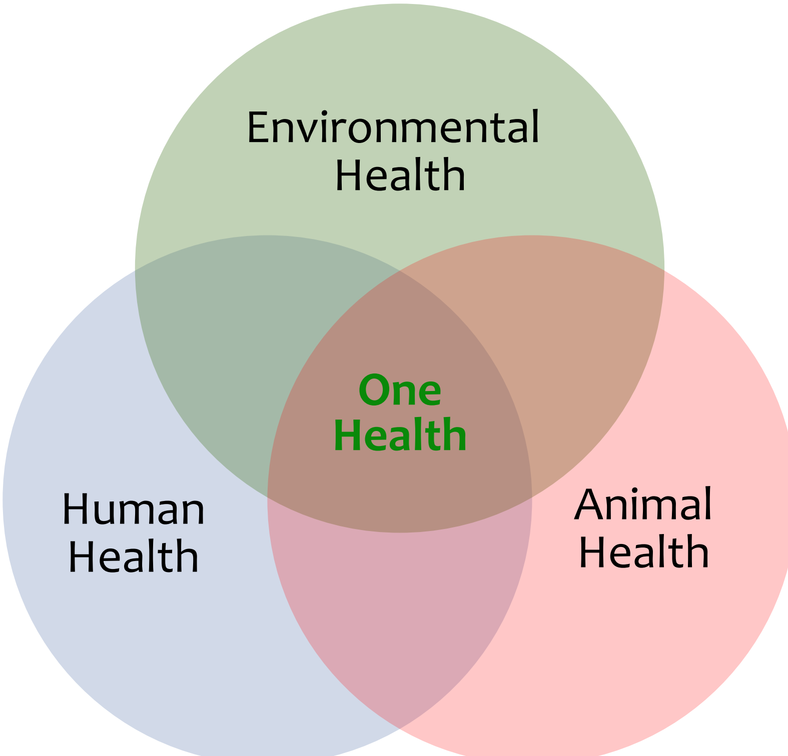
Sustainability and Chemistry
CH5106: L9 AD

Instructors: Sayam Sengupta
Swaminathan Sivaram
Amitava Das



One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems

The chemical pollutant challenge for humanity: Discussion and questions:

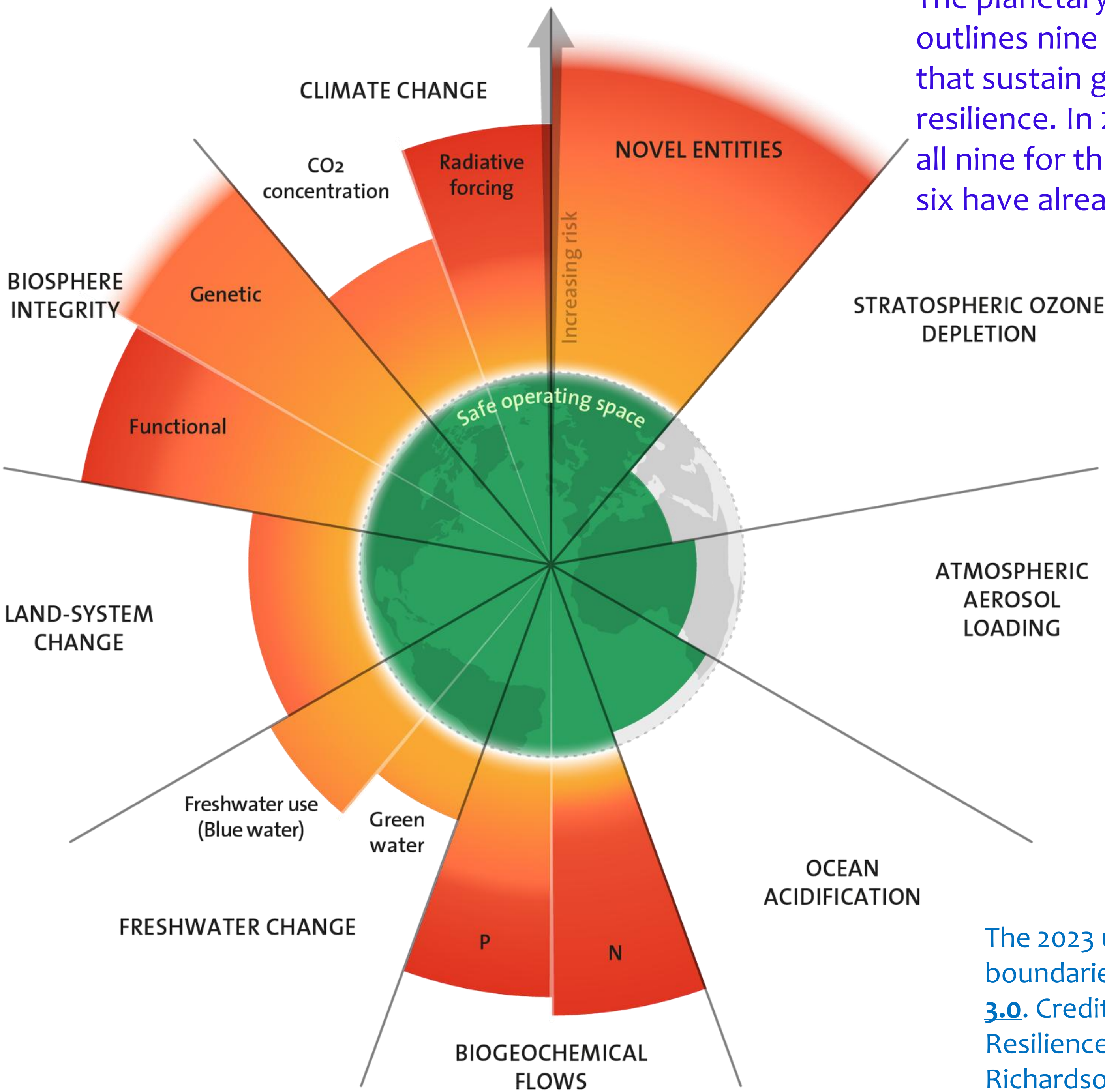
methodological constraints and the varying susceptibility to toxins among humans, only a few reports are showing direct quantitative, whole life-span analyses of fatalities attributed to environmental pollutants. Nevertheless, compilation of the substantial evidence of the health burden caused by chemical pollution both shows and predicts the impairment of normal human life expectancy by direct exposure to pollutants, food contamination and fertility decline.

The concept of the planetary boundary is so pertinent in this regard.

It is likely humanity is approaching a dangerous tipping point due to our release of geogenic, anthropogenic synthetic chemicals. This raises the issue that, as yet, no scientifically credible estimate has been made of humanity's combined chemical impact on the Earth and on human health. This gap exists as the 'global boundaries' chart was unable to include a boundary for chemical emissions because of a lack of data and a suitable methodology.

Consequently, humanity is unaware of how near or far it is from exceeding the Earth's capacity to 'absorb' or safely process our total chemical releases, which grows by many billions of tonnes with each passing year. This represents a potential catastrophic risk to the human future and merits global scientific scrutiny on the same scale and urgency as the effort devoted to climate change.

The planetary boundaries framework outlines nine key Earth system processes that sustain global stability and resilience. In 2023, scientists quantified all nine for the first time and found that six have already been transgressed.



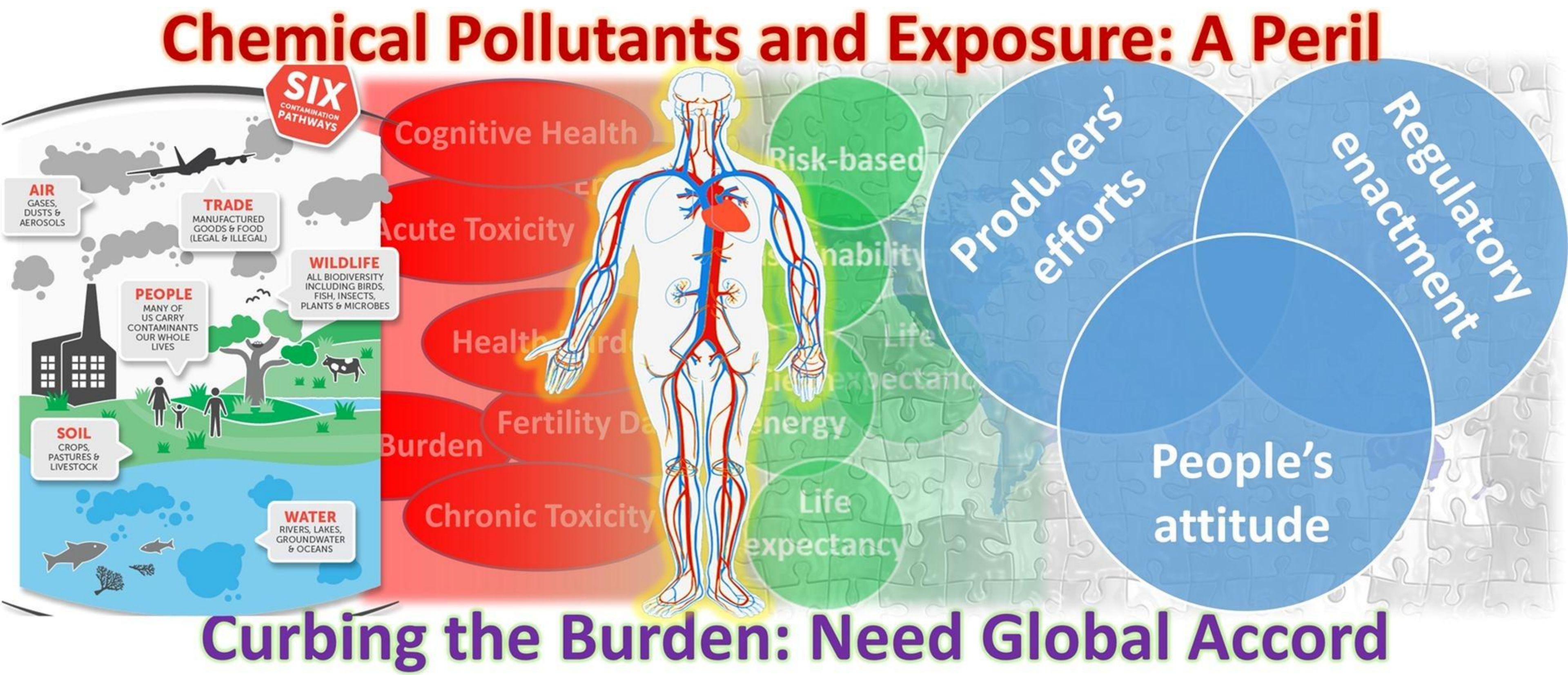
Emerging contaminants (ECs) are a diverse group of unregulated pollutants increasingly present in the environment. These contaminants, including pharmaceuticals, personal care products, endocrine disruptors, and industrial chemicals, can enter the environment through various pathways and persist, accumulating in the food chain and posing risks to ecosystems and human health.

Emerging contaminants pose significant risks to wildlife and ecosystems by disrupting animal hormones, causing genetic alterations that diminish diversity and resilience, and altering soil nutrient dynamics and the physical environment.

Ecotoxicology and Environmental Safety 278 (2024) 116420

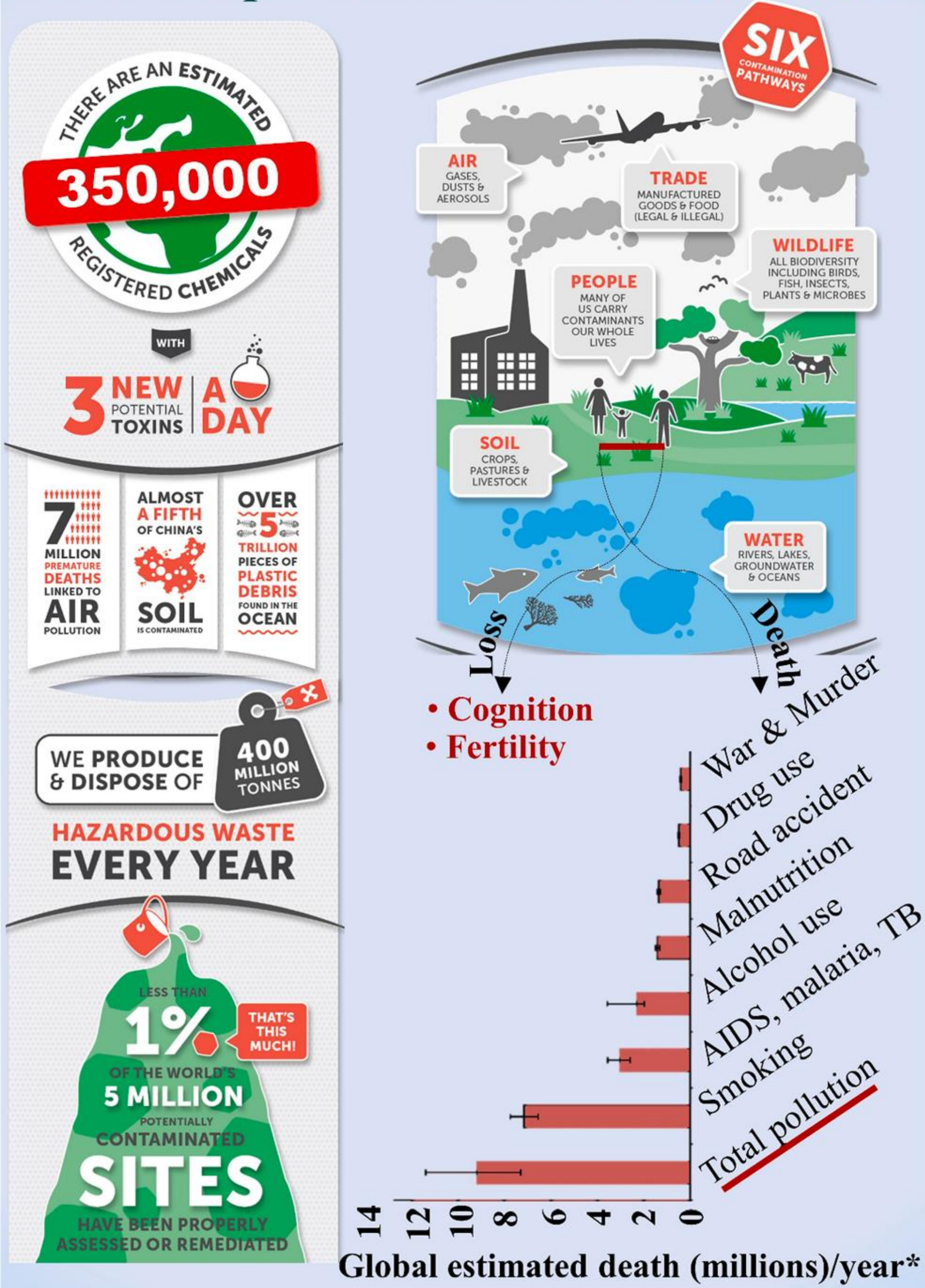
One Health is a collaborative, multisectoral, and transdisciplinary approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognises that the health of humans is interconnected with the health of animals and the environment, and therefore requires integrated efforts from medical, veterinary, agricultural, and environmental sciences to prevent and manage complex health challenges effectively.

Chemical pollution poses an escalating threat to humanity—undermining male fertility, cognitive health, and food security—yet critical knowledge gaps remain about the risks from chemical dispersal, mixtures, and recombination in the environment.



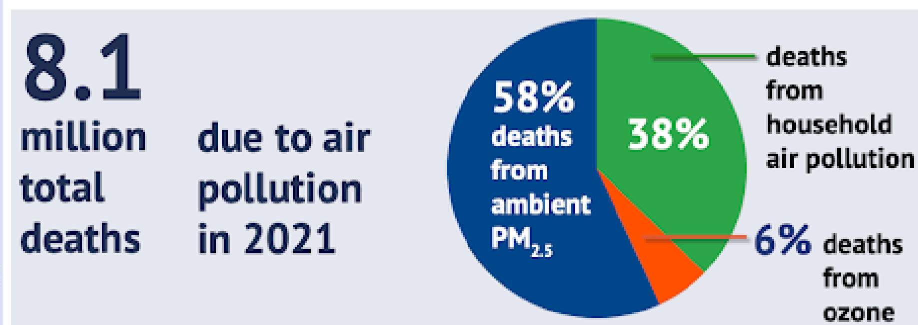
Environment International, 2021, 156, 106616

Chemical pollutant: Global PICTURE



Chemical pollution moves through six major pathways—soil, air, water, wildlife, people, and trade—causing severe environmental and health impacts. Pollution-related deaths, estimated at 9–10 million annually, exceed those from any other major risk factor, far surpassing the 2 million global deaths from COVID-19 in its first year (WHO 2021).

Fig. 1. The number of "silent" deaths caused by environmental pollution exceeds any other widely recognized risk factor.



https://healthpolicy-watch.news/air-pollution-kills-a-child-every-minute/, **2024 data.**

[Environment International 156 (2021) 106616]

International regulation of toxic chemicals began with treaties such as the Vienna Convention for the Protection of the Ozone Layer (1985) and the Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal (1989). These were followed by the Stockholm Convention on Persistent Organic Pollutants (2001) and the Minamata Convention on Mercury (2013). Among these, the Stockholm Convention is the most comprehensive one for POP, entering into force on 17 May 2004. However, its progress has been modest: of an estimated 350,000 synthetic chemicals in circulation, only 26 (<0.01%) have been banned, with just nine additional substances currently under review. in Annexes B and C. [http://www.pops.int/TheConvention/ThePOPs/AllPOPs/tabid/2509/Default.aspx (access: 05 February, 2021)]

[Environment International 156 (2021) 106616]

Pollution impacts on cognitive health:

Recent studies have revealed significant impacts of various industrial pollutants on the human brain and central nervous system. Fine particles, designated PM10, PM2.5, or ultrafine PM0.1, which commonly arise from industrial waste, ash and the combustion products of fossil fuel, can migrate into the brain through the olfactory bulb, the neural structure responsible for the sense of smell. Ultrafine particles also produce cytokines that inflame the lungs or the nasal epithelium and further attack brain cells.

- A 20-year meta-study in China found that children exposed to **fluoride**-contaminated drinking water had a fivefold higher incidence of impaired cognitive performance compared to unexposed children (Tang et al., 2008).
- In vivo studies indicate that per- and poly-fluoroalkyl substances (**PFAS**) are potentially neurotoxic to human neuroblastoma cells. PFAS exposure can alter methylation regulation in brain-derived neurotrophic factor, potentially contributing to behavioural problems (Guo et al., 2017).

Environ. Int. 2021, 156, 106616

Chemical studies show that Al^{3+} binds F^- more strongly than 60 other metal ions. Al is the most abundant metal on earth. It is ubiquitously present in all foodstuffs and drinking water. [Crit Rev Oral Biol Med 14(2):100-114 (2003); Genes & Diseases, 2023, 10, 1470-1493]

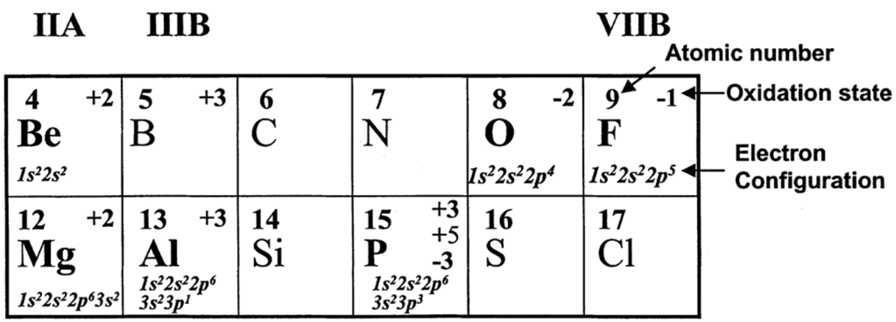
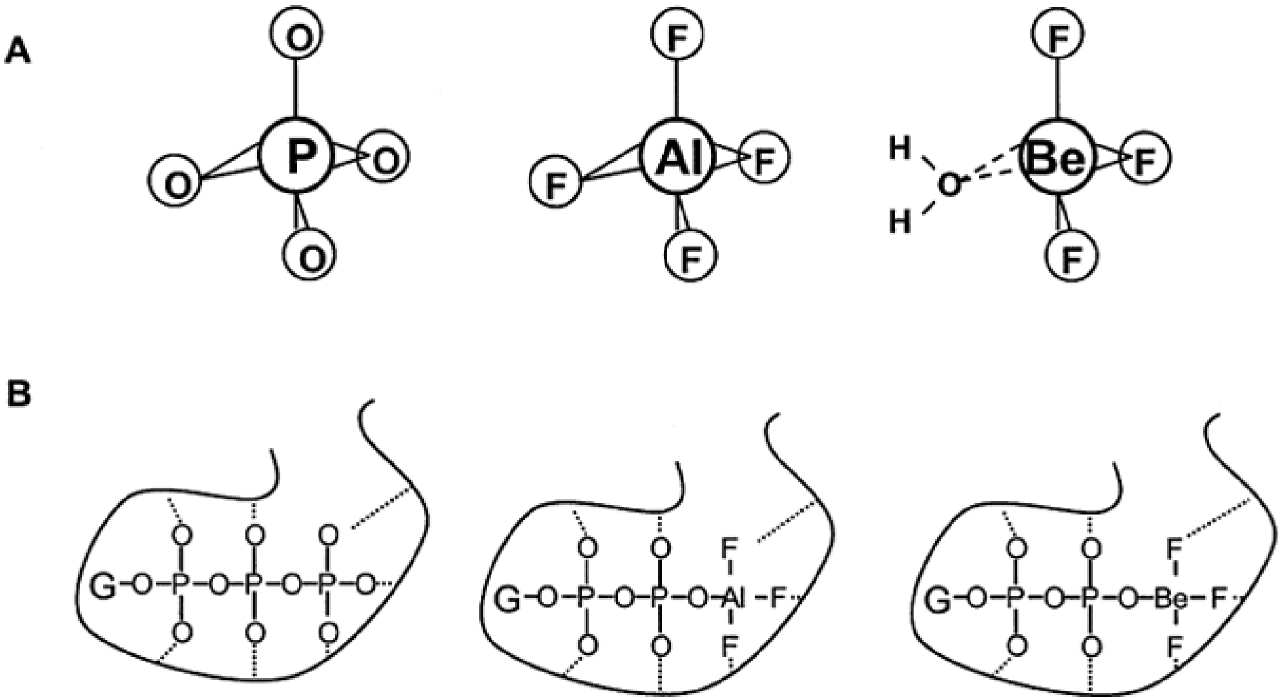
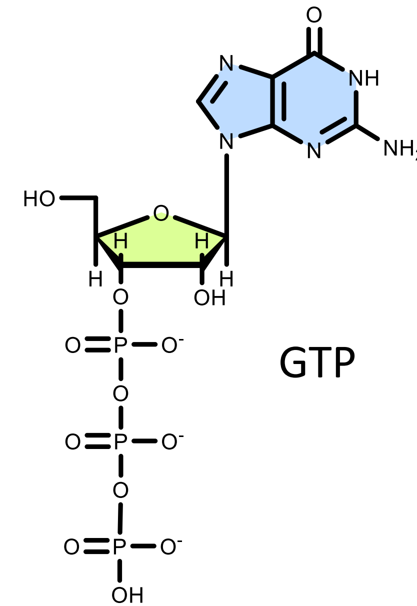


Figure 1. A section of the Periodic Table. For the elements related to phosphate or its analogs, their symbols, atomic numbers, oxidation states, and electron configurations are highlighted.

only a µM level of Al is needed to form biologically effective Al-F complexes. F^- is widely added to human drinking water (1 ppm) and in most toothpastes (500-1500 ppm) to prevent dental caries.

- X In biochemical and cellular research, aluminum fluoride complexes (AlF_x) and beryllium fluoride (BeF_x) are commonly used to interfere with enzyme activity.
- X Both compounds activate G (guanine nucleotide–binding) proteins in eukaryotic cells (Gilman, 1987).
- X AlF_x and BeF_x are small molecules that mimic the chemical structure of phosphate.
- X As phosphate analogues, they modulate the activity of phosphoryl transfer enzymes, including: GTPases; ATPases; Phosphohydrolyases; Phospholipase D
- X Phosphoryl transfer is a fundamental mechanism in cells, underlying both energy metabolism and signal transduction.





Structural similarities among AlF_4^-, $BeF_3(OH_2)^-$, and PO_4^{3-}. All three compounds exhibit tetrahedral geometry. BeF_3^- has an electron-deficient beryllium atom. Be completes an octet by accepting a pair of electrons from a water molecule. (B) The proposed phosphate model for AlF_4^- and BeF_3^- activation of heterotrimeric G proteins. AlF_4^- and BeF_3^- bind with GDP and mimic the -phosphate of GTP.

Structural similarities:

- **AlF_4^-** is structurally similar to **PO_4^{3-}** (both are tetrahedral).
- **Al–F bond length ≈ P–O bond length** in phosphate.
- **BeF_3^-** also mimics phosphate because of its similar tetrahedral structure.

A G protein is a molecular switch within a cell that relays signals from activated cell-surface receptors to intracellular effectors, functioning as a signal transducer.

Phosphate model of G protein activation:

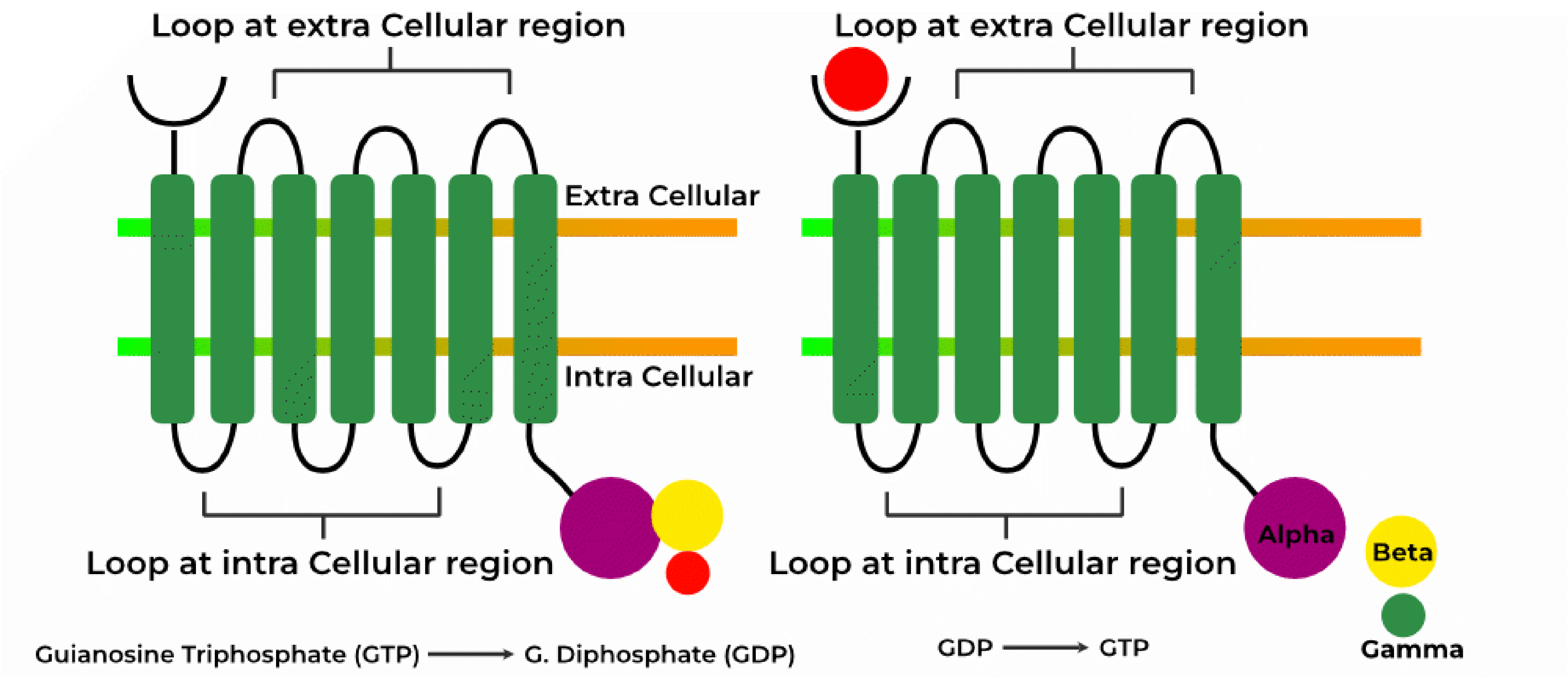
- G protein normally binds GDP permanently.
- **AlF_4^- (or BeF_3^-)** binds to the GDP phosphate.
- This mimics the presence of the γ-phosphate of GTP.
- As a result, the G protein adopts the **active G • GTP-like conformation**.

- Relay signals from **cell-surface receptors** to **intracellular effectors**.
- Function as **signal transducers** in pathways.
- Named for binding **guanine nucleotides (GDP & GTP)**.
- Regulate diverse processes: **growth, metabolism, sensation**.

Stabilization of active state:

- F^- is highly electronegative and forms strong hydrogen bonds with amino acids.
- This makes **AlF_4^- and BeF_3^- resistant to hydrolysis** by GTPase activity.
- Thus, the G protein loses its ability to hydrolyse its bound GTP back to GDP, preventing it from returning to its inactive form.

Only eukaryotes, including yeast, choanoflagellates, and mammals, have G protein-coupled receptors. Light-sensitive substances, smells, pheromones, hormones, and neurotransmitters are among the ligands that bind to and activate these receptors. Their sizes range from tiny molecules to peptides to big proteins. Numerous disorders involve G protein-coupled receptors. [https://www.geeksforgeeks.org/biology/g-protein-coupled-receptor/]

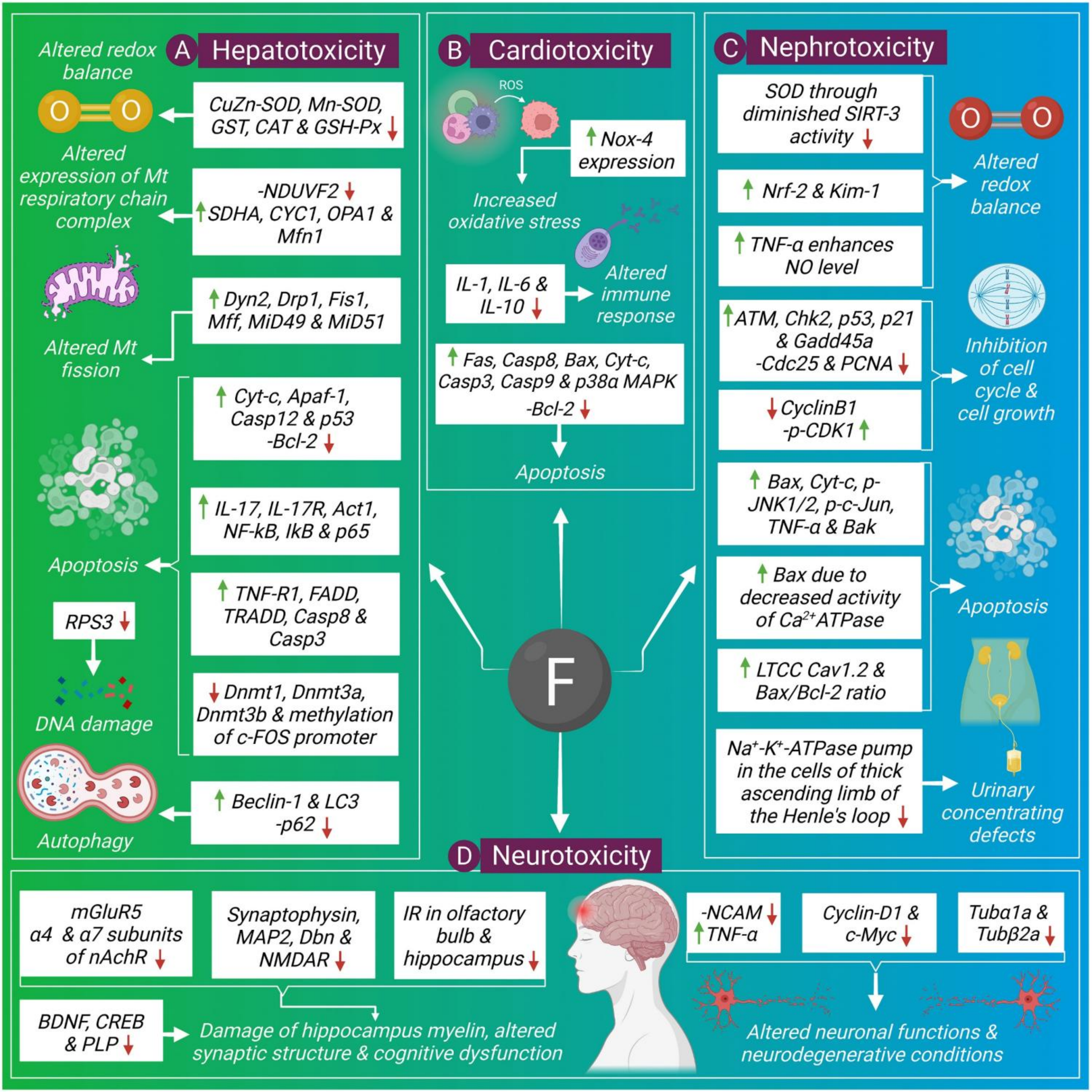


Farley et al. (Science, 1983, 222, 330-332) made the first observation that F^- directly increases the proliferation and alkaline phosphatase activity of avian osteoblastic cells in culture. The optimal F^- concentration for this action is about 10 mM/L, which is within the plasma fluoride level in osteoporosis patients receiving F^- treatment (5-30 mM/L).

Fluorosis is an occupational disease among workers in the Al-smelting industry. A high rate of osteosclerosis occurs in the miners of cryolite (Na_3AlF_6). Studies suggest that F^- alone did not affect cell proliferation. In the presence of Al, F^- forms AlF_4^-, which structurally resembles phosphate (PO_4^{3-}) and binds to G-proteins at phosphate sites.

Mimicking phosphate (γ-phosphate of ATP/GTP):

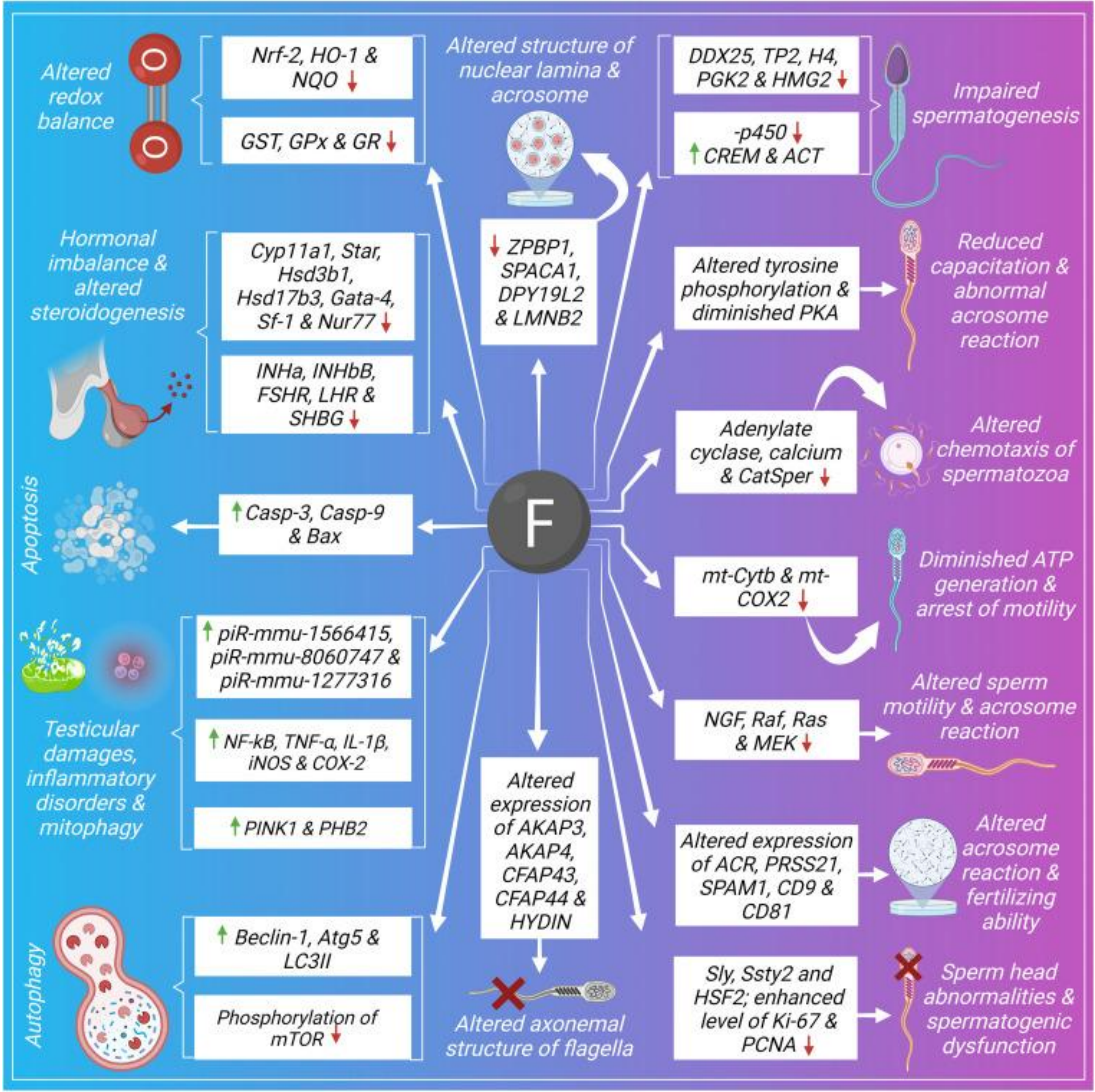
Enzymes and G-proteins contain a binding pocket for the γ-phosphate of ATP or GTP, whose binding and hydrolysis regulate their on/off switch. AlF_4^- can occupy this pocket in place of the γ-phosphate, and because of its structural similarity to PO_4^{3-}, the protein cannot distinguish the difference. As a result, AlF_4^- "tricks" enzymes and G-proteins into adopting the active state without actual ATP or GTP hydrolysis, thereby hijacking normal signalling pathways and promoting uncontrolled growth.



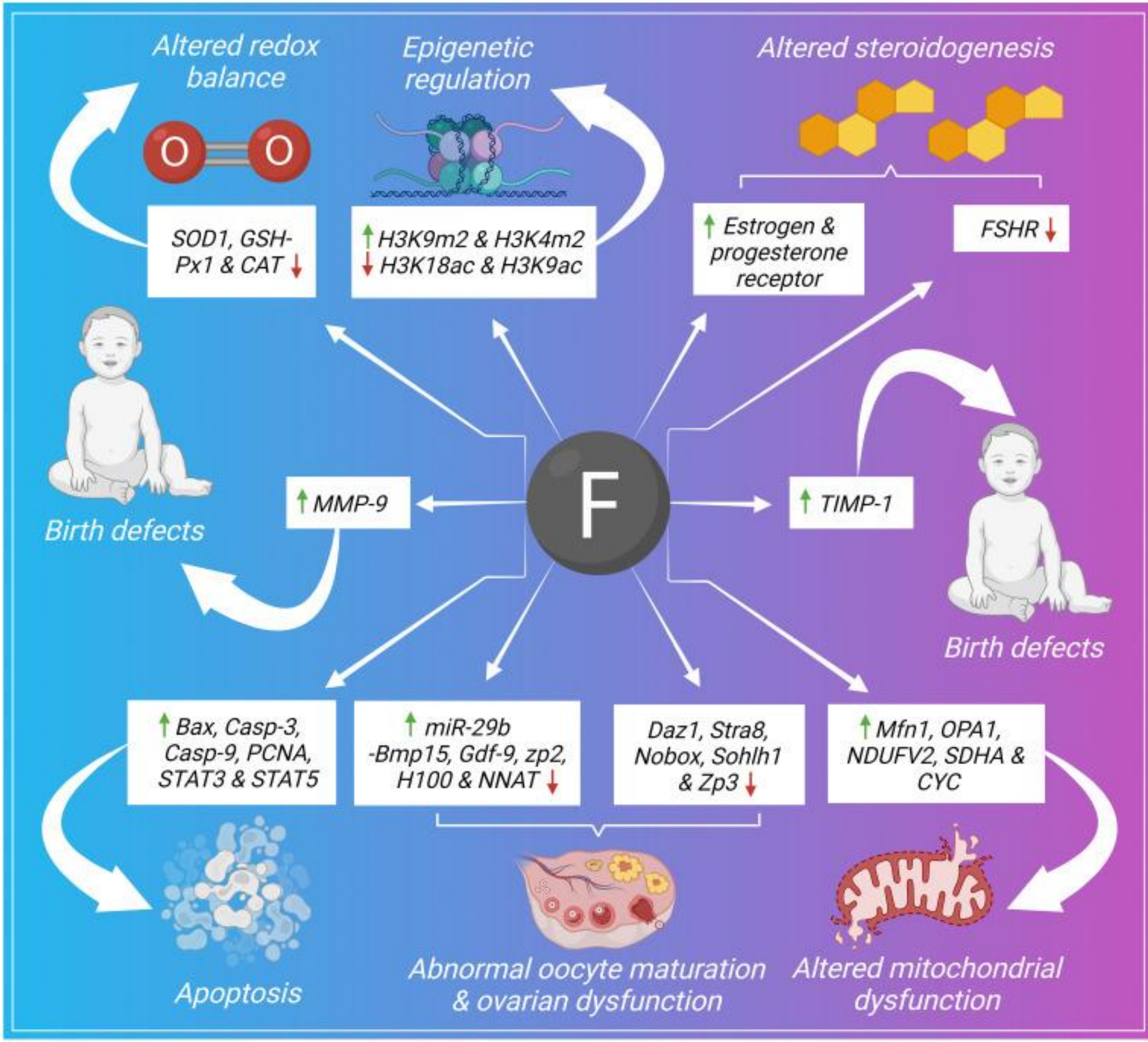
Signaling pathways of F^--induced hepatotoxicity (A), cardiotoxicity (B), nephrotoxicity (C), and neurotoxicity (D)

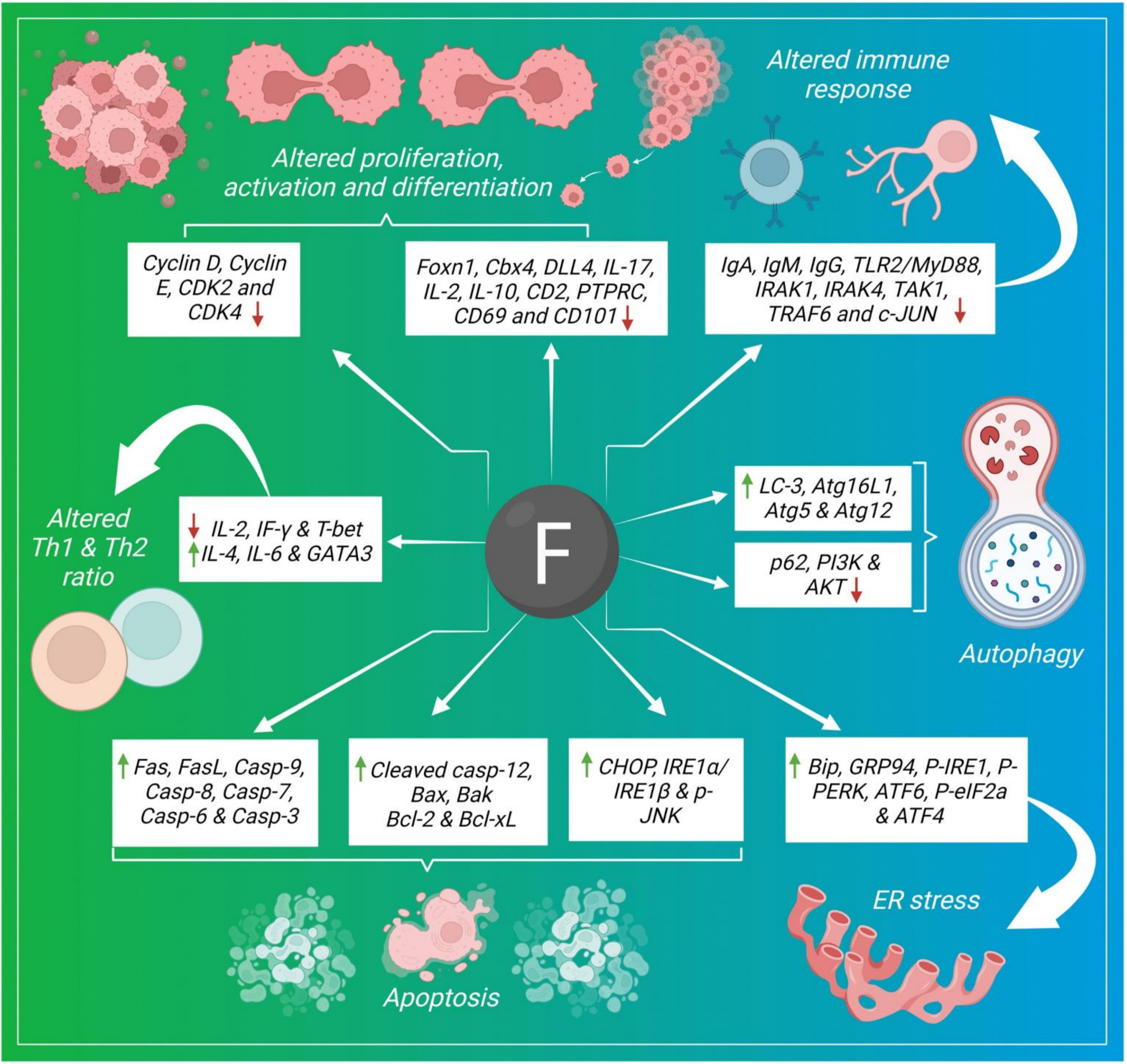
Genes & Diseases, 2023, 10, 1470-1493

Signaling pathways of fluoride induced male reproductive toxicity. Genes & Diseases, 2023, 10, 1470-1493

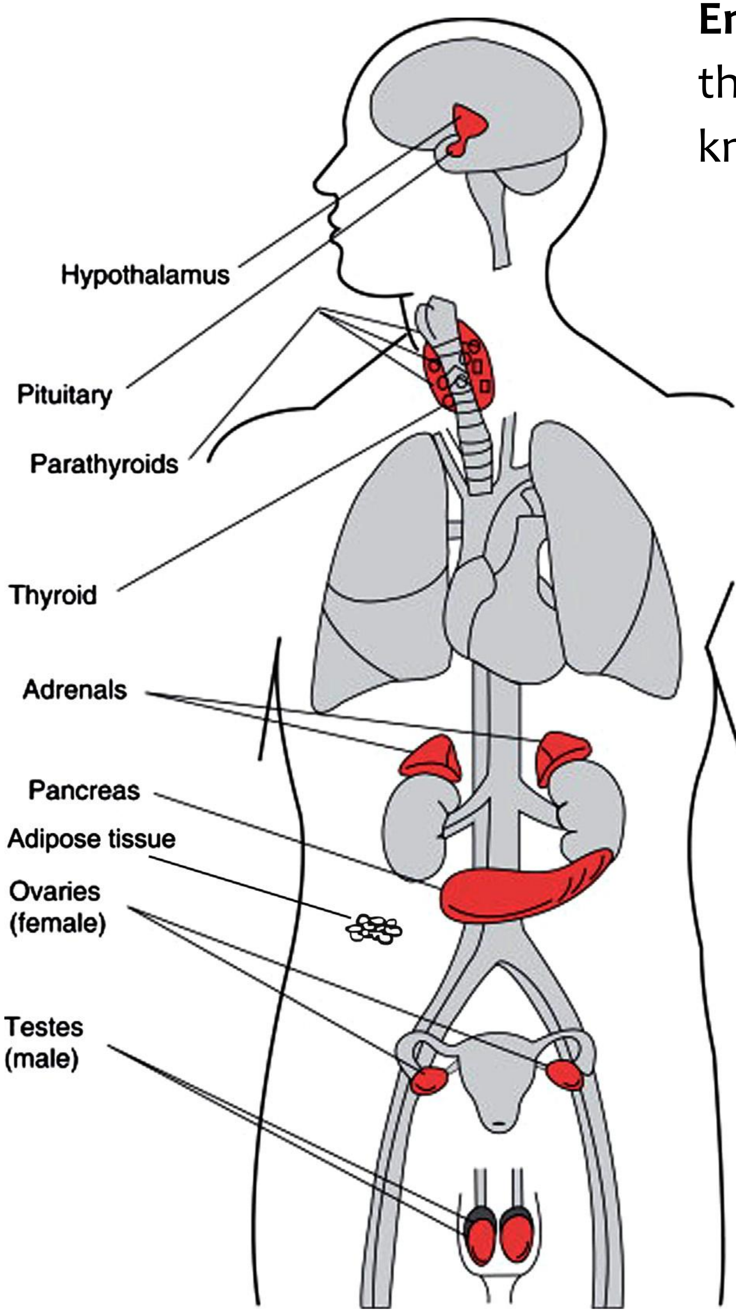


Signaling pathways of fluoride induced female reproductive toxicity. Genes & Diseases, 2023, 10, 1470-1493





Signalling pathways of fluoride induced immune system disorders Genes & Diseases, 2023, 10, 1470-1493



Endocrine disruptors are natural or man-made chemicals that may mimic or interfere with the body's hormones, known as the endocrine system

The Endocrine System:

Endocrine glands, distributed throughout the body, produce the hormones that act as signalling molecules after release into the circulatory system. This controls many biological processes like normal growth, fertility, and reproduction. Hormones act in extremely small amounts, and minor disruptions in those levels may cause significant developmental and biological effects.

Encyclopedia of Toxicology, 2014 (third ed.) Volume 2, Page 332 http://dx.doi.org/10.1016/B978-0-12-386454-3.00377-8

Endocrine-disrupting chemicals interfere with reproduction in humans, and advances in molecular technologies are providing insight into the causative mechanisms, which include gene mutation, DNA methylation, chromatin accessibility and mitochondrial damage. There is compelling evidence that frequent exposure to environmental pollutants has a large potential to reduce overall fertility by DNA methylation, apoptosis and chromatin/DNA fragmentation. [Nat. Chem. 11, 1071–1072 (2019); [Environment International 156 (2021) 106616]

Biodiversity loss and damage to crops and livestock:
Biodiversity across Earth's surface layer, from bedrock to canopy, underpins life-supporting ecosystem services. Excessive use of agrichemicals and industrial pollutants has driven major biodiversity losses. Neonicotinoid pesticides, for example, have decimated global honeybee populations, creating a crisis for crop pollination. Similarly, pesticide contamination has caused the loss of over 40% of stream invertebrate taxa in some regions. [Nat. Chem. 11, 1071–1072 (2019); [Environment International 156 (2021) 106616]

Chemicals That May Disrupt Your Endocrine System

According to the Endocrine Society, there are nearly 85,000 human-made chemicals in the world, and 1,000 or more of those could be endocrine disruptors, based on their unique properties. The following are among the most common and well-studied.

- X **Atrazine** (commonly applied herbicides)
- X **Bisphenol A (BPA)** is used to make polycarbonate plastics and epoxy resins. BPA based polymers and resins.
- X **Dioxins** (byproduct of certain manufacturing processes) Also released into the air from waste burning and wildfires.
- X **Perchlorate** (Used in explosives, and fireworks)
- X **Per- and polyfluoroalkyl substances (PFAS)** (firefighting foam, nonstick pans, paper, and textile coatings, etc).
- X **Phthalates** (liquid plasticizers, food packaging, cosmetics, fragrances, children's toys, and medical device tubing, Cosmetics (nail polish, hair spray, aftershave lotion, cleanser, and shampoo).
- X **Polychlorinated biphenyls (PCBs)** (electrical equipment, such as transformers, and are in hydraulic fluids, heat transfer fluids, lubricants, and plasticizers) were banned in 1979.

Impact of pollution on fertility and fetal health:

Chemical pollutants have well-established detrimental impacts on human fertility. For example, male reproductive systems were reported to be adversely affected by some frequently used or emitted pollutants, such as dioxins, polycyclic aromatic hydrocarbons, BFRs (brominated flame retardants) and nonylphenol, and male fertility has been reported in several studies to have declined by half or more globally.

[Environment International 156 (2021) 106616]

BFRs are added to a wide variety of combustible materials to prevent fires from starting, slow their spread, and provide time to escape. However, these chemicals are often additive, so they leach out into the environment. Governments have restricted the use of polybrominated diphenyl ether flame retardants based on evidence that they are persistent and bioaccumulate and have adverse effects on health. The phasing out of these “legacy” flame retardants has resulted in their replacement with alternatives, such as tetrabromobisphenol A and the organophosphate esters.**[Andrology. 2020;8:915–923]**

Tri-n-butyl phosphate (TnBP), a typical alkyl organophosphate ester is widely used as an emerging flame retardant for polybrominated diphenyl ethers alternatives, but the potential toxicity and mechanism are unclear. In this study, the reproductive toxicity of TnBP and its related mechanisms were explored using the Caenorhabditis elegans (C. elegans) model.

After TnBP (100–1000 μ g/L) exposure: TnBP toxicity in C. elegans arises from a combination of oxidative stress, DNA damage, apoptosis, and mitochondrial dysfunction, with SKN-1/Nrf2, CEP-1/p53, and xenobiotic metabolism pathways playing central roles. **[Ecotoxicol. Environ. Saf. 2021, 227, 112896; Environ Sci. Pollut. Res. Int. 2023, 30, 85578-85591]**

Exposure to environmentally relevant concentrations of TnBP impaired gonad development (crucial for sexual differentiation and reproduction, involving a complex interplay of genetic and environmental factors) and reduced reproductive capacity in C. elegans. **[Ecotoxicology and Environmental Safety 227 (2021) 112896]**

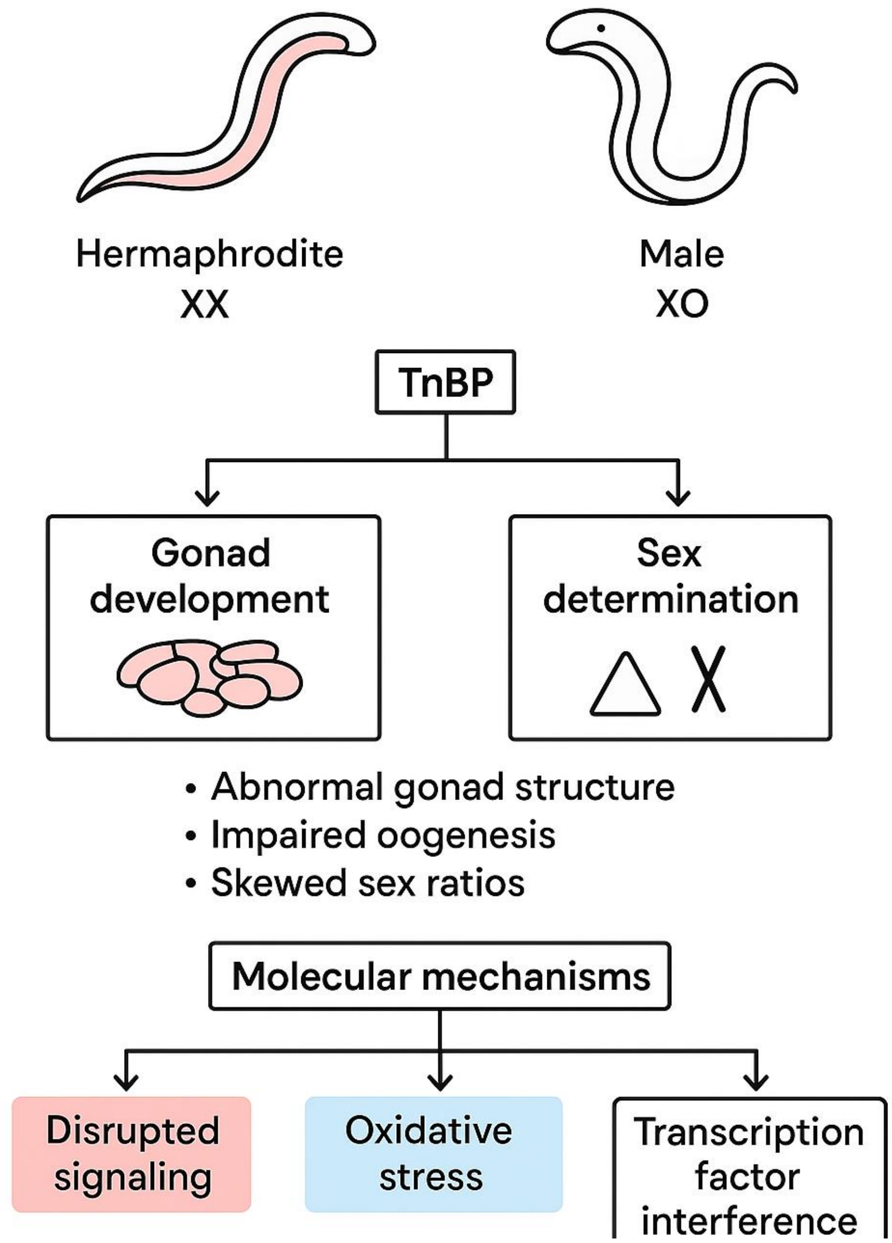
The organophosphate chemical triisobutyl phosphate (TnBP) was used as a case study for exploration of the approach, as its emission to the environment was expected to be inevitable when used as a flame retardant. TBP is also used as a highly polar solvent. It is mainly used as an antifoaming agent in various aqueous systems where it can destroy foam and act as a foam inhibitor.

Effects on Sex Determination & Reproduction

- ***C. elegans*** normally has two sexes: [Ecotoxicology and Environmental Safety 227 (2021) 112896]
  - ✓ **Hermaphrodites (XX)** – produce both sperm (early) and oocytes (later). This allows self-fertilization, though they can also mate with males. Represent about **99.9%** of the natural population.
  - ✓ **Males (XO)** – produce only sperm.
- TnBP exposure can disturb **sex-specific gene regulation**, leading to:
  - ✓ Skewed sex ratios (altered proportion of males vs. hermaphrodites).
  - ✓ Impaired sperm or oocyte function → reduced fertility.

Likely mechanisms: disruption of **hormone-like signalling, oxidative stress,** and interference with **transcription factors** (e.g., TRA, FEM, HER-1: proteins that control gene expression by binding to specific DNA sequences and regulating the conversion of DNA into RNA--transcription) that govern sex fate.

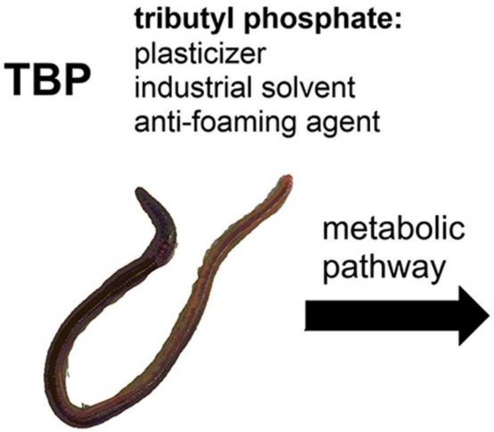
TnBP Effects on Gonad Development and Sex Determination in *C. elegans*



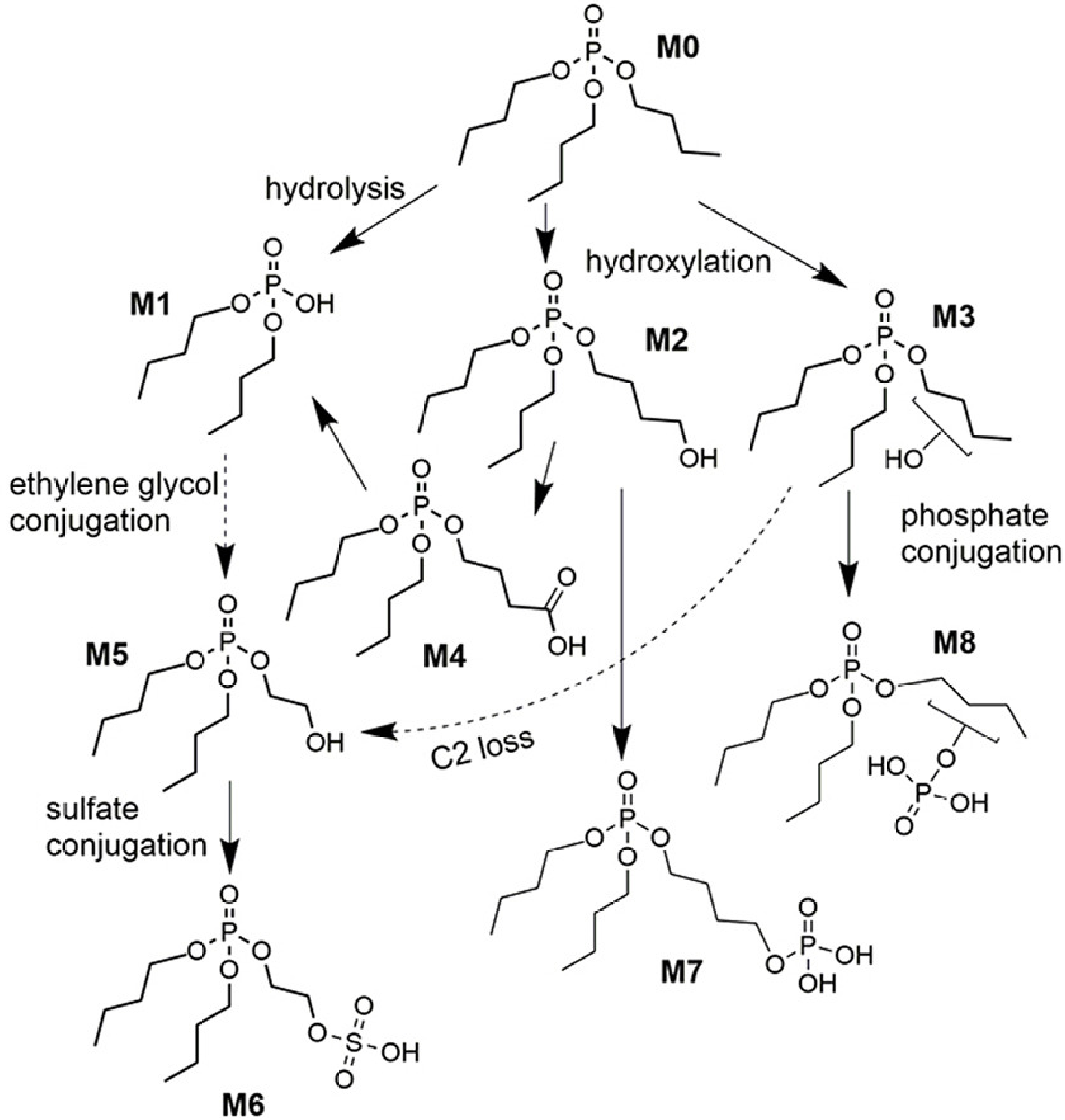
AI generated

Tri-n-butyl phosphate (TnBP) detected in all environmental matrices.

TnBP, when metabolized in the earthworm (*Perionyx excavates*), does not show overt toxicity, unlike in C. elegans:



Metabolism of TnBP in the earthworm, Perionyx excavatus



Reproductive toxicity, Estrogen-disrupting effects of TnBP Ecotoxicol. Environ. Safety 2021, 227, 112896; Environ Pollut. 2018, 234, 389-395

Metabolism of TnBP in earthworm (*Perionyx excavates*):

Studies indicate that *Perionyx excavatus* can metabolize TBP through **phase I and phase II detoxification pathways**, likely involving **hydrolysis and conjugation reactions**. These processes convert TBP into **less harmful metabolites** that can be excreted, thereby preventing accumulation and toxic effects. Unlike in C. *elegans*, where TnBP induces oxidative stress, apoptosis, and DNA damage, the earthworm's **efficient biotransformation capacity** appears to mitigate toxicity. This highlights species-specific differences in organophosphate metabolism and suggests that *P. excavatus* may tolerate environmental TBP exposure without significant impairment. **Environmental Pollution; 2018, 234, 389-395**

For hydrophobic xenobiotics, the major detoxification pathway is by bonding of highly polar compounds, thus making them hydrophilic, which can then be easily excreted.

Tri-n-butyl phosphate (TnBP) Exposure:

The production volume of TnBP is estimated at 3,000 – 5,000 tonnes worldwide. The major uses of TnBP in industry are as a component of aircraft hydraulic fluid and as a solvent for rare earth extraction and purification. No current consumer product uses of TnBP have been identified. The primary occupational exposure to TnBP results from its use as an ingredient in aircraft hydraulic fluids. The potential for exposure to TBP varies with the type of maintenance activity but is almost always via a dermal pathway.

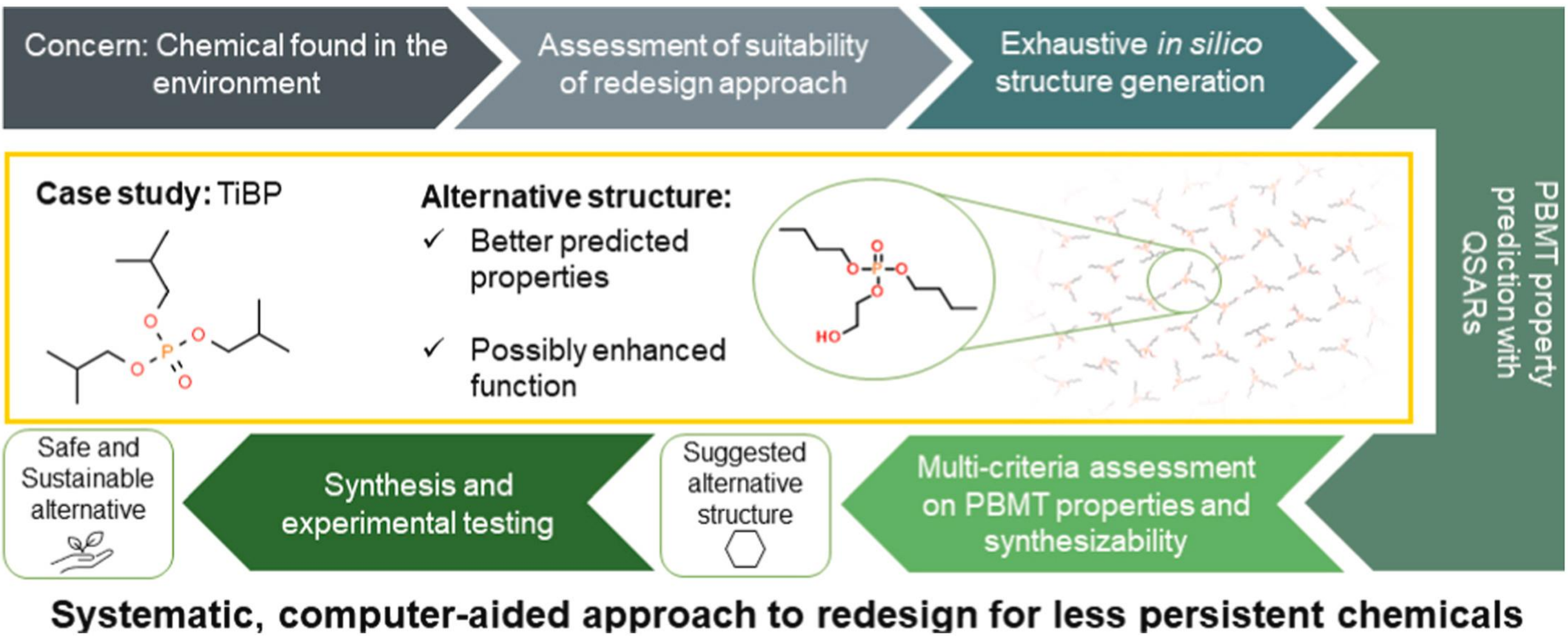
$$\boxed{BCF = \frac{Concentration_{Biota}}{Concentration_{Water}}}$$

A bioconcentration factor (BCF) is a measure of how much a substance accumulates in an organism's tissues to the concentration of the substance in the surrounding environment.

BCF can also be related to the octanol-water partition coefficient, K_{ow}. The octanol-water partition coefficient (K_{ow}) is correlated with the potential for a chemical to bioaccumulate in organisms and can be predicted via software for structure-activity relationship (SAR) or through a linear equation.

https://www.elsevier.com/en-in/industry/4-key-chemicals-industry-trends

Chemosphere, 2022, 296, 134050



Quantitative structure-activity relationship

Persistence (P), bioaccumulation (B), mobility (M) and toxicity (T) potency properties

Impact of Brominated Fire Retardants (BFRs) on fertility and foetal health

- Male reproductive systems are adversely affected by pollutants such as dioxins, polycyclic aromatic hydrocarbons, Brominated Fire Retardants (BFRs), and nonylphenol, contributing to a global decline in male fertility by 50% or more (Andrology., 8 (2020), pp. 915-923).
- Brominated Flame Retardants (BFRs) act as endocrine-disrupting chemicals, and depending on type and exposure level, may cause permanent damage to male reproductive systems.
- PFAS exposure in mice disturbs testicular lipid profiles in male offspring, lowering sperm counts and testosterone later in life (Environ. Sci. Technol., 51 (2017), pp. 8782-8794).

Sertoli cells provide structural and nutritional support for developing sperm cells within the seminiferous tubules, forming the crucial blood-testis barrier and producing substances like Androgen-Binding Protein (ABP) that are vital for spermatogenesis.

Leydig cells, located in the interstitial space between these tubules, are responsible for synthesizing and secreting testosterone, the primary male hormone that drives the development of male secondary sexual characteristics and maintains sperm production

Brominated flame retardants (BFRs) can interfere with male fertility through several mechanisms:

Endocrine disruption:

- BFRs mimic or block natural hormones, especially androgens and thyroid hormones.
- They disturb testosterone production and signalling, crucial for sperm development.

Oxidative stress:

- BFR exposure increases reactive oxygen species (ROS).
- ROS damage sperm DNA, lipids, and proteins, reducing sperm quality and motility.

Altered spermatogenesis:

- BFRs impair testicular function by disrupting Sertoli and Leydig cells.
- This leads to reduced sperm count and abnormal morphology.

Epigenetic changes:

- BFRs can modify DNA methylation and histone regulation.
- Such changes affect gene expression linked to fertility.

Bioaccumulation:

Being lipophilic, BFRs accumulate in fatty tissues, persist in the body, and exert long-term reproductive toxicity.

In short: BFRs harm male fertility by disrupting hormones, damaging sperm through oxidative stress, and impairing testicular cell function.

Exposure to BFRs → Mechanisms → Effects on Male Fertility

Exposure to Brominated Flame Retardants (BFRs)

↓

- **Endocrine disruption** → lowers testosterone → impaired sperm development
- **Oxidative stress** → ROS damage DNA/proteins → reduced sperm motility & quality
- **Testicular toxicity** → damages Sertoli & Leydig cells → low sperm count, abnormal sperm
- **Epigenetic changes** → altered gene expression → long-term fertility issues
- **Bioaccumulation** → persistent in body → prolonged reproductive harm

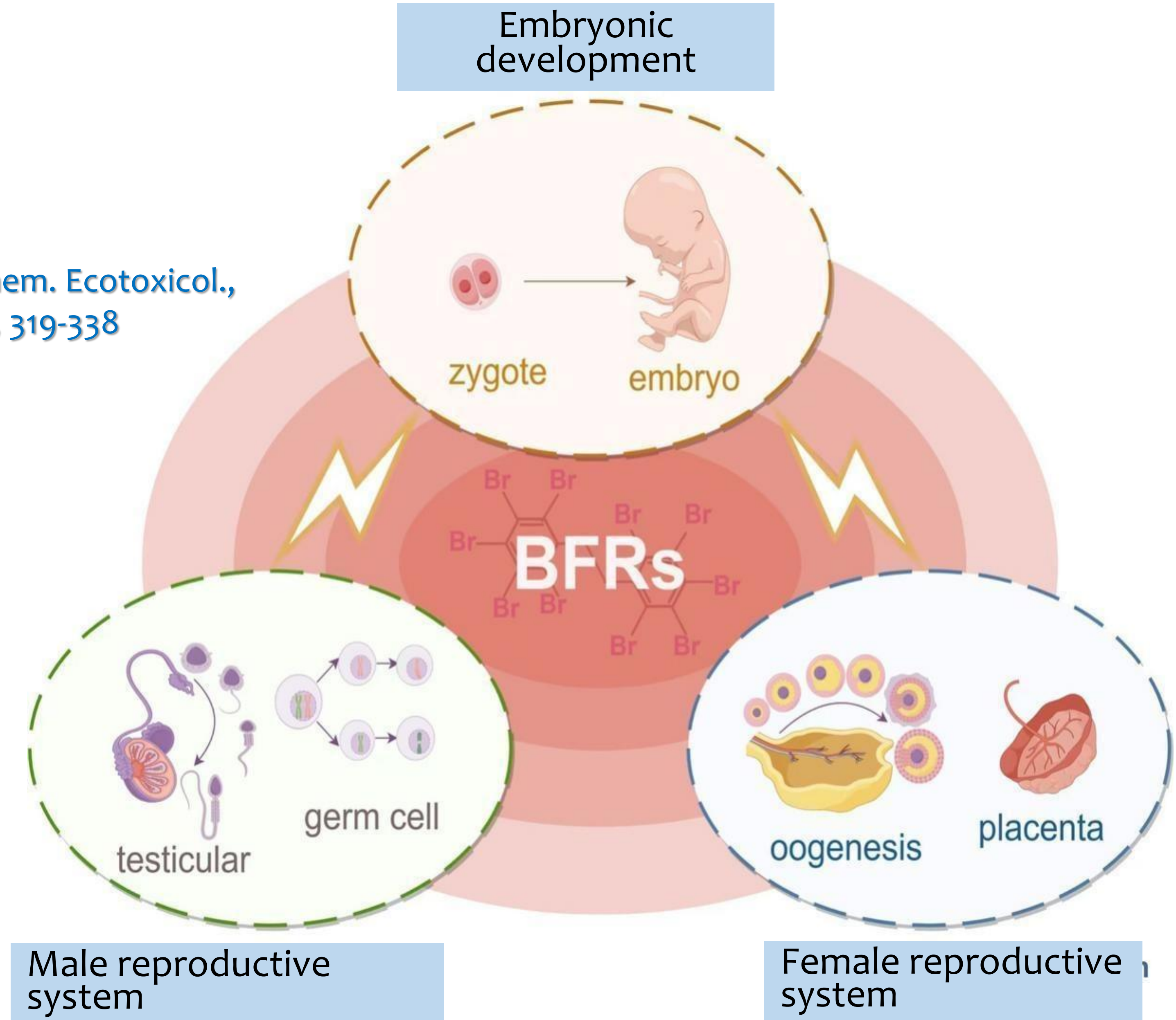
Outcome: Male infertility (poor sperm quality, reduced count, impaired function)

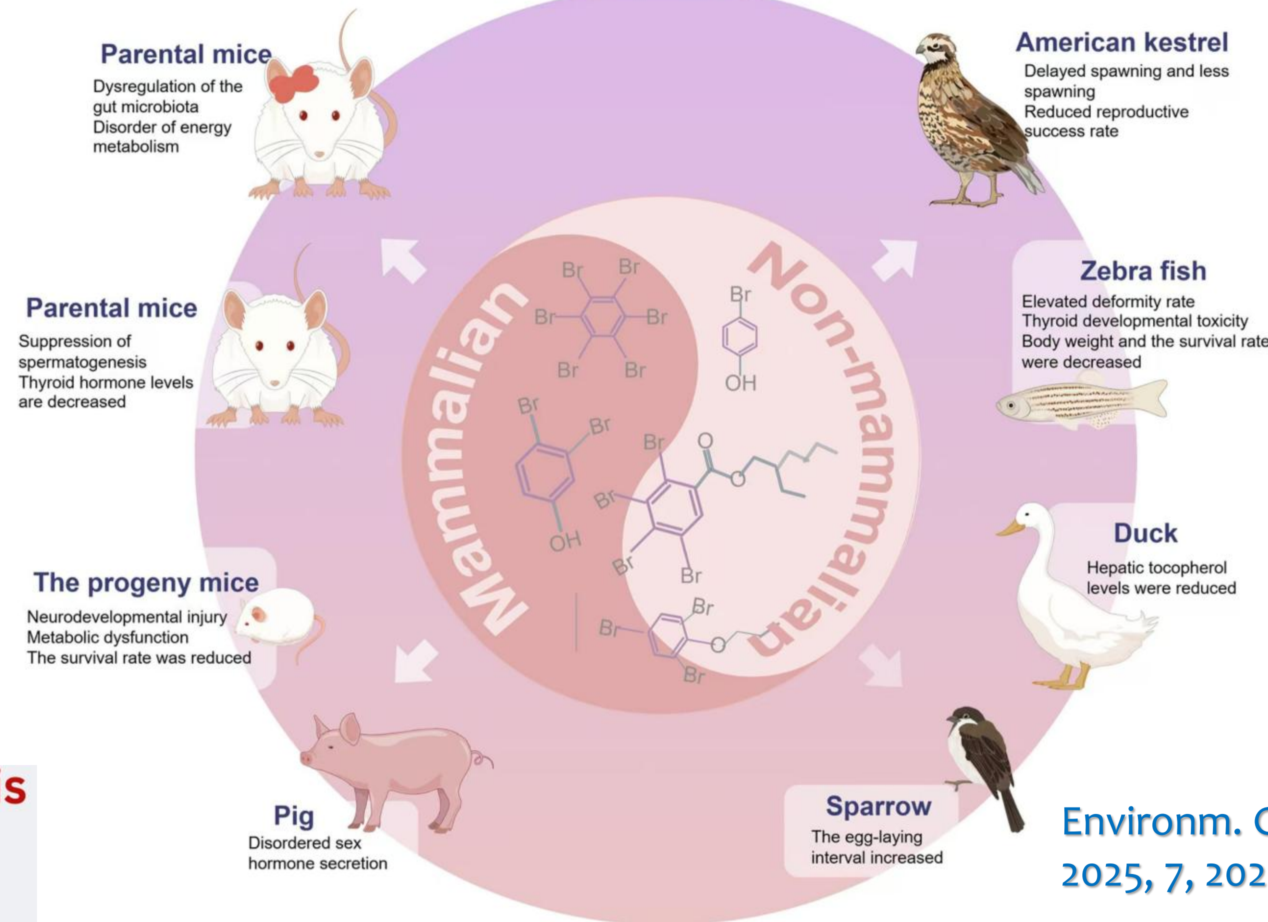
Epigenetic changes are **heritable modifications in gene expression** that occur **without altering the DNA sequence itself**.

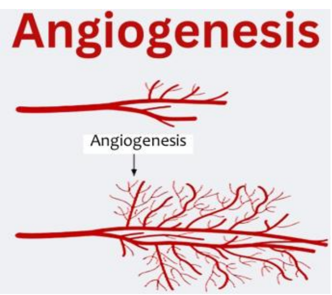
- **DNA methylation** – adding/removing methyl groups on DNA.
- **Histone modification** – chemical changes to histone proteins that affect chromatin structure.
- **Non-coding RNAs (e.g., microRNAs)** – regulate how genes are turned on or off.

Epigenetic changes act like "switches" that control **when and how strongly genes are expressed,** without changing the genetic code.

Environm. Chem. Ecotoxicol., 2025, 7, 2025, 319-338

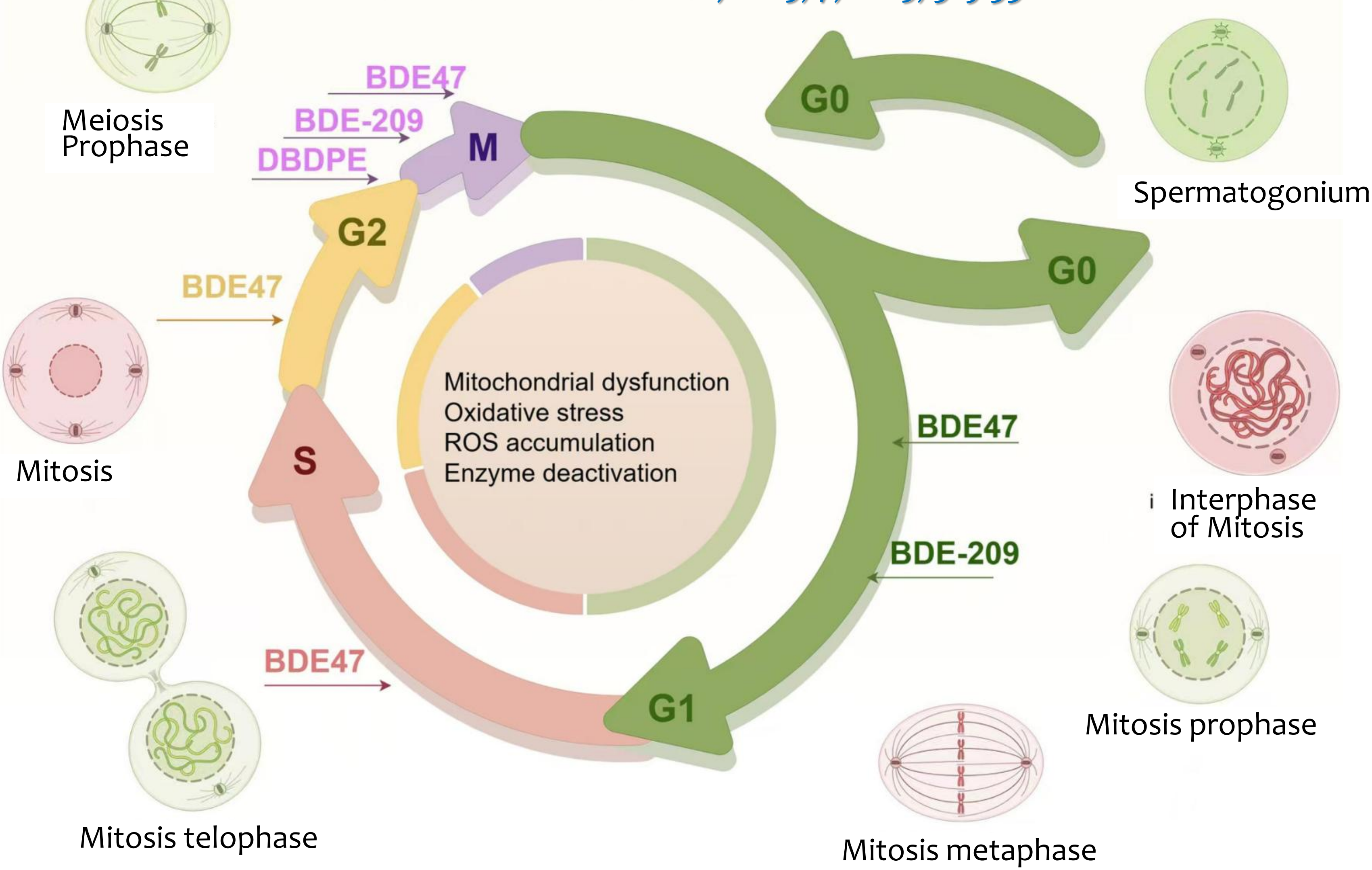






Environm. Chem. Ecotoxicol., 2025, 7, 2025, 319-338

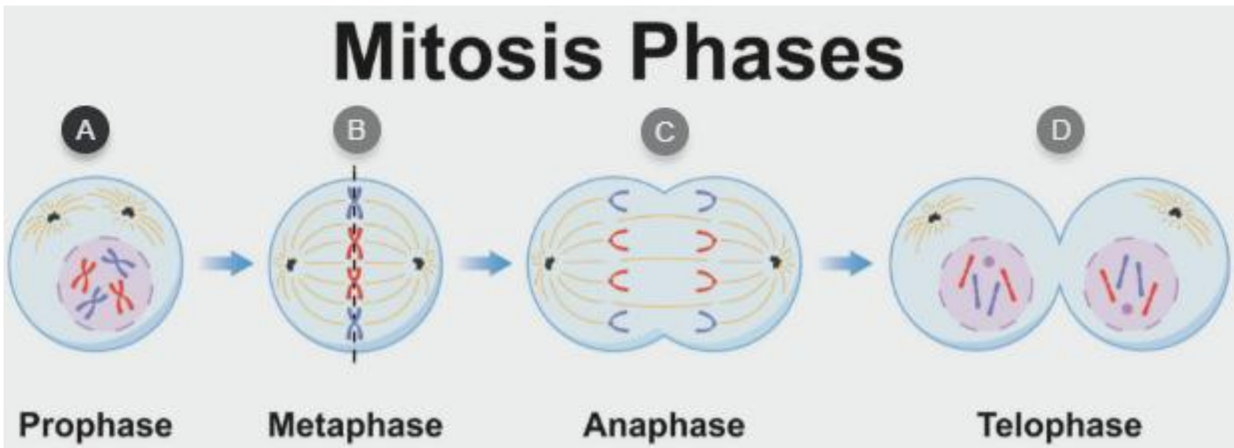
In mammals, BDE-47 impairs placental angiogenesis, while BDE-209 hinders testosterone synthesis and sperm formation. In zebrafish, BDE-47 reduces egg output and larval survival, and TBPH with TBBPA suppress reproduction in bluegill sunfish. In birds, DE-71 and HBCD delay egg laying, thin shells, and lower reproductive success in American kestrels.



BFRs disrupt the reproductive cell cycle via oxidative stress, proenzyme (or zymogen) inactivation, mitochondrial dysfunction, and elevated ROS. BDE-47 arrests mouse spermatogonia in G1 and hinders spermatocyte progression, BDE-209 causes G1 and early meiotic arrest in spermatocytes, while DBDPE impairs oocyte development during late meiosis I.

M Phase (Mitosis Phase)

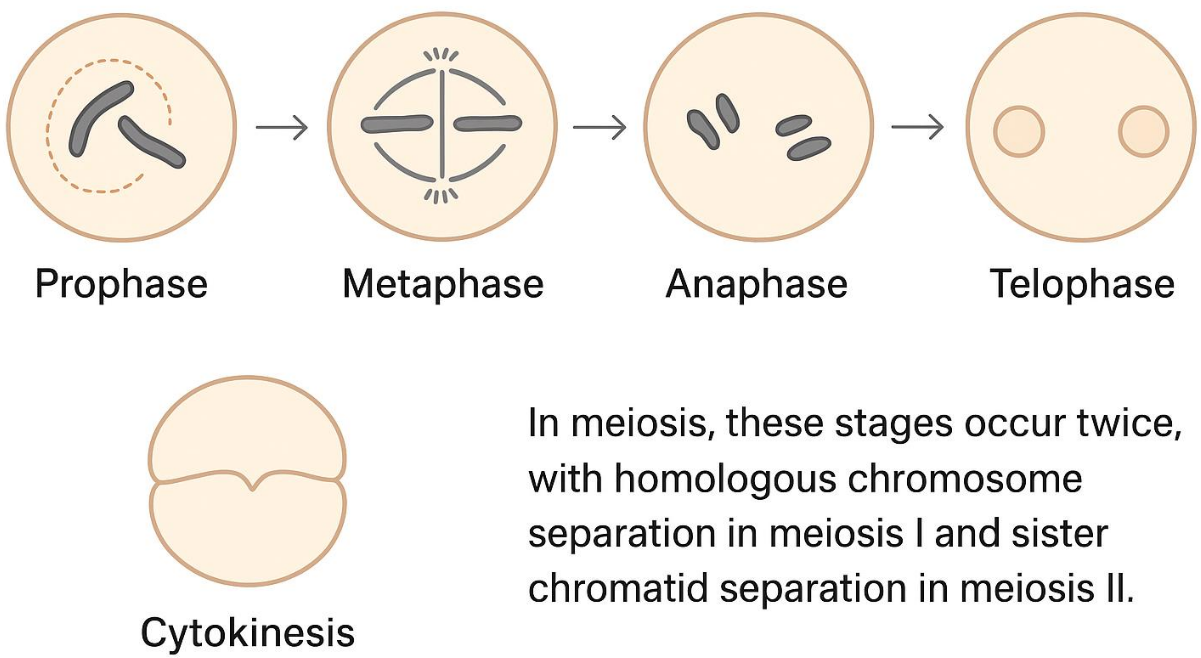
Mitosis is the process in which chromosomes split longitudinally into two identical halves and move to opposite poles, organizing into two daughter nuclei genetically identical to the parent cell. This process is divided into four main stages: Prophase, Metaphase, Anaphase, and Telophase.



This diagram shows the different phases of mitosis. Mitosis is a type of cell division in which a single cell divides into two genetically identical daughter cells. This process is essential for the growth, repair, and maintenance of multicellular organisms. Let's take a look at each phase, beginning with prophase.

- ✓ **Interphase:** Cell grows; DNA is replicated (not a division phase but preparatory).
- ✓ **Prophase:** Chromosomes condensation (the process where long, dispersed DNA chromatin fibres in the nucleus are compacted and organised into tightly coiled, rod-shaped chromosomes).
- ✓ **Metaphase:** Chromosomes align at the cell's equatorial plate.
- ✓ **Anaphase:** Sister chromatids separate and move toward opposite poles.
- ✓ **Telophase:** Nuclear membranes reform, chromosomes de-condense.

Cell division progresses through prophase (chromosome condensation), metaphase (alignment at the equator), anaphase (chromatid separation), and telophase (nuclear reformation), followed by cytokinesis. In meiosis, these stages occur twice, with homologous chromosome separation in meiosis I and sister chromatid separation in meiosis II.



Cytokinesis: The physical process of cell division where the cytoplasm splits, forming two daughter cells after mitosis or meiosis. Occurs in all eukaryotic cells (plants, animals, fungi)

Interphase is called the "resting phase" of cell cycle but studies show active synthesis of RNA, protein, and genetic material occurring during this phase.

The interphase further comprises into following phases:

1. **G1 Phase (Gap 1):** Cells mainly grow during this phase but does not undergo DNA replication. It performs normal functions.
2. **S phase (Synthesis):** DNA synthesis occurs, resulting in the replication of the genetic material.
3. **G2 phase (Gap 2):** The cell continues to grow, synthesizing proteins and preparing for mitosis or meiosis.
4. **Quiescent Stage (G0):** Cells in G0 are metabolically active but have exited the cell cycle. Some cells (e.g., neurons, cardiac muscle) remain permanently in G0, while others (like liver cells) can re-enter the cycle under specific signals (growth factors, injury).

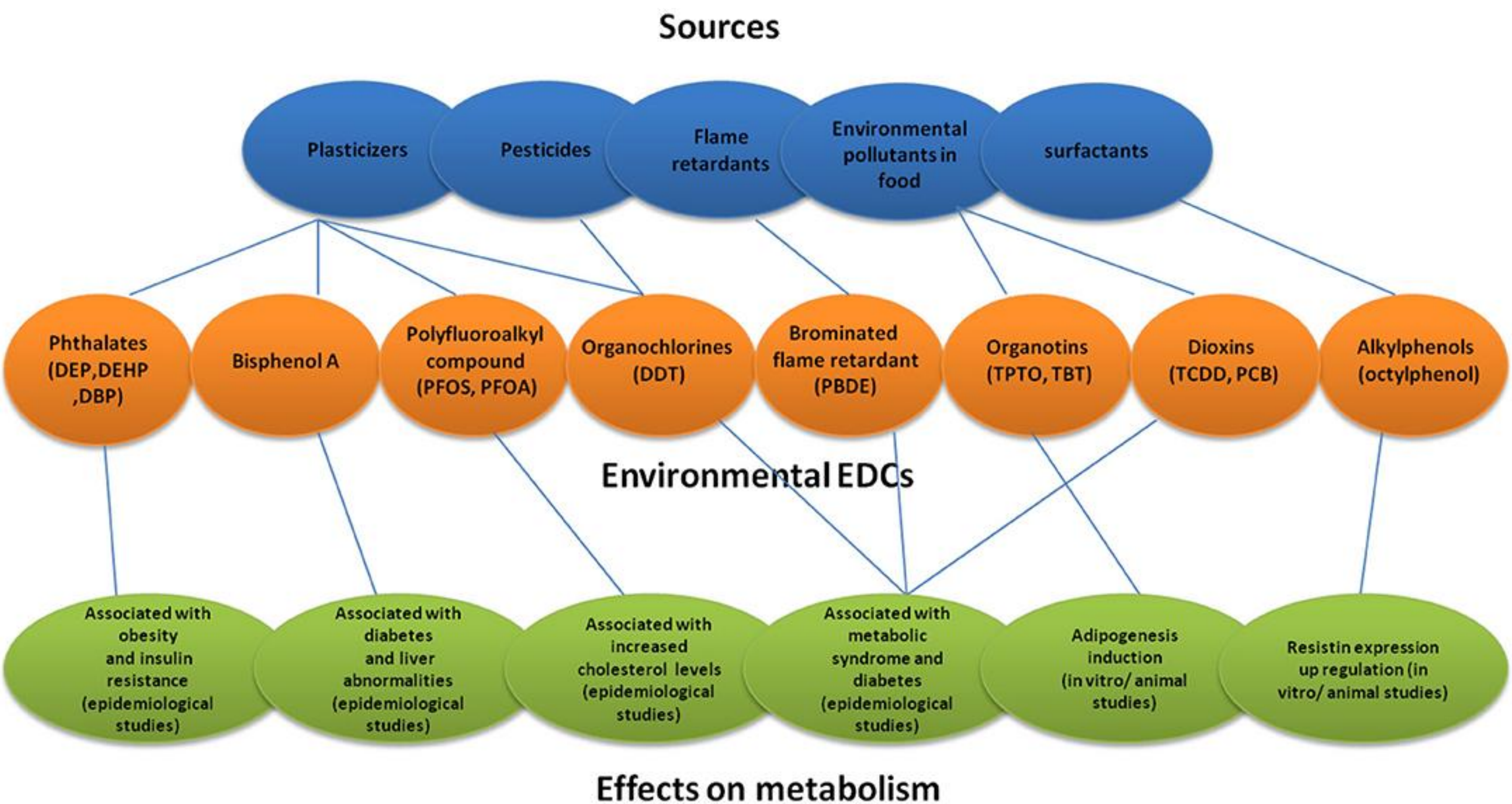
https://www.geeksforgeeks.org/biology/cell-division/

- Exposure to organochlorines may cause reproductive damage in Inuit (people from parts of Greenland and Alaska and European populations, though the effect on fertility remains uncertain (Environ. Health Perspect. 2008, 116, 269–2772).
- The past 50 years have seen a 50% reduction in sperm counts in Western and Asian populations, attributed to environmental toxicant buildup rather than genetics (Transl. Androl. Urol. 2020;9(6):2797-2813).
- Everyday chemical exposures, including endocrine-disrupting chemicals (EDCs), are identified as the primary drivers of declining sperm quality and male fertility (Front. Public Health 8:553850, doi: 10.3389/fpubh.2020.553850).
- Prenatal exposure to chemicals can interfere with male reproductive system differentiation in utero, leading to testicular dysgenesis syndrome, reduced sperm production, cryptorchidism, hypospadias, and testicular cancer (Human Reproduction Update, 2023, 29, 157–176, 2023).

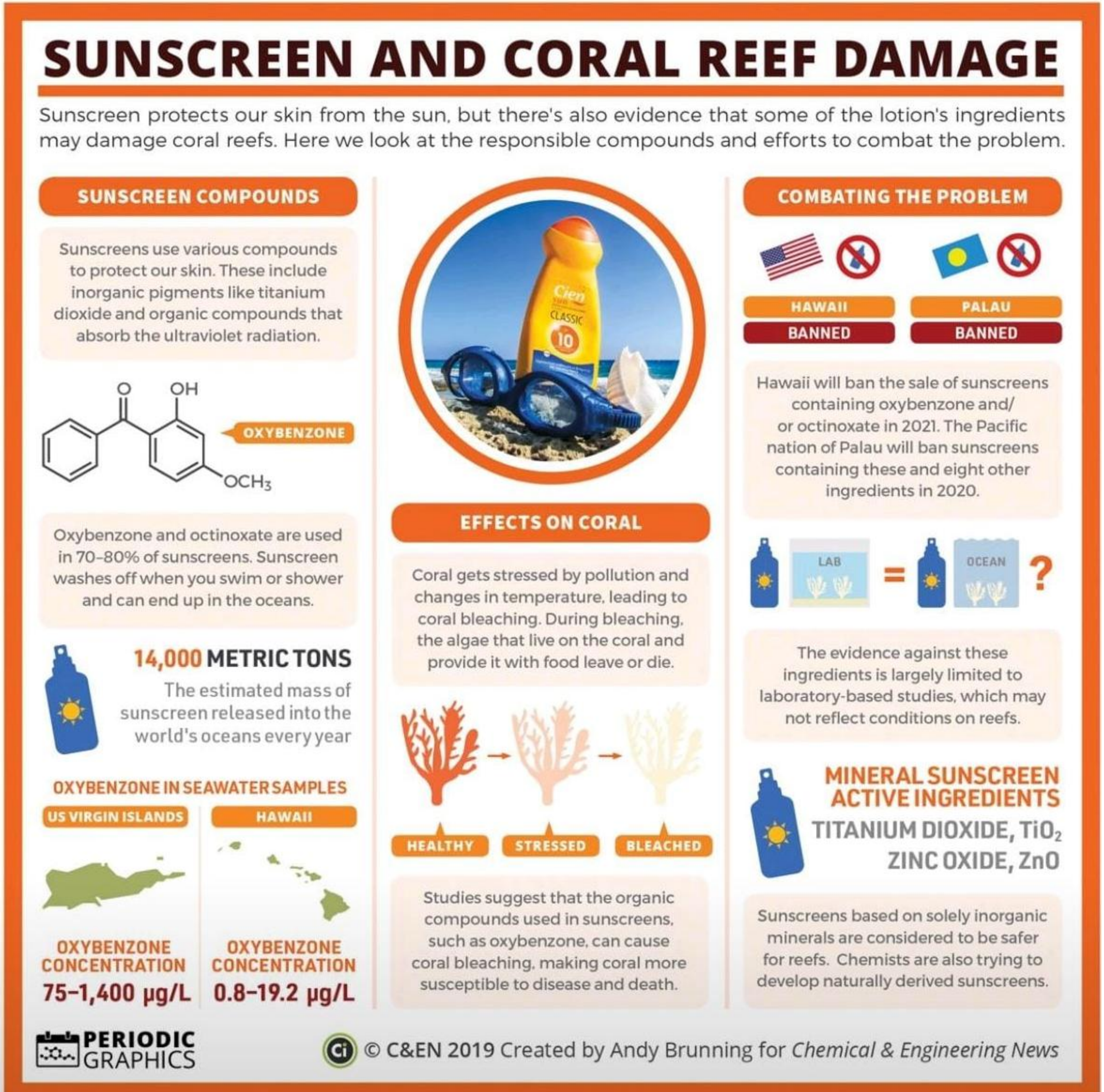
Prenatal exposure to pollutants can lead to developmental issues and lower IQ in children

- Exposure of pregnant women to chemicals and ultrafine particulate matter may cause teratogenic damage, including mitochondrial effects.
- Neurotoxic metals such as arsenic, lead, and mercury can impair offspring cognition or contribute to ADHD, depending on dose, timing, and metal type.
- Blood mercury levels of 1.50–2.44 pg/L in first-trimester women in Avon, UK, showed no adverse cognitive effects in children.
- In contrast, lead exposure in embryonic stem cells (1 μM) disrupted oxidative stress response genes.
- Prenatal exposure to volatile and airborne chemicals has been associated with low birth weight and premature birth.
- In Mexico City, maternal fluoride exposure (~0.90 mg/L urine) from salt and water sources was linked to adverse child behaviour.
- A maternal urinary fluoride level of 0.5 mg/L corresponded to a 3.2% reduction in child cognition and 2.5% lower IQ.
- Widely used fluorine compounds, such as PFAS, pose health risks through soil and groundwater contamination.
- Although the link between prenatal PFAS exposure and child cognition is unclear, PFAS may compromise placental and obstetric health.
- PFAS detection in cord serum (1.23–3.87 ng/mL median) warns of their persistence and transfer across generations.

Environ. Int. 2021, 156, 106616



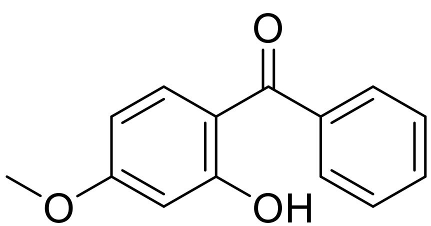
Front. Public Health 8:553850, doi: 10.3389/fpubh.2020.553850



Journal of Science Policy and Governance, 2024, 24, https://doi.org/10.38126/JSPG240106

Although oxybenzone protects against UV-induced (290 to 370 nanometers) photo-oxidation, both the anemone and a mushroom coral formed oxybenzone–glucoside conjugates that were strong photo-oxidants. Algal symbionts sequestered these conjugates, and mortality correlated with conjugate concentrations in animal cytoplasm. Many commercial sunscreens contain structurally related chemicals, and understanding metabolite phototoxicity should facilitate the development of coral-safe products.

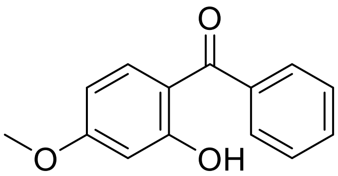
Oxybenzone



The concentration of oxybenzone at a coral reef can vary widely, depending on factors such as tourist activity and water conditions. Coral-bleaching events on Australia’s Great Barrier Reef, for example, have been linked more closely to trends in water temperature than to shifts in tourist activity. “Mass bleaching happens regardless of where the tourists are,” Hughes says. “Even the most remote, most pristine reefs are bleaching because water temperatures are killing them.”

The metabolic products of oxybenzone-based sunscreen threaten the survival of bleached corals, which have already lost their symbiotic algal partners that could have helped minimize the toxic effects of the chemicals. [Science, 2022, 376, 578-579]

Oxybenzone



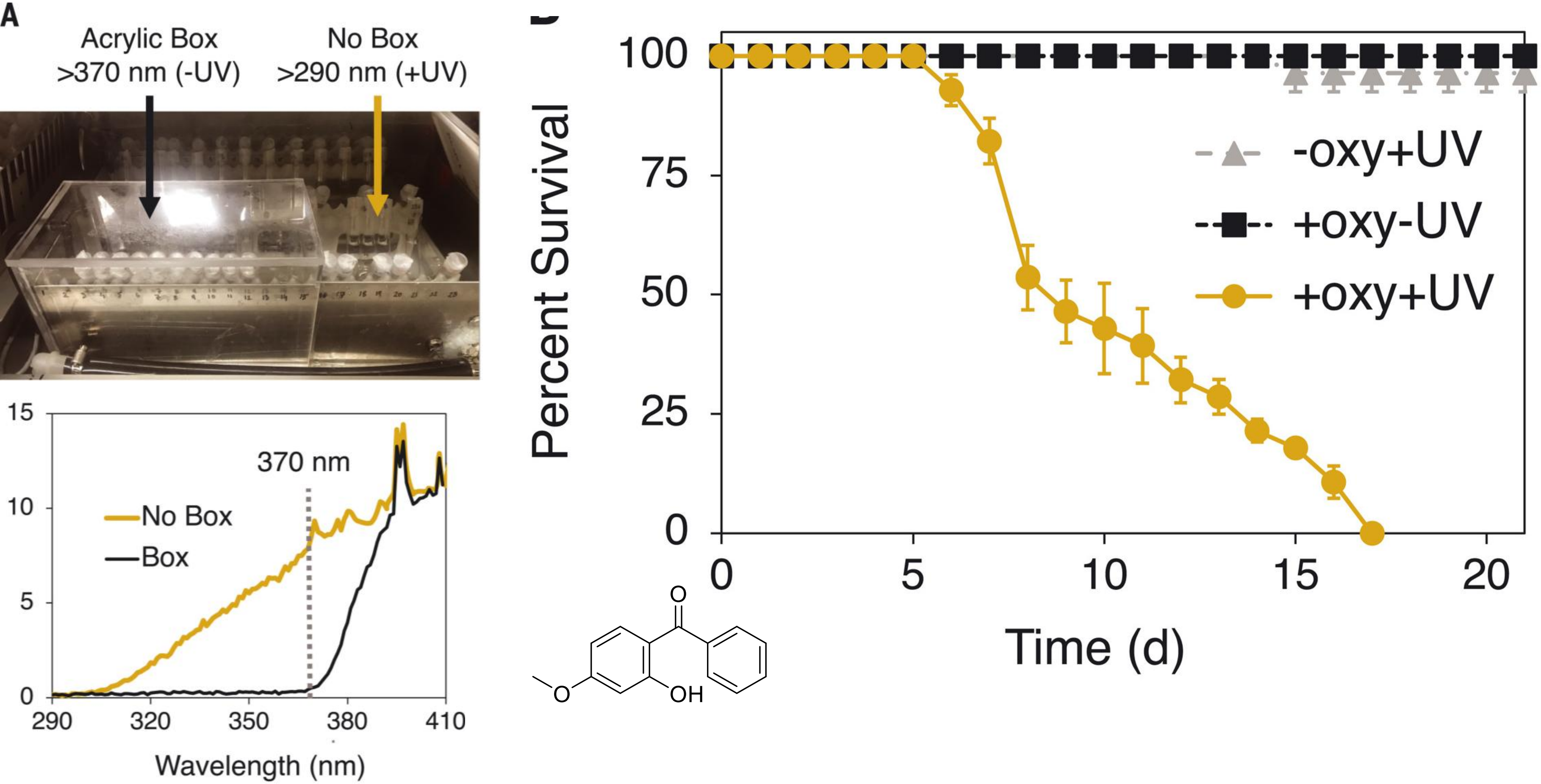
A possible relaxation mechanism is the rotation of excited OH groups toward the bulk (water or aq. phase) and the formation of a hydrogen bond after which energy dissipation occurs rapidly due to the increased anharmonicity of the OH vibrational potential. [PNAS, 2013, 18780-18785]

Symbiotic anemones engage in mutually beneficial relationships, primarily with fish and crustaceans, where both organisms benefit from the interaction. One common example is the relationship between clownfish and sea anemones, where the anemone provides protection and a safe haven for the clownfish, while the clownfish helps to clean the anemone and provides it with nutrients.

Molecular Phylogenetics and Evolution
Volume 56, Issue 3, September 2010, Pages 868-877

Clownfish hiding within the anemone in Seacoast Science Center tank.

https://www.seacoastsciencecenter.org/2025/01/30/send-in-the-clowns/

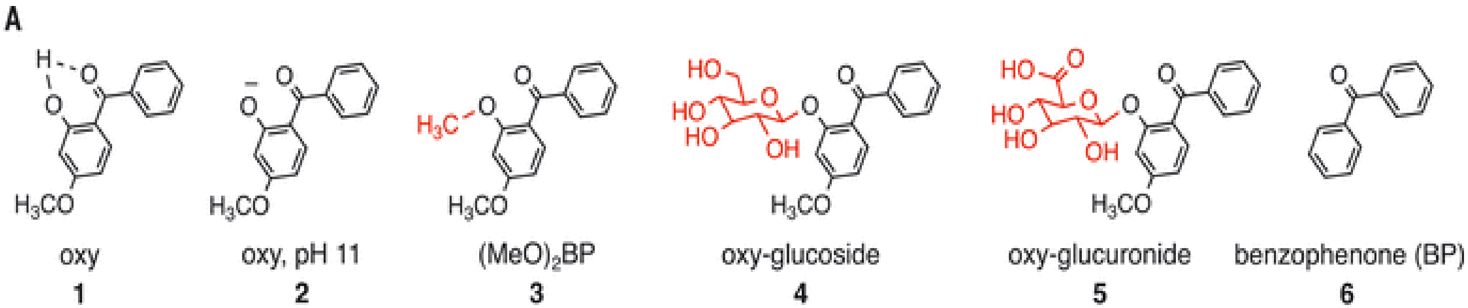


We exposed symbiotic anemones to 8.8 mM (2 mg/liter) oxybenzone in artificial seawater at 27°C in a solar simulator that approximates the 24-hour diurnal sunlight cycle. Mortality was 100% within 17 days. By contrast, negligible mortality was observed over 21 days when exposed to simulated sunlight without oxybenzone or to 8.8 mM oxybenzone without UV light.

Science, 2022, 376, 644-648

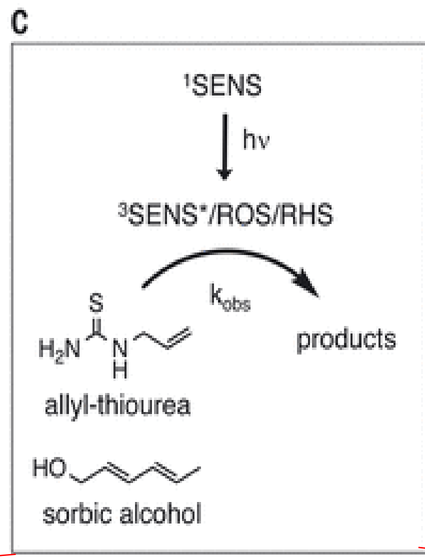
Conversion of oxybenzone sunscreen to phototoxic glucoside conjugates by sea anemones and corals.

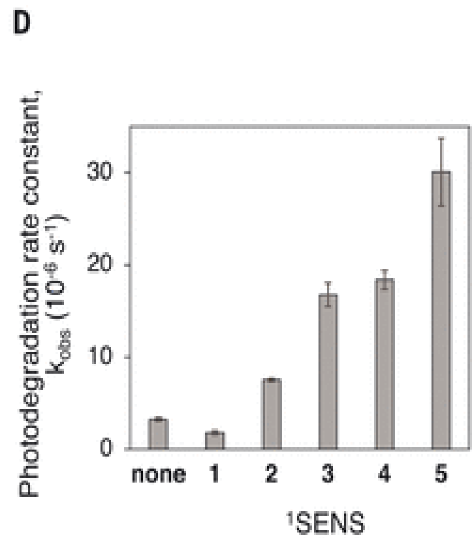
Science, 2022, 376, 644-648, DOI: (10.1126/science.abn2600)



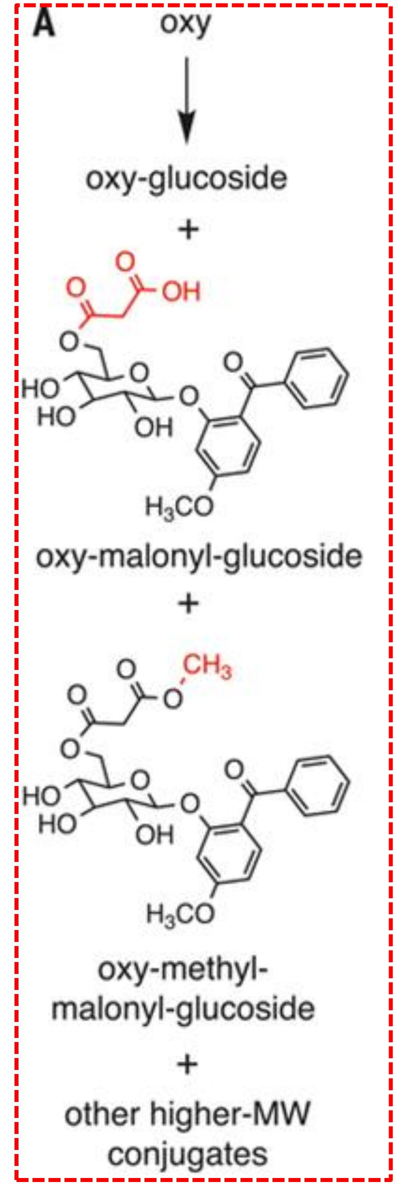
Allyl-thiourea and sorbic alcohol as probes forreactive species. ^{1}SENS, photosensitizing molecule in its ground state; ^{3}SENS*, photosensitizing molecule in its excited, triplet state.

RHS: Reactive halogen species.





Photoexcitation of sensitised molecules to excited triplet states. This excited triplet state degrades biomolecules either directly or indirectly via reactive oxygen species (ROS)and/or reactive halogen species (RHS)



Hypothesized scheme of oxybenzone (oxy) metabolism

Once in a high-energy state, the hydroxyl (–OH) group of oxybenzone can normally dissipate excess energy as heat. However, when corals metabolize oxybenzone, this protective pathway is lost. The resulting oxybenzone glucoside conjugate still absorbs light but can no longer safely release the energy. Instead, it generates reactive oxygen species (ROS), triggering a radical chain reaction that damages cellular components and tissues. In effect, corals transform oxybenzone from a sunscreen into its opposite—a phototoxin.

This suggests that corals that have bleached are even more vulnerable to the sunscreen chemical. Bleaching happens when corals respond to stresses such as increasing ocean temperatures by expelling the symbiotic algae that live in their cells and are a major source of food and energy for the corals. This exodus causes them to turn white. In the group's experiments, bleached sea anemones died about 5 times faster than healthy ones.

https://cen.acs.org/environment/pollution/Sunscreen-chemical-kills-corals-scientists/100/web/2022/05 [C&E News May 9, 2022].

Chemicals That May Disrupt Your Endocrine System

According to the Endocrine Society, there are nearly 85,000 human-made chemicals in the world, and 1,000 or more of those could be endocrine disruptors, based on their unique properties. The following are among the most common and well-studied.

•**Atrazine** (commonly applied herbicides)

•**Bisphenol A (BPA)** is used to make polycarbonate plastics and epoxy resins. BPA based polymers and resins.

•**Dioxins** (byproduct of certain manufacturing processes) Also released into the air from waste burning and wildfires.

•**Perchlorate** (Used in explosives, and fireworks)

•**Per- and polyfluoroalkyl substances (PFAS)** (firefighting foam, nonstick pans, paper, and textile coatings, etc).

•**Phthalates** (liquid plasticizers, food packaging, cosmetics, fragrances, children's toys, and medical device tubing, Cosmetics (nail polish, hair spray, aftershave lotion, cleanser, and shampoo).

•**Polychlorinated biphenyls (PCBs)** (electrical equipment, such as transformers, and are in hydraulic fluids, heat transfer fluids, lubricants, and plasticizers) were banned in 1979.

Examples of ‘One Health’.

- **COVID-19 pandemic:** Likely originating from an animal reservoir, SARS-CoV-2 demonstrated how zoonotic diseases can rapidly cross species barriers and spread globally. A One Health approach—combining wildlife surveillance, safe agricultural practices, and strong human healthcare systems—was essential in understanding and responding to the pandemic.

- **Antimicrobial Resistance (AMR):** The misuse of antibiotics in human medicine, livestock production, and agriculture accelerates the development of resistant microbes. Resistant bacteria can spread between animals, humans, and the environment (e.g., through food chains, water systems, or direct contact). Addressing AMR requires coordinated One Health strategies, such as prudent antimicrobial use, improved infection prevention, and environmental monitoring.