric acid, salts of borates and boron oxide. Natural deposits of borates are borax and kernite. Tourmaline contains about 10 % boron. Boron is released to the environment from natural

Bulletin Board

Hazard Alert

AUG. 02, 2024

sources such as volcanoes and geothermal steam. Traces are present in rocks, soil, water and some food.

- **Transport sources:** Mobile sources are normally not associated with the emission of boron.
- **Consumer products:** Heat-resistant household glassware (Pyrex), laboratory glassware, some soap, some pesticides, some cosmetics and laundry products, some leather products and some cement products.

Routes of Exposure

- **Inhalation** – Minor route of exposure for the general population. Predominant route of exposure for boron workers.
- **Oral** – Predominant route of exposure for the general population via ingestion of boron in food and drinking water.
- **Dermal** – Minor route of exposure.

HEALTH EFFECTS [4]

Acute Health Effects

The severity of health effects will depend on how much boron a person has been exposed to, for how long, and current state of health. Once different borates are dissolved in the acid of gastric juices, they cannot be distinguished from each other on chemical or toxicological grounds. Both boric acid and borax may enter the body by absorption from the gastrointestinal tract or through mucous membranes. Although absorption can occur through undamaged skin, it is slow and toxic effects are less likely. However, absorption through damaged skin can be rapid and complete. Ingestion of large borate quantities is unlikely, but may be harmful if it occurs. Ingestion or absorption through the skin can cause nausea, abdominal pain, diarrhoea and persistent vomiting (vomitus and faeces may sometimes contain blood), which may be accompanied by headache and weakness, lethargy, restlessness, tremors, intermittent convulsions, and characteristic erythematous (abnormally red) lesions on the skin. In severe cases, shock with fall in arterial pressure, tachycardia (increase in heart rate) and cyanosis (blue skin colour) may occur. Central nervous system stimulation followed by depression, gastrointestinal disturbance (haemorrhagic gastroenteritis) and erythematous skin eruptions (giving rise to a boiled lobster appearance) may be present. The kidneys (producing oliguria (small volume of urine), albuminuria (presence of albumin in the urine), anuria (absence of or defective excretion of urine)) and, rarely, the liver (jaundice) may also be involved. Excretion

Bulletin Board

Hazard Alert

AUG. 02, 2024

occurs mainly through the kidneys with about half excreted in the first 12 hours and the remainder over 5-12 days. Toxic symptoms may be delayed for several hours. The mean lethal dose of sodium borate or boric acid probably exceeds 30 grams in adults and death occurs due to vascular collapse in the early stages or to central nervous system depression in later stages. Children are thought to be more susceptible to the effects of borate intoxication. Breathing moderate levels of boron dust or fume can result in irritation of the nose, throat, and eyes.

There is little information on the health effects of long-term exposure to boron. Most of the studies are on short-term exposures. Chronic intoxication with boric acid may give rise to anorexia, loss of strength, confusion and loss of hair (alopecia). Reproductive effects, such as low sperm count, were seen in men exposed to boron over the long-term.

The International Agency for Research on Cancer (IARC), and the United States Environmental Protection Agency (EPA) have not classified boron for human carcinogenicity.

SAFETY

First Aid Measures [5]

- **Eye Contact:** Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention if irritation occurs.
- **Skin Contact:** Wash with soap and water. Cover the irritated skin with an emollient. Get medical attention if irritation develops.
- **Inhalation:** If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.
- **Serious Inhalation:** Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. Seek medical attention.
- **Ingestion:** Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Bulletin Board

Hazard Alert

AUG. 02, 2024

Workplace Controls & Practices [4]

Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protective Equipment [5]

The following personal protective equipment is recommended when handling boron:

- Safety glasses;
- Lab coat;
- Dust respirator (Be sure to use an approved/certified respirator or equivalent);
- Gloves.

Personal protective equipment recommended for large spills:

- Splash goggles;
- Full suit;
- Dust respirator;
- Boots;
- Gloves;
- A self-contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

REGULATION

United States

OSHA: The Occupational Health and Safety Administration has limited workers' exposure to an average of 15 mg/m³ for boron oxide in air for an 8-hour workday, 40-hour workweek.

EPA: The Environmental Protection Agency has determined that exposure to boron in drinking water at concentrations of 4 mg/L for 1 day or 0.9 mg/L for 10 days is not expected to cause any adverse effects in a child. In addition, the agency has determined that lifetime exposure to 1 mg/L boron is not expected to cause any adverse effects.

Bulletin Board

Hazard Alert

AUG. 02, 2024

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6. <http://www.sciencelab.com/msds.php?msdsId=9923126>

Bulletin Board

Gossip

AUG. 02, 2024

New CRISPR Approach Enables "Seamless" Gene Insertions

2024-07-31

Researchers in Switzerland have created a new method to generate knock-ins in *Drosophila melanogaster*, a common laboratory model.

The approach, named SEED/Harvest, combines CRISPR-Cas9 technology with the single-strand annealing (SSA pathway).

"Since we would like to introduce and analyze changes in the DNA throughout the genome for our research, the method must be both precise and efficient," said Dr. Markus Affolter, professor at the the Biozentrum University of Basel and the study's lead author. "The SEED/Harvest method is both. It combines the most robust screening of successful insertions and all the advantages of seamless tagging."

SEED/Harvest enables proteins to be labeled in specific tissue and cell types

There are many reasons why scientists might want to generate knock-ins within laboratory organisms: to study the function of specific genes, model diseases, understand how proteins function and interact or simply to conduct basic research.

When CRISPR-Cas9 was established as a gene-editing tool several years ago, it transformed this line of research.

In the CRISPR-Cas9 system, a guide RNA (gRNA) guides the Cas9 enzyme – which can be likened to a pair of molecular scissors – to a specific location within the genome, where it binds to the targeted sequence. After binding, Cas9 cuts both strands of DNA triggering the cell's DNA repair system into motion.

This repair process allows researchers to introduce targeted changes into the genome. The gold standard method for generating knock-ins typically takes advantage of homology directed repair (HDR). Here, a repair template carrying the desired genetic insertion is used by the cell's molecular machinery to repair the break, and the repair template is incorporated into the genome. Et voila, you have inserted a new gene into the genome!

"However, HDR rates are often low in vivo, and thus, an efficient way for screening correct insertions is required," Affolter and colleagues explained.

Bulletin Board

Gossip

AUG. 02, 2024

To support screening, researchers have explored the feasibility of two-step knock-in approaches, whereby a marker is also inserted into the targeted DNA site, before being removed after screening. But current process can introduce scars.

“Scarless editing is fundamental for many purposes, such as internal tagging of proteins or the generation of point mutants, cases in which scars could disrupt the protein sequence in unpredictable ways,” Affolter and colleagues said.

That’s why the researchers have developed SEED/Harvest, which they described as a “seamless” approach. It’s a method comprising two steps. First, scientists introduce a marker into the desired DNA site that sits within an exon, also known as a protein-coding region. Next, the marker is removed and the DNA breakpoints are repaired by the SSA pathway.

“After insertion of the SEED cassette and screening, the screening marker is seamlessly removed by a subsequent CRISPR-triggered repair event, resolved by SSA. In this step, the repeats anneal and the region in between is removed, resulting in the scarless removal of the 3xP3-dsRED marker and ultimately resulting in the desired gene editing,” the researchers explained.

Technology Networks, 31 July 2024

<https://technologynetworks.com>

Weight-loss power of oats naturally mimics popular obesity drugs

2024-07-22

Let’s face it, dietary fiber is not the most scintillating topic, even though for the last 50 years it’s been well accepted that it’s valuable for good gut health. But we’re now coming to understand that fiber itself is an umbrella term, and one particular type – which is abundant in a common breakfast food – may trigger the same beneficial metabolic functions that GLP-1 agonists like Ozempic do, without the price tag or side-effects.

“We know that fiber is important and beneficial; the problem is that there are so many different types of fiber,” said Frank Duca, an associate professor at the University of Arizona. “We wanted to know what kind of fiber would be most beneficial for weight loss and improvements in glucose homeostasis so that we can inform the community, the consumer and then also inform the agricultural industry.”

Bulletin Board

Gossip

AUG. 02, 2024

In a study led by Duca, researchers undertook a thorough analysis of how different types of fiber impacted the gut microbiota, which play such an important role in how food is processed in our digestive system. They looked at pectin, beta-glucan, wheat dextrin, starch and cellulose, all plant-based fibers, and found that one in particular punched above its weight when it came to naturally fighting obesity.

Many previous studies, such as one that compared a high-fiber diet with one rich in fermented foods, only looked at ‘fiber’ as a single unit of nutrition. While as a whole, both soluble and insoluble forms of dietary fiber have wide-ranging health benefits – from satiety to lowering blood cholesterol levels – the sum of the parts has not offered insight to its weight-loss potential.

Here, the researchers quickly homed in on one type of fiber, beta-glucan, which has previously been singled out as playing a role in moderating the appetite and satiety hormones peptide YY (PYY) and glucagon-like peptide-1 (GLP-1). Last year, a study out of the University of Agriculture, Faisalabad in Pakistan demonstrated that oats in particular, high in beta-glucan, impacted those hormones in ways beneficial for weight management.

In this latest study, the researchers allocated mice into five groups to all be fed high-fat, high-sucrose diets (HFD). Each group’s diet also consisted of either 10% cellulose (control), pectin, beta-glucan, wheat dextrin or resistant starch. Health markers were measured over 18 weeks, assessing percentages of weight gain, fat mass and lean mass. They also looked at the effect of the diets on blood glucose levels after eating, up to two hours after consumption.

What they found was that the animals on the 10% beta-glucan diets had significantly less weight gain despite their high-fat, high-sugar diet, as well as significantly less fat mass yet significantly higher retention of lean mass. These mice also demonstrated sustained energy expenditure, measured by their movements over 24-hour periods.

The beta-glucan cohort were also the only group to show improved insulin sensitivity and beneficial blood-sugar levels throughout the 18 weeks.

Further analysis indicated that the animals on the beta-glucan-supplemented diets had developed the kind of microbiota that set them up for all of these positive health outcomes, altering the gut’s bacteria and the molecules produced through digestion. These molecules, known as

Bulletin Board

Gossip

AUG. 02, 2024

metabolites, are thought to be the key piece of the puzzle when it comes to how fiber encourages weight loss.

They found that one metabolite, butyrate, was the driver of this effect. Butyrate, a short-chain fatty acid (SCFA) is produced by certain gut bacteria in the fiber fermentation process, stimulates the release of GLP-1, which we've come to understand plays such an important role in communicating to the brain that feeling of 'fullness' when we eat. Semaglutide drugs like Ozempic synthetically create this gut-brain scenario, though in a more potent way that doesn't face the same kind of rapid deterioration as when it occurs naturally.

"Part of the benefits of consuming dietary fiber is through the release of GLP-1 and other gut peptides that regulate appetite and body weight," Duca said. "However, we don't think that's all of the effect. We think that there are other beneficial things that butyrate could be doing that are not gut-peptide-related, such as improving gut barrier health and targeting peripheral organs like the liver."

Butyrate has previously been shown to induce the burning of brown fat in mice, which suggests that beta-glucan was helping fuel that specific lipid high-calorie fat availability, reducing the 'white fat' accumulation that is a hallmark of weight gain and obesity.

"Only β -glucan (beta-glucan) supplementation during HFD-feeding decreased adiposity and body weight gain and improved glucose tolerance compared with HFD-cellulose, whereas all other fibers had no effect," the researchers noted. "This was associated with increased energy expenditure and locomotor activity in mice compared with HFD-cellulose. All fibers supplemented into an HFD uniquely shifted the intestinal microbiota and cecal short-chain fatty acids; however, only β -glucan supplementation increased cecal butyrate concentrations. Lastly, all fibers altered the small-intestinal microbiota and portal bile acid composition."

Oats, as well as barley, have the highest concentrations of beta-glucan, but it's also found in rice, mushrooms and seaweed. Oats contain around 3-5% of this fiber per cup of dry cereal, and cooking (not baking) does not diminish its concentration. Duca now hopes to work on developing 'enhanced fibers' that can boost the release of butyrate during digestion.

The study was published in The Journal of Nutrition.

New Atlas, 22 July 2024

<https://newatlas.com>

Bulletin Board

Gossip

AUG. 02, 2024

Chemical and transportation industries could get a boost with new catalyst coating

2024-08-01

Coupling electrochemical conversion of the greenhouse gas CO₂ with renewable electricity sources—such as solar and wind—promises green production of high-demand chemicals and transportation fuels. Carbon dioxide coupling products such as ethylene, ethanol and acetic acid are particularly useful as feedstocks for the chemical industry and powering vehicles.

While designs for efficient and scalable electrolyzers (which use electricity to drive chemical transformations) with industrially relevant current densities have been developed, commercialization efforts have been hindered by the stability and selectivity of the catalysts.

To tackle this challenge, Lawrence Livermore National Laboratory (LLNL) and collaborators have developed a catalyst coating platform that uses physical vapor deposition (PVD), which offers precise control over thickness, composition, morphology and porosity.

To date, only copper and its alloys have been demonstrated to efficiently convert CO₂ into multi-carbon products, such as ethylene, ethanol, acetate and propanol. The challenge in catalyst development is to decouple catalyst performance from catalyst integration-related effects.

This is specifically true when comparing catalysts that have been fabricated and integrated with different methods and are tested in different electrolyzer configurations, or prepared from inks with varying compositions.

"We came up with a new scalable and tunable catalyst platform that allows catalyst composition to be tuned without changing catalyst morphology or catalyst integration in the electrolyzer," said LLNL materials scientist Juergen Biener, a lead author of a paper published in the journal *Small*. Other LLNL researchers include Zhen Li, Stephen Weitzner, Sneha Akhade and Xie Liu.

The team, which also includes researchers from the University of Delaware, Washington University and the University of Pennsylvania and industry partner Twelve Benefits Corporation, used their PVD platform to systematically explore the performance of copper-based dilute alloy catalysts that are difficult to synthesize and integrate otherwise.

Bulletin Board

Gossip

AUG. 02, 2024

Guided by theory, the team developed several copper-based dilute alloy catalysts that promote coupling of the intermediate carbon monoxide toward the desired multicarbon products.

“The results demonstrate the power of using dilute alloys to systematically tune the energy landscape of CO₂ electrolysis to increase the effectiveness of creating cleaner feedstocks for the chemical and transportation industries,” said LLNL scientist Joel Varley, who led the simulation efforts of this work.

Beyond providing fine control over coating uniformity, thickness and composition, PVD methods produce less waste and are less labor-intensive than traditional electrodeposition methods, making them more cost effective despite higher capital costs. The development could lead to improvements in the chemical and transportation industries.

Phys Org, 1 August 2024

<https://phys.org>

Glassy gel is hard as plastic and stretches 7 times its length

2024-06-19

When you think of gel, you might imagine goo – but a new gel-like material has been engineered to be soft enough to stretch to almost seven times its original length while still being strong and clear, like glass.

Michael Dickey at North Carolina State University says his team discovered these “glassy gels” when his student, Meixiang Wang, was experimenting with ionic liquids and kept finding unexpected mechanical properties. The materials they devised are more than 50 per cent liquid, but as strong as the plastics used for water bottles, while also being very stretchy and sticky. “There are a bunch of cool things about them,” he says.

Each glassy gel consists of long molecules called polymers mixed with an ionic liquid, a fluid that is essentially a salt in liquid form. The gel is a transparent solid that can withstand up to 400 times atmospheric pressure, but also stretch very easily up to 670 per cent. Dickey says that this could make it well-suited for building soft robotic grippers or 3D printing deformable materials.

He and his colleagues made glassy gels from several different mixtures of polymers and liquid salts and found that their strength and stretch depended on the precise ratio used.

Bulletin Board

Gossip

AUG. 02, 2024

“Just by changing the ratio of two ingredients, you can go from something very stretchy like a rubber band, to something almost as hard as glass,” says Dickey.

This is because the materials get their stretchiness from the ionic liquid settling into spaces between the stiffer polymer molecules and pushing them apart, while their strength comes from the electrostatic attraction between the liquid’s charged particles and the polymers, which prevents them from fully breaking away from each other.

The glassy gels can also self-heal – a cut or break can be repaired by applying heat, which makes molecules on the broken edges reconnect. Richard Hoogenboom at Ghent University in Belgium says this could make them useful in some instances when conventional plastics are used, but the formula may have to be tweaked so that it only softens at temperatures high enough so this doesn’t happen accidentally.

New Scientist, 19 June 2024

<https://newscientist.com>

New Shingles Vaccine May Cut Risk of Dementia

2024-07-26

A new study suggests that the new, more effective recombinant shingles vaccine can also reduce the risk of dementia, similar to the vaccine’s discontinued predecessor.

The study is published in Nature Medicine.

Links to dementia risk

Shingles is caused by a reactivation of the chickenpox-causing herpes zoster virus. After first infection, commonly during our childhood years, the virus is never fully eradicated, and it lies dormant in our nervous system.

The virus can flare up again to cause shingles, a painful and serious condition that affects many elderly people. Interestingly, evidence emerged after the introduction of the shingles vaccine suggesting that it may reduce the risk of dementia.

This vaccine – Zostavax® – has now been withdrawn in many countries in favor of a more effective recombinant vaccine – Shingrix®. However, it was unclear whether the newer vaccine had a similar effect on dementia risk.

Bulletin Board

Gossip

AUG. 02, 2024

Delaying dementia onset?

To find out if this was the case, University of Oxford researchers studied the electronic records of over 200,000 people aged over 65 in the US. They looked at over 100,000 people who received the previous vaccine from 2014–2017 and the same number who received the recombinant vaccine from 2017–2022.

The participants were followed up for four to six years after vaccination to determine how many were diagnosed with dementia.

The findings revealed that there was indeed a lower risk of dementia among those who received the recombinant vaccine in the 6 years post vaccination, with a 17% delay in the onset of dementia. This translates to an extra 164 days lived without the disease compared to those who received Zostavax.

“There was already some evidence that the old live vaccine was able to reduce the risk of Alzheimer’s disease,” said Prof. Andrew Doig, professor of biochemistry at the University of Manchester. “This work shows that the new recombinant vaccine is even more effective, decreasing the likelihood of being diagnosed with dementia, if the new vaccine is used rather than the old one.”

The recombinant shingles vaccine was also linked to lower dementia risks when compared against other vaccines routinely given to older people, including influenza and tetanus/diphtheria/pertussis vaccines.

Additionally, the effect on dementia risk was observed for both men and women but was greater in women.

Further research needed

“The study is very well-conducted and adds to previous data indicating that vaccination against shingles is associated with lower dementia risk. More research is needed in future to determine why this vaccine is associated with lower dementia risk,” said Prof. Tara Spires-Jones, director of the Centre for Discovery Brain Sciences at the University of Edinburgh.

Findings should stimulate further studies to probe the mechanism behind this association, such as large-scale randomized control trials.

“The next question is, how does vaccination exert this dementia protection effect?” said Prof. Robert Howard, professor of old age psychiatry at University College London. “Is it through suppression of

Bulletin Board

Gossip

AUG. 02, 2024

virus or is the induced immune response targeting a step in the molecular pathology of Alzheimer’s disease?”

Technology Networks, 26 July 2024

<https://technologynetworks.com>

‘Miracle’ filter turns store-bought LEDs into spintronic devices

2024-07-25

Traditional electronics use semiconductors to transmit data through bursts of charged carriers (electrons or holes) to convey messages in “1s” and “0s.” Spintronic devices can process an order of magnitude more information by assigning binary code to the orientation of electrons’ magnetic poles, a property known as spin -- an “up” spin is a 1, a “down” is a 0.

A major barrier to commercial spintronics is setting and maintaining the electron spin orientation. Most devices tune spin-orientation using ferromagnets and magnetic fields, a burdensome and unreliable process. Decades of research has shown that carriers lose their spin orientation moving from materials with high-conductivity to low-conductivity -- for example, from metallic ferromagnets to undoped silicon and conjugated polymer materials that make up most modern semiconductors.

For the first time, scientists transformed existing optoelectronic devices into ones that can control electron spin at room temperature, without a ferromagnet or magnetic field.

Most optoelectronic devices, such as LEDs, only control charge and light but not the spin of the electrons. In the new study led by the University of Utah physicists and researchers at the National Renewable Energy Laboratory (NREL), replaced the electrodes of store-bought LEDs with a patented spin filter, made from hybrid organic-inorganic halide perovskite material. The LEDs produced circularly polarized light, a tell-tale sign that the filter had injected spin-aligned electrons into LED’s existing semiconductor infrastructure, a massive step forward for spintronics technology.

“It’s a miracle. For decades, we’ve been unable to efficiently inject spin-aligned electrons into semiconductors because of the mismatch of metallic ferromagnets and non-magnetic semiconductors,” said Valy Vardeny, Distinguished Professor in the Department of Physics & Astronomy at the U and co-author of the paper. “All kinds of devices that

Bulletin Board

Gossip

AUG. 02, 2024

use spin and optoelectronics, like spin-LEDs or magnetic memory, will be thrilled by this discovery.”

The study was published in the journal Nature on June 19, 2024.

Spin filters

In 2021, the same collaborators developed the technology that acts as an active spin filter made of two successive layers of material, called chiral hybrid organic-inorganic halide perovskites. Chirality describes molecule’s symmetry, where its mirror image cannot be superimposed on itself. Human hands are the classic example; hold yours out, palms facing away. The right and left hands are arranged as mirrors of one another -- you can flip your right hand 180° to match the silhouette, but now the right palm is facing you while the left palm faces away. They’re not the same.

Some molecules, such as DNA, sugar and layers of chiral hybrid organic-halide perovskites, have their atoms arranged in chiral symmetry. The filter works by using a “left-handed” oriented chiral layer to allow electrons with “up” spins to pass, but block electrons with “down” spins, and vice versa. At the time, the scientists claimed the discovery could be used to transform conventional optoelectronics into spintronic devices simply by incorporating the chiral spin filter. The new study did just that.

“We took an LED from the shelf. We removed one electrode and put the spin filter material and another regular electrode. And voila! The light was highly circularly polarized,” said Vardeny.

Chemists from the NERL fabricated the spin LEDs by stacking several layers, each with specific physical properties. The first layer is a common transparent metallic electrode; the second layer’s material blocks electrons having spin in the wrong direction, a layer that the authors call a chirality-induced spin filter. The spin-aligned electrons then recombine in the third layer, a standard semiconductor used as an active layer in regular LEDs. The injected spin aligned electrons cause this layer to produce photons that move in unison along a spiral path, rather than a conventional wave pattern, to produce the LED’s signature circular polarized electroluminescence,

“This work demonstrates the unique and powerful ability for these emerging ‘hybrid’ semiconductors to combine and take advantage of the interplay of the distinct properties of organic and inorganic systems,” said Matthew Beard, coauthor of the study of NREL. “Here the chirality is borrowed from the organic molecules and provides control over spin

Bulletin Board

Gossip

AUG. 02, 2024

while the inorganic component both orients the organic component and provides conductivity or control over charge.”

Once they installed the filter into a standard LED, Xin Pan, research assistant in the Department of Physics & Astronomy at the U, confirmed that the device worked as intended, namely by spin-aligned electrons. However, more research is needed to explain the exact mechanisms at work to create the polarized spins.

“That’s the \$64,000 question for a theorist to answer,” said Vardeny. “It’s really a miracle. And the miracle is without knowing the exact underlying mechanism. So that’s the beauty of being experimentalist. You just try it.”

The authors assert that other scientists can apply the technique using other chiral materials, such as DNA, in many contexts.

Science Daily, 25 July 2024

<https://sciencedaily.com>

Valuable “super-black” material derived from plasma-treated wood

2024-07-31

Vantablack, which is the world’s darkest material, could be in for some competition. Canadian scientists have created a super-black substance that has the potential to be cheaper, hardier and easier to manufacture ... and it’s made out of wood.

Trademarked as Nxylon (“niks-uh-lon”) the material takes its name from Nyx, the Greek goddess of the night, and xylon, which is the Greek word for wood. It is being developed at the University of British Columbia, by a team led by Prof. Philip Evans.

Nxylon was discovered accidentally, when Evans and PhD student Kenny Cheng were trying to make wood more water-repellent via exposure to high-energy plasma. When the surface of sawn basswood-tree samples received the plasma treatment, the cut-open ends of the porous cells that made up the wood changed in structure.

Putting it simply, that new light-absorbing structure caused the entire treated surface layer of the wood to take on a velvety “extremely black” appearance. When the material was analyzed by colleagues at Texas A&M University, it was found to reflect less than 1% of visible light. By contrast, regular black paint typically reflects at least 2.5%.

Bulletin Board

Gossip

AUG. 02, 2024

And what's more, it was determined that wood from other species of trees – besides basswood – can also be used. The surface layer that changes structure is only about 0.5 to 1 mm thick. This means that a multitude of thin sheets of Nxylon could be produced from a single slab of wood.

Among other things, the material may find use in better-performing telescopes and other optical devices, more efficient solar cells, and even consumer goods such as jewelry and luxury watches. In the case of the latter two, Nxylon could be a less expensive and more sustainable alternative to black hardwoods like ebony and rosewood.

Although Nxylon currently reflects slightly more light than Vantablack, Evans believes that should change once the technology is developed further. Additionally, whereas Vantablack is composed of fragile, costly, vertically oriented forests of carbon nanotubes, such is not the case with Evans' material.

"Nxylon is made from a renewable material, wood, and we could make about 200,000 watch faces from one basswood tree," he tells us. "We have worked out how to make the surface less fragile. Nxylon sheets can be made in 30 minutes [...] I'm sure we could speed up the process with a device designed for commercial production."

A paper on the research was recently published in the journal *Advanced Sustainable Systems*. Plans call for the technology to be commercialized via a spinoff company, the Nxylon Corporation of Canada.

New Atlas, 31 July 2024

<https://newatlas.com>

Researchers develop an energy efficient, reusable, and versatile catalytic system using abundant cobalt

2024-08-01

Controlling the crystal phase of cobalt nanoparticles leads to exceptional catalytic performance in hydrogenation processes, report scientists from Tokyo Tech.

Produced via an innovative hydrosilane-assisted synthesis method, these phase-controlled reusable nanoparticles enable the selective hydrogenation of various compounds under mild conditions without the use of harmful gases like ammonia. These efforts could lead to more sustainable and efficient catalytic processes across many industrial fields.

Bulletin Board

Gossip

AUG. 02, 2024

Hydrogenation—the chemical reaction of hydrogen gas with another compound—is fundamental in industries such as food, pharmaceuticals, materials, and petrochemicals.

Traditionally, noble metals like palladium and rhodium serve as catalysts in these reactions. However, these materials are scarce and expensive, and their mining is plagued by environmental concerns. Moreover, they demand highly controlled and energy-intensive conditions to function effectively.

In recent years, cobalt has emerged as a promising alternative to noble metal catalysts for hydrogenation. Cobalt nanoparticles (Co NPs) can catalyze hydrogenation reactions efficiently, requiring lower temperatures and pressures than noble metal catalysts.

Despite the theoretical significance of the crystal phase of Co NPs in their catalytic performance, studying this has been challenging due to the lack of methods to produce Co NPs with a specific crystal phase of similar size.

Fortunately, a research team from Tokyo Institute of Technology and Osaka Metropolitan University has found a solution to this issue. As reported in their latest study, which was published in the *Journal of the American Chemical Society*, they devised a new method to selectively produce Co NPs with two very distinct crystal phases in a convenient and consistent way.

"We previously reported that nickel NPs can be readily synthesized by the reduction of nickel complexes in the presence of hydrosilanes through a technique we dubbed the hydrosilane-assisted method," explains Professor Michikazu Hara, who led the study.

"We hypothesized hydrosilanes would act not only as reducing agents for Co cations, but also as ligands on the metal complexes to control the growth of metal particles. Therefore, we attempted to synthesize Co NPs with a controlled crystal phase via the simple addition of appropriate coordination compounds and specific diol solvents."

Through careful testing, the research team found their predictions were right, and the hydrosilane-assisted method could reliably produce two types of Co NPs depending on the reaction conditions: face-centered cubic (fcc) Co NPs and hexagonal close-packed (hcp) Co NPs. They then ran several hydrogenation experiments to explore the differences in catalytic performance between both types of Co NPs.

Bulletin Board

Gossip

AUG. 02, 2024

Interestingly, they observed that hcp-Co NPs were far superior to fcc-Co NPs. In the hydrogenation of benzonitrile into benzyl amine, hcp-Co NPs achieved a much higher selectivity, exhibiting a yield of 97% compared to fcc-Co NPs' 80%.

Moreover, hydrogenation using hcp-Co NPs required a pressure of roughly half that of fcc-Co NPs, rendering the entire process more energy-efficient. This notable feat is not limited to the production of benzyl amine only, as Hara says, "Worth noting, the proposed Co NP-based catalytic system displayed compatibility with a diverse range of nitriles and carbonyl compounds."

Considering that cobalt is abundant, and the proposed Co NP-base catalyst is reusable and does not require harmful gases such as ammonia, this work could serve as a stepping stone towards more sustainable and cost-effective hydrogenation technologies.

In turn, this may lower the price and environmental impact of many industrial commodities, drugs, and even food products, leading to an overall better future for humanity in multiple ways.

Phys Org, 1 August 2024

<https://phys.org>

Breakthrough in plant disease: New enzyme could lead to anti-bacterial pesticides

2024-08-01

Plant diseases pose significant challenges to agricultural productivity, presenting formidable hurdles that require urgent attention. Left unchecked, these diseases can spread rapidly, inflicting widespread damage on crops and leading to reduced yields and substantial economic losses. Therefore, accurately identifying the pathogens responsible for these diseases is crucial. This identification allows for targeted interventions that minimize risks and effectively mitigate the agricultural impacts.

Xanthomonas species are notorious plant pathogens that affect a broad spectrum of hosts, including key crops like rice, wheat, and tomatoes. These pathogens augment their pathogenicity by utilizing α -1,6-cyclized β -1,2-glucohexadecaose (C β G16 α) to suppress essential plant defense mechanisms, such as the expression of pathogenesis-related proteins and the accumulation of callose.

Bulletin Board

Gossip

AUG. 02, 2024

In a recent breakthrough published on June 19, 2024, in the Journal of the American Chemical Society, a team of researchers led by Associate Professor Masahiro Nakajima from Tokyo University of Science unveiled a significant discovery. They identified XccOpgD, a glycoside hydrolase (GH186) found in *X. campestris pv campestris* which plays a pivotal role in the biosynthesis of C β G16 α . The research team also included Mr. Sei Motouchi from Tokyo University of Science, Principal Scientist Shiro Komba from the Institute of Food Research, NARO, and Hiroyuki Nakai from Niigata University.

"Glycan structures are intricate and multifaceted and fulfill diverse crucial roles in nature and organisms. Enzymes synthesize and degrade glycans, exhibiting diverse structures and functions that correspond to the glycan diversity. However, our understanding of these enzymes is still limited, which drives the search for new enzymes with varied new potentials," explains Prof. Nakajima, elaborating on the study's rationale.

The team conducted biochemical analysis to elucidate the role of XccOpgD in C β G16 α biosynthesis. Advanced techniques such as X-ray crystallography were employed as structural analysis to unravel the enzyme's catalytic mechanism and substrate specificity.

These efforts have yielded profound insights. XccOpgD belongs to the GH186 family, essential for regulating bacterial cell wall components. Unlike the first identified GH186 enzymes, XccOpgD exhibits an unprecedented enzymatic mechanism known as anomer-inverting transglycosylation.

"Reactions of typical GH enzymes are classified into four types by combination of retaining or inverting, and reaction with water (hydrolysis) or sugar (transglycosylation) theoretically. However, one classification is missing somehow in a long history of researches on carbohydrate associated enzymes and we discovered the missing classification. This breakthrough was made possible by unique structural environment, opening new possibilities for enzyme-based glycosylation," explains Prof. Nakajima. Moreover, the sugar chains synthesized through this mechanism are not merely minor components but rather essential structures utilized by various Gram-negative bacteria in nature for pathogenic purposes.

Detailed studies revealed that linear β -1,2-glucan was converted to cyclic compound and the compound was identified as C β G16 α using nuclear magnetic resonance. Structural analysis of the Michaelis complex identified crucial substrate binding residues, further elucidating specific interactions along the glucan chain. Notably, XccOpgD utilizes an anomer-

Bulletin Board

Gossip

AUG. 02, 2024

inverting transglycosylation mechanism, with D379 and D291 playing pivotal roles as catalysts.

These findings deepen our understanding and open avenues for developing targeted strategies against *Xanthomonas*-induced plant diseases. "We are expecting a pesticide concept targeting this enzyme homolog in the future. Unlike fungicides that promote the emergence of drug-resistant bacteria in soil, targeting this enzyme could potentially inhibit pathogenicity without causing sterilization. Enzyme homologs identified in this study may serve as promising structure-based drug targets, offering a potential solution to the issue of drug-resistant bacteria," says a hopeful Prof. Nakajima.

The discovery of XccOpgD and its role in C β G16 α biosynthesis marks a major breakthrough in agriculture. It promises enhanced resilience and food security while mitigating environmental impacts linked to conventional pesticides. Overall, this advancement offers sustainable solutions to global agricultural challenges, promoting environmental stewardship and economic viability for farmers worldwide.

Science Daily, 1 August 2024

<https://scientistdaily.com>

Does honey ever go bad?

2024-07-12

Honey is a pantry staple that can be safe to eat for ages. But does honey ever go bad? And why is honey so resistant to spoiling?

It appears that this thick, sticky, sweet nectar owes its properties to chemicals imparted by its makers — honeybees. Astonishingly, there are at least 300 types of honey known today that are produced by more than 20,000 honeybee species.

"The composition of the honey depends on the type of honeybees," Kantha Shelke, a food scientist at Johns Hopkins University and founder of Corvus Blue LLC, a food science and nutrition research firm based in Chicago, told Live Science in an email.

After collecting nectar from flowers, bees turn the sucrose, a complex mix of glucose and fructose, into highly concentrated simple sugars. While honey is mostly sugars, it also contains more than a dozen other substances, such as enzymes, minerals, vitamins and organic acids. Honey also contains flavonoid and phenolic compounds, which are known to be

Bulletin Board

Gossip

AUG. 02, 2024

anti-inflammatory and antioxidants. These compounds are responsible for honey's medicinal properties.

The multitude of chemicals that coalesce when honeybees create honey makes this natural sweetener inhospitable to microbes that usually spoil food.

Honey's high sugar content makes it hygroscopic, meaning it can suck moisture from the environment, and even absorb the water from surrounding microbial cells. Honey also has a low level of available water in which microbes can grow.

After turning flower nectar into simple sugars, bees regurgitate the sweet liquid and pass it on to other bees in the hive. As the nectar sits inside the bees' stomachs, glucose oxidase breaks down the glucose and turns it into gluconic acid and hydrogen peroxide. When the bees finally place and fan the digested nectar in the comb, water slowly evaporates and turns this sweet liquid viscous.

The presence of gluconic, as well as acetic, formic, and citric acid, makes honey even more acidic than coffee. This pH range is lower than what most microbes can tolerate. And the hydrogen peroxide in honey may stop bacteria from forming a slimy network called biofilm that usually sticks to surfaces.

All of these chemicals stop microbes from degrading honey. But while honey remains safe to consume for a long period, it does change over time.

"Honey constituents undergo changes because of crystallization, fermentation, oxidation, and thermal effects. The changes also depend on the type of honey (light or dark) and source, or region which vary with the season and the plants foraged by the honeybee," Shelke said. "Some of these changes influence the nutritional and sensory attributes including appearance."

When heated or stored for a long time, honey can undergo a Maillard reaction, the same chemical reaction that caramelizes sugar and turns it brown. As sugars become dehydrated, they produce a potentially toxic compound, 5-hydroxymethylfurfural (HMF). HMF is also found in many other food products including breakfast cereals, dried fruits and milk.

The safe levels of HMF for daily consumption are still poorly understood. Some research has suggested HMF can fuel cancer, while others suggest the compound can prevent allergic reactions. The Codex Alimentarius

Bulletin Board

Gossip

AUG. 02, 2024

Standard, an international standard on food safety, has set an upper limit of 40 mg/kg HMF for honey products. But this limit varies among the different types of honey. For instance, sunflower honey can reach this HMF limit after being properly stored for 18 months, while acacia honey takes about five years to reach the same amount of HMF.

Heating leads to HMF production, but cooling causes honey to crystallize. As honey cools, the sugar content becomes too saturated and unable to stay in solution. This can also happen when moisture escapes the honey during storage, causing the sugars to form crystals, Shelke said.

According to one study, the sensory and chemical properties of honey are best preserved when stored at 75 degrees Fahrenheit (24 degrees Celsius), or around room temperature.

Because of all these variables, “handling and packaging can greatly affect the shelf life of honey,” Shelke said. “Raw honey — with intact enzymes and other beneficial compounds — is minimally processed and can last ‘forever’ if stored in a sealed container.”

Likewise, pasteurized honey can last several years. But because it lacks some of the enzymes and antimicrobial compounds, it may be susceptible to microbial damage if not sealed or stored properly, Shelke added.

Of note, caretakers should avoid feeding honey to infants, because spores from the bacterium *Clostridium botulinum* can contaminate honey. These spores can withstand pasteurization temperatures. Once ingested, they can release a toxin into babies’ intestines and cause infant botulism, a condition that can be fatal. The spores are generally harmless to adults as their mature digestive systems purge the toxin.

This article is for informational purposes only and is not meant to offer medical advice.

Live Science, 12 July 2024

<https://livescience.com>

Bulletin Board

Curiosities

AUG. 02, 2024

PFAS Can End Up in Breast Milk, and Rice and Red Meat May Be Prime Sources

2024-07-24

People who consume high amounts of certain foods during pregnancy may have high levels of “forever chemicals” in their lactation milk, according to a recent study published in *Science of the Total Environment*.

After assessing the diets and milk samples of 426 participants, researchers from Dartmouth College found that a higher intake of white rice, red meat, eggs, tea and tomatoes during pregnancy was associated with higher lactation concentrations of perfluorooctanesulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) – 2 of the most harmful per- and polyfluoroalkyl substances (PFAS).

PFAS in food, PFAS in milk

PFAS contamination is a mounting issue around the world. The group of surfactants were first mass produced in the mid-20th century to waterproof consumer products like pans, paints and packaging. They’re now known as forever chemicals because they have an almost-unbreakable highly fluorinated alkyl chain backbone that makes them extremely chemically stable, and difficult to degrade naturally.

This robustness is all the more troubling considering the recent wave of research linking the chemicals to cancers, high cholesterol and low birth weights. Avoiding them doesn’t seem to be an option, either; most Americans already have some levels of PFAS in their blood, according to the US Department of Health and Human Services.

But some people may still be more exposed to PFAS than others depending on their location and the kind of food and beverages they consume. Recent research from the Dartmouth College group found that seafood, particularly lobster and other crustaceans, can host high levels of PFAS.

To see if such products and other foodstuffs could confer PFAS into human breast milk, the researchers accessed data from the New Hampshire Birth Cohort Study, an ongoing study involving over 3,000 participants who were enrolled while pregnant. Between 2013 and 2018, 426 of the participants provided milk samples when 6 weeks postpartum.

These samples were then tested for PFAS levels, and the results were compared with the participants’ responses to a dietary questionnaire.

Bulletin Board

Curiosities

AUG. 02, 2024

A higher intake of white rice, red meat, eggs, tea and tomatoes during pregnancy was associated with higher PFOS and PFOA concentrations in the milk samples.

Rice appeared to be the food most packed with two forever chemicals. After performing a statistical analysis, the researchers found that an increased serving per day of white rice during pregnancy was associated with a 7.5 % and 12.4 % higher milk PFOS and PFOA concentration, respectively.

Rice crops can absorb PFAS from tainted soil, but contamination can also occur when the grains are boiled in PFAS-contaminated water or cooked and stored in PFAS-coated cookware and containers.

Red meat and eggs appeared to be the next two significant sources of PFAS. Every increased serving/day of eggs or red meat was associated with 7.2 % and 9.3 % higher milk PFOS concentration, while one more serving/day of tea or tomatoes was associated with 5.9 % and 6.4 % higher milk PFOA level.

Previous research has suggested that teabags are a prime source of PFAS contamination.

As for seafood – the food source commonly associated with PFAS – the Dartmouth researchers made a surprising finding: while greater seafood consumption was associated with higher PFAS levels in the blood of participants, this contamination was largely absent from the same participants' milk samples. The researchers say a better understanding of the biological mechanisms underpinning milk transfer of PFAS is needed to elucidate this finding.

For now, the researchers advise anyone worried about breastfeeding to push ahead despite the PFAS concerns. The known harms associated with such PFOS and PFOA contamination, they say, still pale to the boons of breastmilk.

"It seems like the benefits of breastfeeding really outweigh the risks of any kind of potential contamination, that's certainly the Centers for Disease Control stance and the World Health Organization stance at the present moment," Megan Romano, one of the researchers of the study and an associate professor of epidemiology at Dartmouth's Geisel School of Medicine, told Technology Networks.

"But we definitely want to learn more about this. And it's the question that I most commonly get asked by women who live in contaminated

Bulletin Board

Curiosities

AUG. 02, 2024

communities. 'Is it safe for me to breastfeed? Should I be breastfeeding?' We'd like to be able to give them better guidance and more satisfying answers," Romano concluded.

Romano was speaking with Leo Bear-McGuinness, Science Writer and Editor at Technology Networks.

Technology Networks, 24 July 2024

<https://technologynetworks.com>

100% of toxic "forever chemicals" break down overnight in new reaction

2024-07-29

Scientists in Japan have developed a new method for breaking down toxic "forever chemicals" quickly and at room temperature. The technique broke down 100% of certain types of these pollutants overnight, recovering some useful components for reuse.

Per- and polyfluoroalkyl substances (PFAS) are a broad class of chemicals that have excellent stability and resistance to water and heat, largely thanks to their strong carbon-fluorine bonds. This makes them perfect for everything from non-stick cookware to firefighting foam and water-repellant clothing.

But those super-strong bonds have a downside too – since they don't break down, the chemicals tend to linger in the environment essentially "forever," hence their nickname. Worse still, when they accumulate in the human body they've been linked to diabetes, fertility issues, various cancers, immune system disruption, and many other health conditions.

Now, scientists at Ritsumeikan University in Japan have developed a new method for breaking down PFAS. Semiconductor nanocrystals of cadmium sulfide (CdS), some of which are doped in copper, are the active ingredients in a solution that also contains water, a compound called triethanolamine (TEOA), and of course the PFAS chemicals waiting to be treated.

When the solution is exposed to LED lights at wavelengths of 405 nm, the nanocrystals become excited and cause the PFAS molecules to stick to their surface. At the same time, electrons are generated and excited in the solution, until they remove fluorine ions from the PFAS molecules, breaking those sturdy bonds.

Bulletin Board

Curiosities

AUG. 02, 2024

In tests, this method successfully broke down 100% of a particular PFAS, called perfluorooctanesulfonate, in just eight hours. Another, called Nafion, broke down by 81% in 24 hours. This was achieved at a temperature of just 38 °C (100 °F) – far cooler than the 400 °C (752 °F) usually required. The technique also recovers the fluoroine ions, allowing them to be reused for other industrial applications.

The technique is similar to many others that use a catalyst to break down PFAS molecules, but usually UV light is required and often a higher temperature. Other teams have found success with similar reactions using supercritical water, magnetic particles, hydrogen or boron nitride. Ultimately, having a mix of options for breaking down PFAS could be the best solution.

The research was published in the journal *Angewandte Chemie International Edition*.

New Atlas, 29 July 2024

<https://newatlas.com>

A Band-Aid for the heart? New 3D printing method makes this, and much more, possible

2024-08-01

In the quest to develop life-like materials to replace and repair human body parts, scientists face a formidable challenge: Real tissues are often both strong and stretchable and vary in shape and size.

A CU Boulder-led team, in collaboration with researchers at the University of Pennsylvania, has taken a critical step toward cracking that code. They've developed a new way to 3D print material that is at once elastic enough to withstand a heart's persistent beating, tough enough to endure the crushing load placed on joints, and easily shapable to fit a patient's unique defects.

Better yet, it sticks easily to wet tissue.

Their breakthrough, described in the Aug. 2 edition of the journal *Science*, helps pave the way toward a new generation of biomaterials, from internal bandages that deliver drugs directly to the heart to cartilage patches and needle-free sutures.

"Cardiac and cartilage tissues are similar in that they have very limited capacity to repair themselves. When they're damaged, there is no

Bulletin Board

Curiosities

AUG. 02, 2024

turning back," said senior author Jason Burdick, a professor of chemical and biological engineering at CU Boulder's BioFrontiers Institute. "By developing new, more resilient materials to enhance that repair process, we can have a big impact on patients."

Worm 'blobs' as inspiration

Historically, biomedical devices have been created via molding or casting, techniques which work well for mass production of identical implants but aren't practical when it comes to personalizing those implants for specific patients. In recent years, 3D printing has opened a world of new possibilities for medical applications by allowing researchers to make materials in many shapes and structures.

Unlike typical printers, which simply place ink on paper, 3D printers deposit layer after layer of plastics, metals or even living cells to create multidimensional objects.

One specific material, known as a hydrogel (the stuff that contact lenses are made of), has been a favorite prospect for fabricating artificial tissues, organs and implants.

But getting these from the lab to the clinic has been tough because traditional 3D-printed hydrogels tend to either break when stretched, crack under pressure or are too stiff to mold around tissues.

"Imagine if you had a rigid plastic adhered to your heart. It wouldn't deform as your heart beats," said Burdick. "It would just fracture."

To achieve both strength and elasticity within 3D printed hydrogels, Burdick and his colleagues took a cue from worms, which repeatedly tangle and untangle themselves around one another in three-dimensional "worm blobs" that have both solid and liquid-like properties. Previous research has shown that incorporating similarly intertwined chains of molecules, known as "entanglements," can make them tougher.

Their new printing method, known as CLEAR (for Continuous-curing after Light Exposure Aided by Redox initiation), follows a series of steps to entangle long molecules inside 3D-printed materials much like those intertwined worms.

When the team stretched and weight-loaded those materials in the lab (one researcher even ran over a sample with her bike) they found them to be exponentially tougher than materials printed with a standard method

Bulletin Board

Curiosities

AUG. 02, 2024

of 3D printing known as Digital Light Processing (DLP). Better yet: They also conformed and stuck to animal tissues and organs.

“We can now 3D print adhesive materials that are strong enough to mechanically support tissue,” said co-first author Matt Davidson, a research associate in the Burdick Lab. “We have never been able to do that before.”

Revolutionizing care

Burdick imagines a day when such 3D-printed materials could be used to repair defects in hearts, deliver tissue-regenerating drugs directly to organs or cartilage, restrain bulging discs or even stitch people up in the operating room without inflicting tissue damage like a needle and suture can.

His lab has filed for a provisional patent and plans to launch more studies soon to better understand how tissues react to the presence of such materials.

But the team stresses that their new method could have impacts far beyond medicine—in research and manufacturing too. For instance, their method eliminates the need for additional energy to cure, or harden, parts, making the 3D printing process more environmentally friendly.

“This is a simple 3D processing method that people could ultimately use in their own academic labs as well as in industry to improve the mechanical properties of materials for a wide variety of applications,” said first author Abhishek Dhand, a researcher in the Burdick Lab and doctoral candidate in the Department of Bioengineering at the University of Pennsylvania. “It solves a big problem for 3D printing.”

Other co-authors on the paper include Hannah Zlotnick, a postdoctoral researcher in the Burdick Lab, and National Institute of Standards and Technology (NIST) scientists Thomas Kolibaba and Jason Killgore.

Phys Org, 1 August 2024

<https://phys.org>

Bulletin Board

Curiosities

AUG. 02, 2024

Vegan Diet Appears to Slow Aging in 8-Week-Long Study

2024-07-29

Want to look your best? Consider going vegan – that’s the implication from a new trial that compared the aging effects of vegan and omnivorous diets.

After splitting 21 sets of identical twins into 2 groups, which were either fed a vegan or omnivorous diet for 8 weeks, the researchers from Stanford University measured the participants’ DNA methylation levels to determine how much they had biologically aged.

The researchers found that individuals on the vegan diet showed decreases in their “epigenetic aging clocks” – decreases that weren’t observed in their twins fed the omnivorous diet.

The vegan dieters also showed decreases in the ages of their hearts, livers and inflammatory and metabolic systems. Again, these decreases weren’t observed in the omnivorous dieters.

However, before any vegan influencers rush to market themselves as anti-aging gurus, it’s worth acknowledging that other causes could be behind these rejuvenating benefits. For instance, the vegan participants lost more weight over the course of their eight-week diets than the omnivorous participants – weight loss that could account for their slower aging clocks.

The results were published in BMC Medicine.

Turning back the epigenetic clock

DNA methylation is a leading marker for measuring biological aging. The pattern of a person’s DNA methylation is strongly correlated with their aging, making a person’s “epigenetic clock” a viable measurement of their age.

In their trial, the researchers from Stanford and TruDiagnostic (a company that sells epigenetic testing kits) measured the DNA methylation levels of the 42 participants by analyzing blood samples taken at the beginning, middle and end of the 8-week-long diet period.

For their diets, the omnivore twins ate between 170 and 225 grams of meat, 1 egg and 1.5 servings of dairy each day. The vegan half of the cohort were instructed to avoid all animal products. Diets were assessed via 24-hour recalls and participant logs.

Bulletin Board

Curiosities

AUG. 02, 2024

Most of the study participants (77%) were women, with an average age of 39.9.

At the end of the trial, the researchers observed that, unlike the omnivorous participants, the vegan ones exhibited significant decreases in epigenetic age acceleration.

On closer inspection, 5 out of 11 tested organ systems (inflammation, heart, hormone, liver and metabolic systems) showed biological age reductions in the vegan twins, too.

However, these aging differences weren't so clear when other measurements were used. An analysis of the participants' total number of stem cell replication cycles, for instance, showed no significant differences between the vegan and omnivorous dieters.

Nevertheless, by focusing on the epigenetic data, the researchers concluded that vegan diets appear to provide short-term anti-aging benefits. These coveted effects, they say, could be due to the rich antioxidant content and anti-inflammatory properties found in plant products like vegetables and nuts.

They stress that any long-term adherence to a vegan diet, though, should include vitamin and nutrient supplementation.

"This research shows us that certain markers in our DNA, known as epigenetic biomarkers, can give us valuable information about how our diet affects our body at the cellular level," Varun B Dwaraka, head of bioinformatics at TruDiagnostic, told Technology Networks.

"Essentially, this means that by studying these markers, we can better understand how different foods influence our aging process. This insight opens up possibilities for customizing diets in a way that might help people stay healthy and age better, tailoring eating habits according to how someone's body specifically reacts to different foods." "This could be a big step forward in using science to improve health and wellness through personalized nutrition."

Skepticism from others

Others, however, have questioned the conclusions of the study.

In a statement made to the UK's Science Media Centre, Dr. Duane Mellor, a registered dietician and spokesperson for the British Dietetic Association, noted that the weight lost by the vegan participants could easily explain the epigenetic results.

Bulletin Board

Curiosities

AUG. 02, 2024

"Those following the vegan diet ate fewer calories and lost weight which could easily be the reason why the participants DNA was methylated in a healthier way that is associated with longevity," Mellor said.

"Although the study compared a vegan diet to an omnivorous diet, these diets were not entirely matched with vegan participants on average consuming around 200kcal fewer per day, resulting in an average 2 kg weight loss. This was generally caused by those on the vegan diet eating less protein and fat than the omnivore group. It is possible that a reduction in energy intake could potentially have altered how the participants [sic] DNA was changed."

"Another important consideration was that the vegan group were asked to eat twice the number of portions of vegetables, more fruit and more legumes, nuts and seeds than the omnivore group," Mellor continued. "In part this was to replace meat, eggs and dairy foods, but this would mean fiber intake as well as the vitamin and mineral intakes are likely to be different between group, which also could in part explain the differences reported. Finally, the omnivores were asked to eat 6-8oz (175-225g) of meat per day, which seems a lot compared to the UK recommendations."

The study acknowledges partial funding by the Vogt Foundation, which has a mission "to assist plant-based development and protect all animals while supporting organizations that produce animal alternative products or protect animals."

Technology Networks, 29 July 2024

<https://technologynetworks.com>

Breakthrough in plant disease: New enzyme could lead to anti-bacterial pesticides

2024-08-01

Plant diseases pose significant challenges to agricultural productivity, presenting formidable hurdles that require urgent attention. Left unchecked, these diseases can spread rapidly, inflicting widespread damage on crops and leading to reduced yields and substantial economic losses. Therefore, accurately identifying the pathogens responsible for these diseases is crucial. This identification allows for targeted interventions that minimize risks and effectively mitigate the agricultural impacts.

Bulletin Board

Curiosities

AUG. 02, 2024

Xanthomonas species are notorious plant pathogens that affect a broad spectrum of hosts, including key crops like rice, wheat, and tomatoes. These pathogens augment their pathogenicity by utilizing α -1,6-cyclized β -1,2-glucohexadecaose (C β G16 α) to suppress essential plant defense mechanisms, such as the expression of pathogenesis-related proteins and the accumulation of callose.

In a recent breakthrough published on June 19, 2024, in the Journal of the American Chemical Society, a team of researchers led by Associate Professor Masahiro Nakajima from Tokyo University of Science unveiled a significant discovery. They identified XccOpgD, a glycoside hydrolase (GH186) found in *X. campestris* pv *campestris* which plays a pivotal role in the biosynthesis of C β G16 α . The research team also included Mr. Sei Motouchi from Tokyo University of Science, Principal Scientist Shiro Komba from the Institute of Food Research, NARO, and Hiroyuki Nakai from Niigata University.

"Glycan structures are intricate and multifaceted and fulfill diverse crucial roles in nature and organisms. Enzymes synthesize and degrade glycans, exhibiting diverse structures and functions that correspond to the glycan diversity. However, our understanding of these enzymes is still limited, which drives the search for new enzymes with varied new potentials," explains Prof. Nakajima, elaborating on the study's rationale.

The team conducted biochemical analysis to elucidate the role of XccOpgD in C β G16 α biosynthesis. Advanced techniques such as X-ray crystallography were employed as structural analysis to unravel the enzyme's catalytic mechanism and substrate specificity.

These efforts have yielded profound insights. XccOpgD belongs to the GH186 family, essential for regulating bacterial cell wall components. Unlike the first identified GH186 enzymes, XccOpgD exhibits an unprecedented enzymatic mechanism known as anomer-inverting transglycosylation.

"Reactions of typical GH enzymes are classified into four types by combination of retaining or inverting, and reaction with water (hydrolysis) or sugar (transglycosylation) theoretically. However, one classification is missing somehow in a long history of researches on carbohydrate associated enzymes and we discovered the missing classification. This breakthrough was made possible by unique structural environment, opening new possibilities for enzyme-based glycosylation," explains Prof. Nakajima. Moreover, the sugar chains synthesized through this mechanism

Bulletin Board

Curiosities

AUG. 02, 2024

are not merely minor components but rather essential structures utilized by various Gram-negative bacteria in nature for pathogenic purposes.

Detailed studies revealed that linear β -1,2-glucan was converted to cyclic compound and the compound was identified as C β G16 α using nuclear magnetic resonance. Structural analysis of the Michaelis complex identified crucial substrate binding residues, further elucidating specific interactions along the glucan chain. Notably, XccOpgD utilizes an anomer-inverting transglycosylation mechanism, with D379 and D291 playing pivotal roles as catalysts.

These findings deepen our understanding and open avenues for developing targeted strategies against Xanthomonas-induced plant diseases. "We are expecting a pesticide concept targeting this enzyme homolog in the future. Unlike fungicides that promote the emergence of drug-resistant bacteria in soil, targeting this enzyme could potentially inhibit pathogenicity without causing sterilization. Enzyme homologs identified in this study may serve as promising structure-based drug targets, offering a potential solution to the issue of drug-resistant bacteria," says a hopeful Prof. Nakajima.

The discovery of XccOpgD and its role in C β G16 α biosynthesis marks a major breakthrough in agriculture. It promises enhanced resilience and food security while mitigating environmental impacts linked to conventional pesticides. Overall, this advancement offers sustainable solutions to global agricultural challenges, promoting environmental stewardship and economic viability for farmers worldwide.

Science Daily, 1 August 2024

<https://sciencedaily.com>

Weight-loss drugmakers bet billions on boosting supplies

2024-08-01

There is a gush of investment from drugmakers Eli Lilly and Novo Nordisk as the companies hasten to boost production of their new anti-obesity drugs. Demand for these drugs, which mimic the natural hormone glucagon-like peptide 1 (GLP-1), has rapidly outstripped supply and the leading duo are now trying to keep pace with the predicted market growth for these incredibly valuable drugs.

Bulletin Board

Curiosities

AUG. 02, 2024

Earlier this year, Eli Lilly upped its 2024 revenue forecast for its GLP-1 medicines Mounjaro and Zepbound (tirzepatide) by \$2 billion (£1.5 billion) to almost \$9 billion. Meanwhile, there are predictions that GLP-1 drugs could reach over \$125 billion in sales annually for diabetes and obesity by 2033.

To boost supplies, the two leaders are opting to build up their own internal production capacity. Lilly is to invest \$9 billion at a site in Indiana, US, to boost production of tirzepatide. It previously announced expansion at a manufacturing site in Germany, bringing to \$11 billion its global manufacturing investments over the past three years.

Similarly, Novo Nordisk announced a \$4 billion injection into a US manufacturing facility in North Carolina in June. And its parent company, Novo Holdings, agreed a deal to buy Catalent, a contract drug manufacturing organisation (CDMO), for \$16.5 billion with Novo Nordisk expected to acquire three of Catalent's manufacturing sites to bolster production of its drugs Ozempic and Wegovy (semaglutide), once the deal is finalised.

'If you want to meet the future demand, the time to expand is now,' says Ivan Lugovoi, professor of supply chain management at Kühne Logistics University in Hamburg, Germany. It can take three to five years to build, install, validate and qualify a facility to make these drugs. The fill-finish line for pre-filled syringes – needed for the weekly injections of current GLP-1 drugs – are also different from those handling vials and cartridges. 'You need to have specialised technologies in place to process and move those devices,' says Gil Roth, president of the Pharma & Biopharma Outsourcing Association in the US.

Expanding their own production lines will give Eli Lilly and Novo Nordisk greater security over supply, and more control over forecast and production volumes. It should also lower costs by improving their manufacturing process. 'They see this as their main revenue-making drugs, so they want control,' says Lugovoi. But creating in-house capacity comes with its own risks, and Novo's Catalent deal is also raising questions about its implications for drug supplies generally.

Supply security

Novo's purchase of Catalent surprised industry watchers. 'We haven't seen very much CDMO capacity becoming captive in-house capacity for a pharma company,' says Roth. He notes that smaller biopharma companies have often been reluctant to get stuck with bricks and mortar, opting to

Bulletin Board

Curiosities

AUG. 02, 2024

collaborate with a CDMO. The purchase has also drawn the attention of the Federal Trade Commission (FTC) in the US, however, which has requested additional information on the deal.

Politicians and regulators have become increasingly sensitive to drug costs and antitrust issues, and the deal has raised concerns over its potential impact on competition in the pharma industry. David Balto, an attorney and former policy director of the FTC, notes that Catalent is one of only two full service CDMOs in the US, with 87 of the top 100 pharmaceutical manufacturers and 80 of the top biologics relying on it. 'CDMOs play a vital role, in not only manufacturing, but also in helping the pharmaceutical firms go through the regulatory process,' says Balto. 'I don't think there are any kind of conditions that you could put in place to adequately protect consumers.'

Balto warns that the deal could give Novo Nordisk control over GLP-1 drug supply in particular, allowing it 'to dictate the terms of competition to its rivals and effectively raise the cost and reduce the availability of these vital drugs'.

Security of supply matters from a business and political perspective now more than ever, and there is pressure on pharma to ensure supply of essential medicines. 'For politicians, it is very difficult to explain drug shortages,' says Lugovoi. Yet views on the Catalent deal are mixed. 'I don't see problems with this deal,' Lugovoi adds.

CDMO outsourcing could be further hit by legislation winding its way through the US Congress – the BioSecure Act. This alleges that key Chinese instrument makers and CDMOs have ties to the military. The bill would prohibit US pharma from collaborating with specified Chinese CDMOs by blocking certain government contracts, grants and loans to companies that do business with them.

'There is growing industry awareness around Biosecure now, and CDMO customers are taking its prospects very seriously,' says Roth, but he is cautious about predictions. 'It is a fraught situation right now in terms of understanding what it's going to mean, how its going to be implemented and what the fallout is going to be,' he says.

Competition is coming

The spate of investment in manufacturing also signals to any competitors developing their own GLP-1 drugs that this will be a tough market to enter. '[Novo and Lilly] are trying to dissuade others to invest by saying we

Bulletin Board

Curiosities

AUG. 02, 2024

are putting in billions and will have a competitive advantage with our in-house manufacturing,' says Lugovoi.

Those competitors are already on the horizon. Viking Therapeutics has a GLP-1 drug that also hits another receptor (GIP), which completed a phase 2 trial this year in patients with obesity. It also has an oral version moving into phase 2. Meanwhile, Roche recently announced positive results for a once-daily oral GLP-1. Amgen too is developing its own anti-obesity drug, with phase 1 results published early this year.

'For the next two years, I can see Eli Lilly and Novo holding prices, but prices should start to come down in two to three years as more competition arrives,' says Philip Short, fund manager at Flagship Asset Management. Once the medicines come off patents early the next decade, prices may fall precipitously.

That creates a risk for pharma investing in production sites that could become obsolete. 'There is massive investment, but longer term, this market is susceptible to significant change, such as if somebody develops an oral GLP-1,' says Roth. 'Similarly, while current versions of GLP-1s are weekly, companies are working on monthly injections.'

Novo Nordisk and Eli Lilly have enormous business incentives to ensure supply chain resilience. They will also hope that their first mover advantage will allow them to capitalise on other treatments that target the GLP-1 receptor, such as positive trial results for reducing sleep apnea and recent reports on semaglutide given to diabetics with chronic kidney disease. Earlier this year, the US Food and Drug Administration approved injections of semaglutide to reduce the risk of heart attacks and stroke.

Nonetheless, it remains challenging for Lilly and Novo to invest the right amount in their own manufacturing facilities. 'It's a delicate balancing act to get the right supply now without over capitalising on capacity,' says Short.

Chemistry World, 1 August 2024

<https://chemistryworld.com>

Bulletin Board

Curiosities

AUG. 02, 2024

Hydrogel can preserve medications for weeks outside of a fridge

2024-07-17

Many medications must be refrigerated or they lose their effectiveness, but a new method of packing protein-based drugs into a stiff gel could make them last longer at room temperature.

Drugs can break down if they aren't stored properly, which can make them unsafe to use. Exposure to high temperatures, for example, can break the chemical bonds that maintain a drug molecule's shape, disrupting its function. For some drugs, shaking can make their molecules clump together, reducing their efficacy. Matthew Gibson at the University of Manchester in the UK has been working on addressing these challenges for almost 15 years.

He and his colleagues have now developed a method that could make handling protein-based drugs simpler and more practical. He says the new advance came from working with Dave Adams at the University of Glasgow in Scotland, who specialises in making hydrogels. They worked out how to mix proteins with gel ingredients and end up with a stiff white structure that can be loaded into a syringe. In this form, proteins that would usually have to be refrigerated at -20°C (-4°F) withstood temperatures as high as 50°C (122°F) and remained functioning under these conditions for up to four weeks.

The hydrogel gets its stiffness from small molecules combined into large chains, which are then broken by applying force. In syringes, pushing down on the plunger breaks the molecular bonds, turning the gel and protein mixture into a liquid. The hydrogel remnants were too big to enter the syringe's needle, so only the drug leaves the syringe.

The team tested this method with several compounds, including bovine insulin and β -Galactosidase, an enzyme commonly used for gene studies in biology. They also mailed a box filled with containers full of protein-packed hydrogels to themselves and found that the proteins withstood the temperatures and jostling of the journey through the postage system.

Though there are laboratory methods that can keep proteins stable for longer, this approach may be better suited to leave the lab and enter the clinic, says Alex Brogan at King's College London. He says that it would most benefit countries and regions where cold storage is rare and prohibitively expensive. If the new method works with protein-based vaccines, it could make disease prevention more equitable, he says.

Bulletin Board

Curiosities

AUG. 02, 2024

Gibson says that he and his team are confident they could make their hydrogel at industrial scales, but they want to conduct more studies on its longevity and safety. While using it with vaccines is on their wish list, in the short term the method could also be used to store, transport and administer semaglutide, a drug used to treat diabetes and obesity.

New Scientist, 17 July 2024

<https://newscientist.com>

Health-threat 'forever chemicals' removed from water with 3D-printed ceramic ink

2024-08-01

Engineers have invented a new way to remove health-harming 'forever chemicals' from water—using 3D printing.

Researchers at the University of Bath say their method, using ceramic-infused lattices (or 'monoliths'), removes at least 75% of perfluorooctanoic acid (PFOA), one of the most common perfluoroalkyl and polyfluoroalkyl substance (PFAS), from water, and could become an important tool in future efforts to eliminate the chemicals from water supplies.

Their findings were published in the Chemical Engineering Journal.

Known as forever chemicals due to the incredibly long time they take to break down—in some cases over 1,000 years—PFAS are man-made and known for causing health issues including harms to reproductive, developmental, cardiovascular systems, and in increasing likelihood of diabetes.

Sources of PFAS include domestic products, often with water-repellent properties, such as non-stick pans, raincoats, paints, fabrics and firefighting foams.

Dr. Liana Zoumpouli, a Research Associate in Bath's Department of Chemical Engineering and a member of the Center for Digital, Manufacturing and Design, says, "PFAS, or forever chemicals," are a major focus in water treatment and public health. We have created an efficient way to remove these chemicals from water without using lots of energy.

"Using 3D printing to create the monoliths is relatively simple, and it also means the process should be scalable. 3D printing allows us to create objects with a high surface area, which is key to the process. Once the monoliths are ready, you simply drop them into the water and let them do

Bulletin Board

Curiosities

AUG. 02, 2024

their work. It's very exciting and something we are keen to develop further and see in use."

While legislators around the world, particularly in the US and EU, have brought in some rules on acceptable levels of PFAS and similar chemicals in drinking water, the researchers say further legislation is likely as the scale of health threats comes into clearer focus.

Co-author Professor Davide Mattia adds, "Currently, these chemicals are not strongly regulated in the UK in drinking water, but there are guidelines, and we expect changes in policy quite soon. Water companies are likely to be looking at integrating systems to deal with them."

Made of ink infused with the ceramic indium oxide, the 4cm monoliths are created by extruding the ink from a 3D printer—like squeezing toothpaste from a tube—and forming it into a lattice shape. Because indium oxide bonds with PFAS, the chemicals immediately stick to the monoliths and can be removed from the water in under three hours, which is compatible with current water treatment plants in the UK and abroad.

While testing has so far found that the monoliths remove 75% of PFAS from water, the team is aiming to increase the efficiency of the process with further refinement.

Testing of the monoliths has surprisingly shown they have become more effective under repeated use—they undergo high-temperature thermal 'regeneration' treatment after each use. This is something the researchers are keen to understand more fully with further experimentation.

Phys Org, 1 August 2024

<https://phys.org>

Drugs and vaccines could be freed from cold chains by hydrogel

2024-07-31

A stiff hydrogel could end the need for vaccines and gene therapies to be refrigerated, potentially revolutionising the storage and transportation of vital, life-saving medicines.

Cold supply chain management is currently the best solution suppliers have for keeping active biological molecules, like mRNA, proteins and viruses, stable during distribution. However, it requires specialised

Bulletin Board

Curiosities

AUG. 02, 2024

handling and infrastructure, and incurs significant energy costs, limiting distribution.

'A single ultralow temperature freezer can use as much electricity per day as a small household,' says study author Matthew Gibson at the University of Manchester. 'Addressing this may help with sustainability but crucially [would] allow advanced therapies to be shared more widely ... to locations with less developed energy infrastructure.'

'My team has been looking at cryopreservation for over a decade,' he adds. 'We have looked in the past at freezing proteins and had noticed that if we stopped the proteins aggregating, they survived the freezing quite well.'

This line of thinking led Gibson and his team to collaborate with Dave Adams at the University of Glasgow, whose group specialises in low molecular weight gelators – molecules that self-assemble into fibrous 3D networks, trapping large volumes of liquids in the process.

Gibson points out that proteins don't just fall apart or unfold at room temperature. The issue is that they clump together and stop functioning. But to aggregate, proteins need to find and interact with one another – something easily done in a room temperature solution where they are free to move. 'The network stops the proteins being able to move so freely and so [they can't] aggregate,' Adams explains.

Hydrogels have been used before in an effort to solve this problem. But where previous iterations have used chemical bonds to 'tie' proteins to the hydrogel's polymers, the current approach yields stiff hydrogels that 'freeze' the proteins in place without the need to alter them.

'Where you attach the polymer can change the structure and function of the biologic greatly,' says Lydia Kisley of Case Western Reserve University, US, who was not involved in the study.

The gel's rigidity, while great for stabilising biologics, also makes the hydrogel susceptible to breaking. However, the team do not see this as a weakness. 'Many people try to get over this in various ways but we saw this as an advantage – if they break easily when you put strain on them, we reasoned it would be possible to use this to get the proteins back again without the need for any fancy chemistry,' Adams says. 'This gives us a cheap way of trapping the proteins, stopping the aggregation and getting the protein back.'

After some initial tests, the team settled on a gel that forms in the presence of a conventional buffer and its mechanical properties can be

Bulletin Board

Curiosities

AUG. 02, 2024

tuned by simply adding a calcium salt. The stiff hydrogel was found to stabilise proteins against thermal denaturation even at 50°C and, unlike other similar technologies, it delivers pure protein from a syringe.

'This is an interesting combination of materials science with biopharmaceuticals to overcome the tedious storage conditions for biologics,' comments Kisley. '[They] take advantage of what many would consider a problem – the breakage of the gel under strain – as instead a positive to release the protein as it is pushed through a filtered syringe. This is a simple, yet overlooked, idea.'

However, these stiff hydrogels are not ready to begin dismantling drugs' cold chains yet. 'The model tests were limited to two relatively small proteins [but] many biologic therapies are large, antibody-based treatments,' says Kisley. 'Would the gelator still be able to self assemble and form the entangled network to trap large biologics? I wonder if the gelator would be able to maintain its properties with large molecules present.'

'Any new technology has limitations,' Gibson responds, 'and we are exploring the range of proteins we can stabilise. Our discovery has an opportunity to be a platform technology but is adaptable to different use cases depending on the stressors involved.'

Chemistry World, 31 July 2024

<https://chemistryworld.com>

The next generation of RNA chips

2024-07-31

An international research team led by the University of Vienna has succeeded in developing a new version of RNA building blocks with higher chemical reactivity and photosensitivity. This can significantly reduce the production time of RNA chips used in biotechnological and medical research. The chemical synthesis of these chips is now twice as fast and seven times more efficient. The results of the research were recently published in the journal Science Advances.

The emergence and approval of RNA-based medical products, such as mRNA vaccines during the COVID-19 pandemic, has brought the RNA molecule into the public eye. RNA (ribonucleic acid) is an information-carrying polymer -- a chemical compound made up of similar subunits -- but with far greater structural and functional diversity than DNA. About 40 years ago, a method was developed for the chemical synthesis of DNA and RNA, in which any sequence can be assembled from DNA or RNA

Bulletin Board

Curiosities

AUG. 02, 2024

building blocks using phosphoramidite chemistry. The assembly of a nucleic acid chain is carried out step by step using these special chemical building blocks (phosphoramidites). Each building block carries chemical 'protecting groups' that prevent unwanted reactions and ensure the formation of a natural link in the nucleic acid chain.

Overcoming challenges

This chemical method is also used in the production of microchips (microarrays), where millions of unique sequences can be synthesised and analysed simultaneously on a solid surface the size of a fingernail. While DNA microarrays are already widely used, adapting the technology to RNA microarrays has proved difficult due to the lower stability of RNA.

In 2018, the University of Vienna demonstrated how high-density RNA chips can be produced through photolithography: by precisely positioning a beam of light, areas on the surface can be prepared for the attachment of the next building block through a photochemical reaction. Although this first report was a world first and remains unrivalled, the method suffered from long production times, low yields and poor stability. This approach has now been greatly improved.

Development of a new generation of RNA building blocks

A team from the Institute of Inorganic Chemistry at the University of Vienna, in collaboration with the Max Mousseron Institute for Biomolecules at the University of Montpellier (France), has now developed a new version of RNA building blocks with higher chemical reactivity and photosensitivity. This advance significantly reduces the production time of RNA chips, making synthesis twice as fast and seven times more efficient. The innovative RNA chips can be used to screen millions of candidate RNAs for valuable sequences for a wide range of applications.

"Making RNA microarrays containing functional RNA molecules was simply out of reach with our earlier setup, but it is now a reality with this improved process using the propionyloxymethyl (PrOM) protecting group," says Jory Lietard, Assistant Professor at the Institute of Inorganic Chemistry.

As a direct application of these improved RNA chips, the publication features a study of RNA aptamers, small oligonucleotides that specifically bind to a target molecule. Two "light-up" aptamers that produce fluorescence upon binding to a dye were chosen and thousands of variants of these aptamers were synthesized on the chip. A single binding

Bulletin Board

Curiosities

AUG. 02, 2024

experiment is sufficient to obtain data on all variants simultaneously, which opens the way for the identification of improved aptamers with better diagnostic properties.

"High-quality RNA chips could be especially valuable in the rapidly growing field of non-invasive molecular diagnostics. New and improved RNA aptamers are critically sought after, such as those that can track hormone levels in real-time or monitor other biological markers directly from sweat or saliva," says Tadija Keki?, PhD candidate in the group of Jory Lietard.

This work was financially supported by a joint grant of the Agence Nationale pour la Recherche/Austrian Science Fund (FWF International Program I4923).

Science Daily, 31 July 2024

<https://sciencedaily.com>

Bulletin Board

Technical Notes

AUG. 02, 2024

(NOTE: OPEN YOUR WEB BROWSER AND CLICK ON HEADING TO LINK TO SECTION)

CHEMICAL EFFECTS

Highly sensitive response to the toxicity of environmental chemicals in transparent casper zebrafish

Microplastic-derived dissolved organic matter: Generation, characterization, and environmental behaviors

Novel herbicide flusulfenam: absolute configuration, enantioseparation, enantioselective bioactivity, toxicity and degradation in paddy soils

ENVIRONMENTAL RESEARCH

Air pollution generated in an industrial region: effect on the cardiovascular health of humans and damage caused to a plant species, *Piper gaudichaudianum* (Piperaceae), used for biomonitoring

Understanding and addressing microplastic pollution: Impacts, mitigation, and future perspectives

Tracking fine particles in urban and rural environments using honey bees as biosamplers in Mexico

PHARMACEUTICAL/TOXICOLOGY

Perfluorooctanesulfonic acid (PFOS) induced cancer related DNA methylation alterations in human breast cells: A whole genome methylome study

Drug metabolism of ciprofloxacin, ivacaftor, and raloxifene by *Pseudomonas aeruginosa* cytochrome P450 CYP107S1

OCCUPATIONAL

Actinium-225 as an example for monitoring of internal exposure of occupational intakes of radionuclides in face of new nuclear-medical applications for short-lived alpha emitting particles

A cross-sectional comparison of gut metagenomes between dairy workers and community controls