BIOCHEMSOC 2023

BioChemistry: Under the Microscope

Contents

Hi all, and welcome to the 6th Edition of “Biochemistry: Under the Microscope”, the BioChemSoc Newsletter. BioChemSoc has been running since 2014, and in this time hundreds of students have created engaging presentations to share their further reading with their peers. Since the BCS Newsletter was introduced in 2021, many amazing articles have been written and submitted by students of all ages, and we are excited to show you our latest submissions!

First of all, we'd like to give a big thank you to everyone who submitted an article! We've had entries on a wide range of fascinating topics, from the mechanism of paracetamol to how sleep affects our brain, and we've loved reading every one of them!

Thank you for all your support this year and we are looking forwards to seeing what you'll present on next. In the meantime, we hope you find this edition an enjoyable read!

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THE WINNER OF THE BIOCHEMSOC ARTICLE COMPETITION IS....

FRANCES WONG

for her article on Paracetamol

Congratulations on your amazing article! We loved reading it and hope you enjoy your prize.

Paracetamol

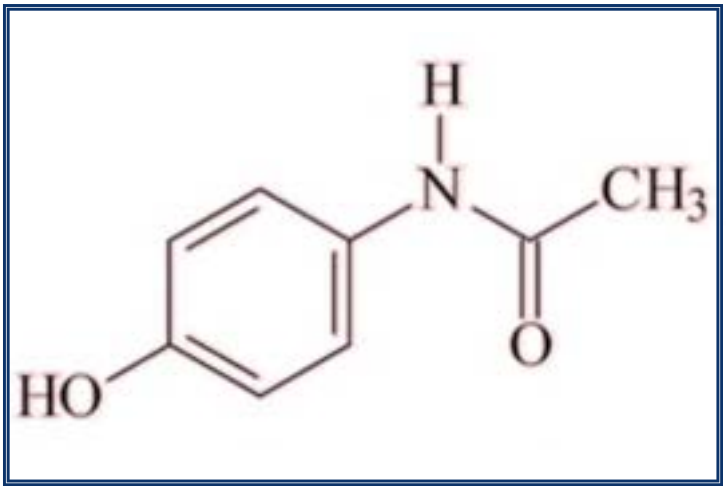
By Frances Wong

Paracetamol, also known as Acetaminophen, is a commonly used medicine that treats mild to moderate pain and fever [1], as the standard antipyretics and analgesics. It was first used clinically in 1893 by von Mering and appeared commercially in the United States in 1950. [2]

Etymology of Paracetamol

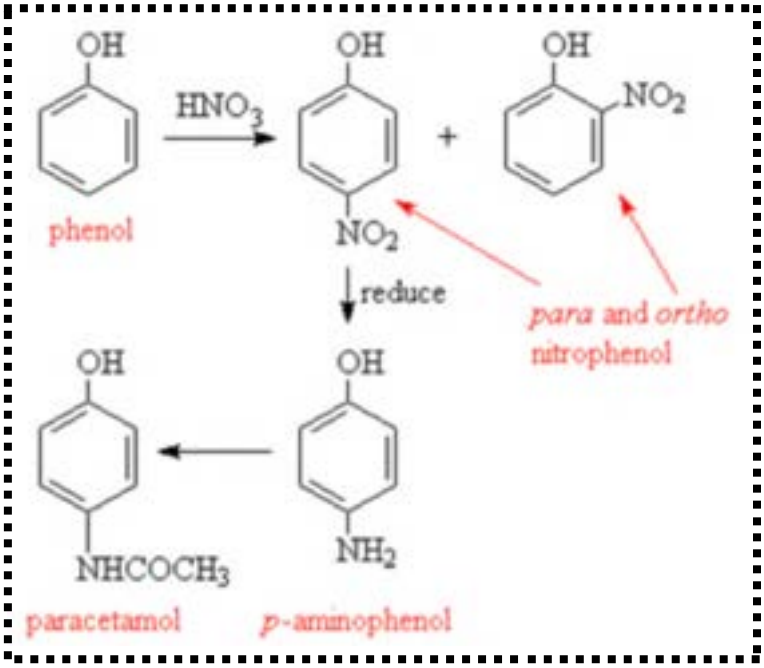
Paracetamol is the shortened form of para-acetylaminophenol [3]

- "Para" describes the molecule with the substituents, acetamide group(-$CONH_2$) and hydroxyl group, at the 1 and 4 positions on an aromatic compound[4]
- "Acet" stands for "acetyl" functional group with the chemical formula -$COCH_3$ [5]
- "Tamol" stands for "aminophenol", which refers to the amino group (-NH_2) and the hydroxyl group(-OH) in the benzene ring



Synthesis of paracetamol [6]

The starting material of paracetamol is phenol. By nitration, nitrophenol is created with the addition of concentrated nitric acid and sulfuric acid. The o-isomer of the mixture is removed by steam distillation. The remaining p-nitro group is then reduced to a p-amino group by the addition of easily oxidised metal and acid. It is then acetylated to make paracetamol.



Paracetamol

By Frances Wong

Mechanisms of action of Paracetamol

Even though paracetamol is one of the medicines that is used broadly worldwide, the exact mechanism of paracetamol is still not clear. There is evidence of several central mechanisms including the inhibition of prostaglandin synthesis and its effect on the endocannabinoid system.

Inhibition of prostaglandin synthesis/ Cyclooxygenase

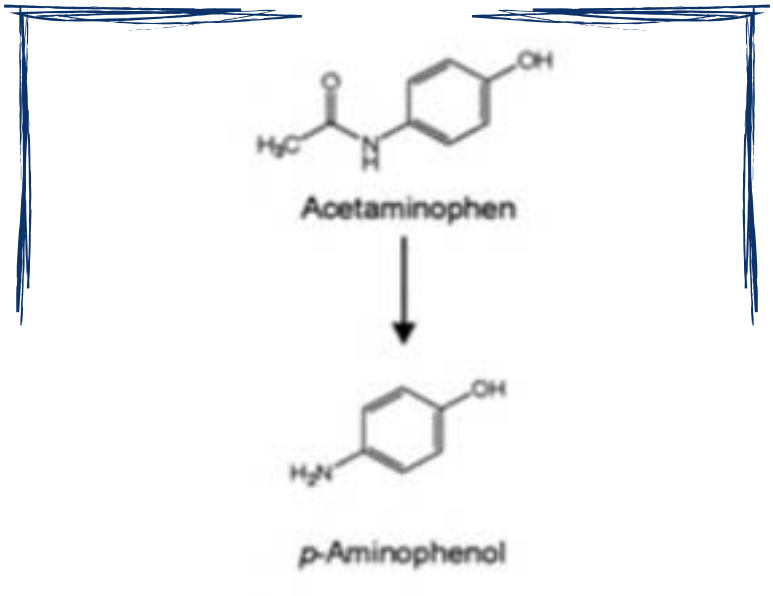
Prostaglandins are groups of lipids with hormone-like actions [7] that are responsible for the generation of the inflammatory response [8]. The cyclooxygenase isoenzymes, COX-1 and COX-2, catalyse the formation of prostaglandins. [9] Paracetamol is a inhibitor of prostaglandin H synthases (COX-1 and COX-2), weakly inhibiting the synthesis of prostaglandins (PGS). [10] It completely inhibits the synthesis of prostaglandin E2 in lipopolysaccharide-stimulated microglia, the resident immune cells of brain that regulate injury repair.[11] By blocking cyclooxygenase, paracetamol helps to reduce pain and fever by decreasing the inflammation in the central nervous system with reduced sensitivity of pain receptors. [12]

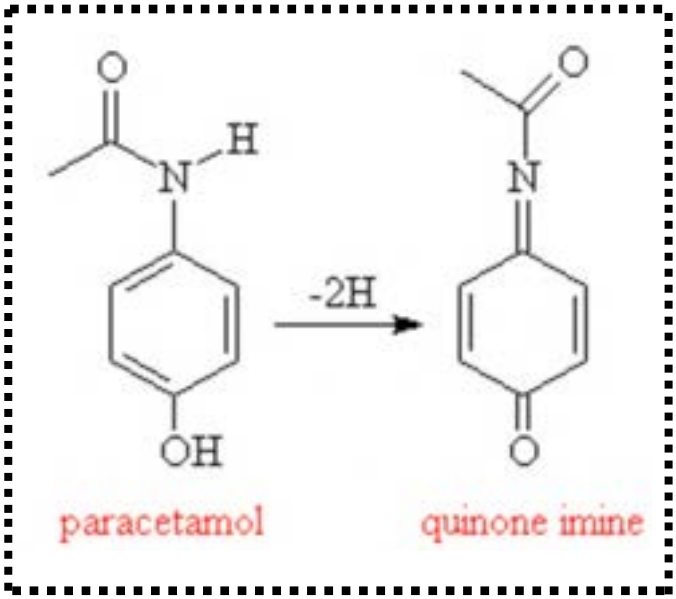
Effect on the Endocannabinoid system

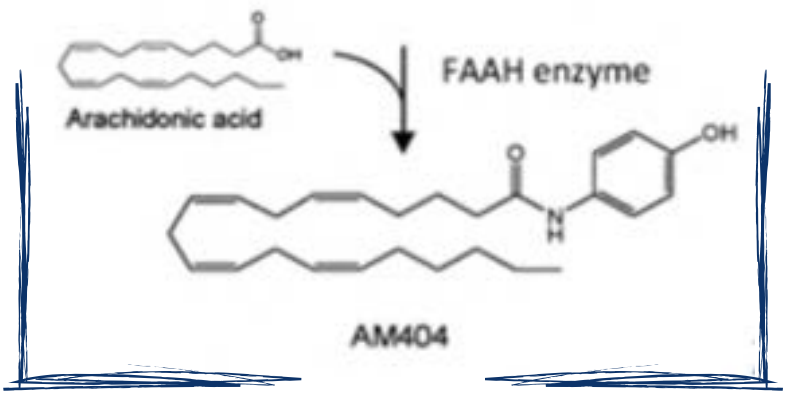
The endocannabinoid system is a neuromodulatory system that play important roles in the central nervous system development, neuronal synaptic communication and synaptic plasticity. [13]The system in comprised of cannabinoid receptors, endogenous cannabinoids (endocannabinoids) and the enzymes responsible for the synthesis and degradation of endocannabinoids. [14] Endocannabinoids are lipid base neurotransmitter that binds to cannabinoid receptors. [15] By lowering the level of cannabinoid receptors, analgesia is produced with dysregulations in the endocannabinoid system. A hypothesis is reported by Hogestatt. In central nervous system, para-aminophenol produced from the acetaminophen metabolism is combined with arachidonic acid to produce AM404. The reaction is catalysed by enzyme FAAH, which is a central enzyme in the ECS where it catabolises endocannabinoids. Am404 acts as an indirect agonist at the CM1 cannabinoid receptors by blocking the reuptake of endocannabinoid, increasing its action in ECS. This may disrupt the normal action of ECS, decreasing sensitivity to pain. [16]

Paracetamol

By Frances Wong







Toxicity [6]

Overdose of paracetamol can cause liver failure. This is caused by an insufficiency of glutathione. When paracetamol enters the body, paracetamol is metabolised into quinone imine, which is highly toxic. Quinone imine can be eliminated in the liver by a tripeptide, glutathione. If there is not sufficient glutathione, quinone imine would not be eliminated and begin to react with nucleic acids and cellular proteins in the liver, causing irreversible damage in the liver.

References

[1]Australia, H. (2023). Paracetamol. [online] www.healthdirect.gov.au. Available at: https://www.healthdirect.gov.au/paracetamol#:~:text=Paracetamol%20is%20a%20medicine%20used

[2]Lf, P. (2000). Paracetamol: Past, Present, and Future. [online] American journal of therapeutics. Available at: https://pubmed.ncbi.nlm.nih.gov/11319582/.

[3]www.merriam-webster.com. (n.d.). Definition of PARACETAMOL. [online] Available at: https://www.merriam-webster.com/dictionary/paracetamol#:~:text=etymology.

[4] byjus.com. (n.d.). Why do we use meta para ortho in physical chemistry? [online] Available at: https://byjus.com/question-answer/why-do-we-use-meta-para-ortho-in-physical-chemistry/.

[5]Wikipedia. (2020). Acetyl group. [online] Available at: https://en.wikipedia.org/wiki/Acetyl_group.

[6]www.ch.ic.ac.uk. (n.d.). Paracetamol. [online] Available at: https://www.ch.ic.ac.uk/vchemlib/mim/bristol/paracetamol/paracet_text.htm.

[7]Cleveland Clinic. (n.d.). Prostaglandins: What It Is, Function & Side Effects. [online] Available at: https://my.clevelandclinic.org/health/articles/24411-prostaglandins#:~:text=Prostaglandins%20are%20a%20group%20of.

[8]Ricciotti, E. and FitzGerald, G.A. (2011). Prostaglandins and Inflammation. Arteriosclerosis, Thrombosis, and Vascular Biology, [online] 31(5), pp.986–1000. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3081099/.

[9]Fa, F. (2004). Cyclooxygenase Enzymes: Regulation and Function. [online] Current pharmaceutical design. Available at: https://pubmed.ncbi.nlm.nih.gov/14965321/.

[10]Graham, G.G., Robins, S.-A., Bryant, K.J. and Scott, K.F. (2001). Inhibition of prostaglandin synthesis in intact cells by paracetamol (acetaminophen). InflammoPharmacology, 9(1-2), pp.131–142. Available at: https://doi.org/10.1163/156856001300248407.

[11]Greco, A., Ajmone-Cat, M.A., Nicolini, A., Sciulli, M.G. and Minghetti, L. (2003). Paracetamol effectively reduces prostaglandin E2 synthesis in brain macrophages by inhibiting enzymatic activity of cyclooxygenase but not phospholipase and prostaglandin E synthase. Journal of Neuroscience Research, [online] 71(6), pp.844–852. Available at: :https://doi.org/10.1002/jnr.10543.

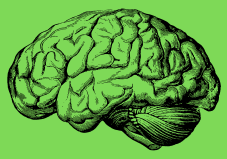
[12]Graham, G. and Day, R. (2018). Curious Kids: How does pain medicine work in the body? [online] The Conversation. Available at: https://theconversation.com/curious-kids-how-does-pain-medicine-work-in-the-body-82495#:~:text=Inside%20our%20bodies%2C%20paracetamol%20is

[13]Skaper, S.D. and Di Marzo, V. (2012). Endocannabinoids in nervous system health and disease: the big picture in a nutshell. Philosophical Transactions of the Royal Society B: Biological Sciences, 367(1607), pp.3193–3200. Available at: :https://doi.org/10.1098/rstb.2012.0313.

[14]Lu, H.-C. and Mackie, K. (2016). An Introduction to the Endogenous Cannabinoid System. Biological Psychiatry, [online] 79(7), pp.516–525. Available at: :https://doi.org/10.1016/j.biopsych.2015.07.028.

[15]Endocannabinoid system (2023) Wikipedia. Available at: https://en.wikipedia.org/wiki/Endocannabinoid_system

[16] Schultz, S., Gould, G.G., Antonucci, N., Brigida, A.L. and Siniscalco, D. (2021). Endocannabinoid System Dysregulation from Acetaminophen Use May Lead to Autism Spectrum Disorder: Could Cannabinoid Treatment Be Efficacious? Molecules, 26(7), p.1845. doi:https://doi.org/10.3390/molecules26071845.



CAN WE MAKE BRAINS?

By Emma Corrigan

HOW ARE BRAIN ORGANOIDS MADE?

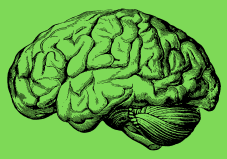
In recent years, brain organoids have been developed in vitro to mimic the characteristics of a developing brain and to model nervous system diseases such as Alzheimer's. Brain organoids are mainly cerebral organoids, which closely resemble structures found in the developing human brain and shows how brain regions interconnect. The process begins with induced pluripotent stem cells (iPSCs), as they have the capacity to differentiate into any type of cell in the body. These iPSCs are differentiated into three-dimensional embryoid bodies which reach a diameter of 400-600 micrometres. After 5 days, the body is put in a neural induction medium, which promotes development of the neuroectoderm (in an embryo, this would give rise to the nervous system). At day 10, the neuroectoderm is induced, which allows it to develop surface buds containing neuroepithelial cells. In the final stage, the organoid is cultivated in a spinning bioreactor, promoting nutrient and oxygen exchange, which allows the organoid to differentiate and mature.

Cross section of an entire brain organoid. Accessed from https://www.viennabiocenter.org/research/key-discoveries/human-brain-organoids/

WHY HAVE SCIENTISTS DEVELOPED BRAIN ORGANOIDS?

Research using brain organoids is still in early stages, but scientists have begun to use them to understand brain development to a more advanced level or to study neurological disorders.

Brain organoids have recently been used to model developmental abnormalities, for example lissencephaly, a genetic disorder which involves having no folds over the surface of your brain. Children suffering from lissencephaly showed slowed development and reduced life expectancy. By using organoids, scientists have found problems with initial patterns of the nerve cells, which can now be studied in more detail.



CAN WE MAKE BRAINS?

By Emma Corrigan

In 2021, Dr Peggy Arthur and her team found that their organoids were able to grow optic-vesicles. These developed in between day 30-60, producing organoids with both neural and non-neural cell types. This meant the organoids also developed light sensitive cells, meaning that in the future these organoids can be used to explore the mechanisms of underlying retinal disorders. Thus, the value of developing brain organoids lies in this, as they are being used to understand disorders which can negatively affect people's lives, in the hopes of being able to one day cure/treat these disorders.

Brain organoids are also being grown from stem cells which are harvested from patients with neurological disorders in the hopes of recreating pathological features, such as amyloid plaques. Models are now being used to discuss the efficacy of drugs to treat Huntington's, Parkinson's, and Alzheimer's. Organoids are also being used to further understand cancers which accept the brain, like Glioblastoma multiforme is a form of brain cancer that is difficult to treat with current treatment options. By using fluorescent markers in organoids, researchers are revealing how abnormal cells metastasise and form tumours within the brain, in the hopes of being able to attack the cancer with better, more effective treatments in the future.

WHAT ARE THE ISSUES SURROUNDING RESEARCH ON BRAIN ORGANOIDS?

Ethics remain a very prevalent topic in research, and a large issue surrounding brain organoids is, as they become more developed, scientists become concerned that they can develop consciousness and ultimately become aware of what is going on in their environment. Many scientists are now calling for more ethics to be put in place for future research on brain organoids, in the hopes of preventing a scenario where a brain organoid becomes aware enough to understand it is being tested on and feel pain. However, now we understand how to use these organoids to change the future of medicine, it has caused some to argue against any degree of unethical conduct in research, which in turn will likely be the cause of future debate in the hopes of finding a balance.

NEUROTRANSMITTERS

By Harini Saseetharan

What are neurotransmitters?

Neurotransmitters are chemical messengers which carry chemical signals from the presynaptic neurone to the postsynaptic neurone. There are 3 possible actions of neurotransmitters:

- excitatory – allow the message to be passed onto the next cell and result in the depolarisation of the postsynaptic neurone e.g., epinephrine and norepinephrine
- inhibitory – block or prevent the chemical message being passed on any further and result in the hyperpolarisation of the postsynaptic neurone e.g., glycine and serotonin
- modulatory – influence the effects of other chemical messengers.

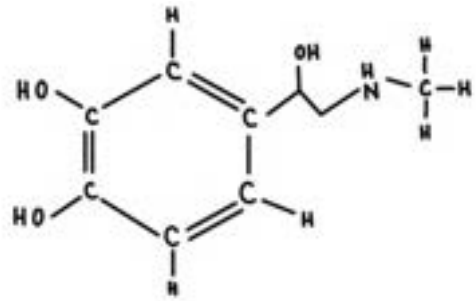
What happens at the synapse between two neurones?

- The action potential reaches the end of the presynaptic neurone.
- Depolarisation of the presynaptic neurone membrane results in calcium ion channels opening
- Calcium ions diffuse into the presynaptic knob down a concentration gradient.
- This causes synaptic vesicles containing neurotransmitters to fuse with the presynaptic membrane
- Neurotransmitters are released into the synaptic cleft via exocytosis.
- The neurotransmitters diffuse across the synaptic cleft and binds with its specific receptor molecule on the postsynaptic membrane.
- This causes sodium ion channels to open.
- Sodium ions diffuse into the postsynaptic neurone.
- This causes action potential, and the impulse is moved along the postsynaptic neurone

Examples of neurotransmitters

Adrenaline

- Also known as epinephrine
- The fight or flight neurohormone
- Secreted by the adrenal glands.
- Released during times of stress or danger.
- Causes heart to beat faster, breathing occurs at a faster rate and you feel very alert.



Noradrenaline

- Also known as norepinephrine
- Excitatory neurotransmitter
- Regulates attention and the fight or flight response.
- Increases heart rate and the blood flow to muscles.
- In large quantities, it causes anxiety.
- In low quantities, it causes poor concentration and problems with sleep.

NEUROTRANSMITTERS

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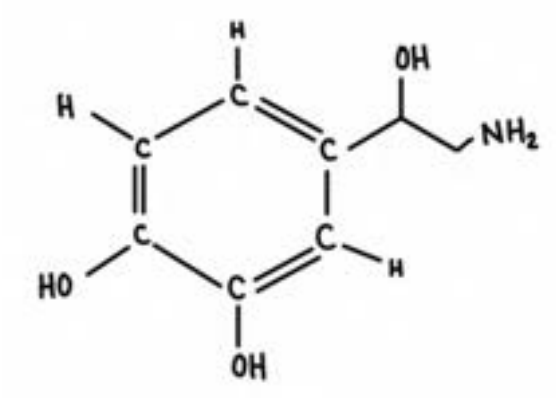
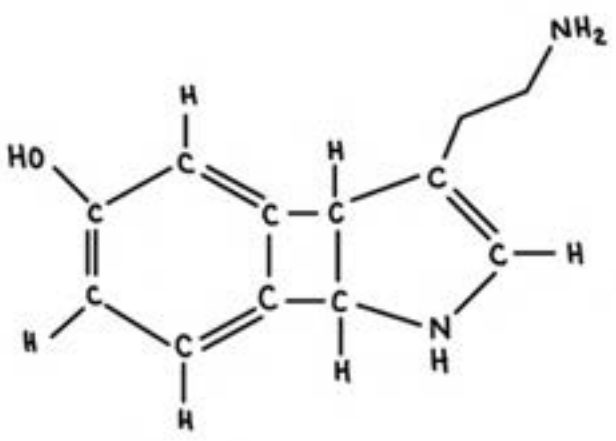


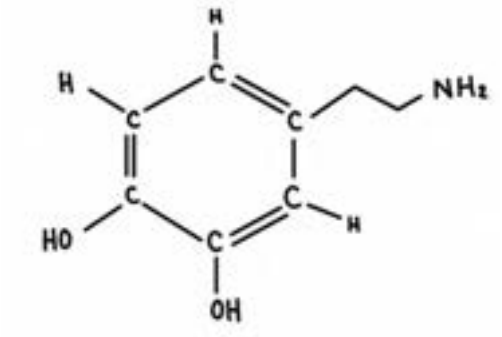
Serotonin

- Contributes to feelings of wellbeing.
- Regulates pain, digestion and sleep mechanisms.
- Low serotonin is associated with depression and anxiety – antidepressants work to increase serotonin levels.
- Naturally produced through exposure to sunlight and exercise
- Has implications in OCD (obsessive compulsive disorder) – low serotonin levels are found to have links with OCD



Dopamine

- The molecule connected to the reward and pleasure perception system.
- Alcohol and many illegal drugs cause an increase of dopamine, which forms somewhat the reason why people get addicted to them.
- Has a role in controlling memory, mood, sleep, concentration, learning and body movements
- Low levels of dopamine have been linked to depression, psychosis and schizophrenia
- High levels of dopamine have been linked to being more competitive, aggressive and having poor impulse control – can lead to binge eating, addiction and ADHD
- In Parkinson's disease, nerve cells that produce dopamine eventually die – this leads to problems with muscle stiffness and movements.



References

1)https://my.clevelandclinic.org/health/articles/22513-neurotransmitters
2)Fullick, A., Locke, J., Bircher, P., (2015) *A Level Biology for OCR A*. Oxford University Press
3)Magrini, M (2021) *The Brain A User's Manual.* London
4)https://my.clevelandclinic.org/health/body/23038-adrenaline#:~:text=What%20is%20adrenaline%3F,because%20it%20happens%20so%20fast
5)https://www.healthdirect.gov.au/dopamine#:~:text=my%20dopamine%20levels%3F-,What%20is%20dopamine%3F,send%20messages%20to%20each%20other.

Biosynthesis of sunscreen

By Eleanor Gao

What is biosynthesis? [1]

Biosynthesis is a process in which living organisms produce complex molecules and compounds in their own cells. Just like most other reactions, enzymes are used as a catalyst, and an energy source (for example ATP) is always needed.

During biosynthesis, small monomers such as amino acids, sugars (for example glucose), and fatty acids can all be assembled into larger macromolecules or compounds.

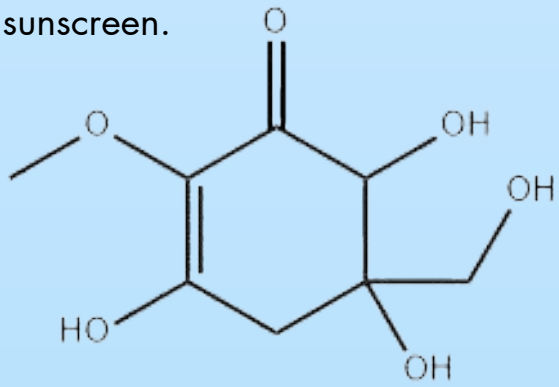
Protein synthesis is an example of biosynthesis, as new polypeptides are produced from the amino acids each tRNA brings along during translation.

Natural Sunscreens Used in Organisms? [2]

The fishes, plants and microorganisms that live in the upper ocean and on reefs are always exposed to intense and unrelenting sunlight, however they are restricted to this area of the ocean as their food - such as insects, algae and plankton (for fish such as zebrafish) all live here, and the abundant sunlight allows for photosynthesis (for cyanobacteria and plants). And most of all, living closer to sunlight provides the temperature that is necessary for the survival of all of these organisms.

However, with the sunlight also comes potentially deadly UV radiation. Cyanobacteria (bacteria that are capable of photosynthesis) and algae that live in shallow water produce their own sunscreens, especially since they are smaller and can be the most severely affected by UV radiation. These natural sunscreens are actually mycosporine-like amino acids. Mycosporine-like amino acids are UV absorbing compounds and can also act as potent antioxidants.

Some fish, birds, amphibians and reptiles living in shallow water have the genes to produce gadusol, a compound that can act as a sunscreen.



Gadusol, $C_8H_{12}O_6$, used in organisms as a natural sunscreen

Biosynthesis of sunscreen

By Eleanor Gao

Gadusol absorbs UV radiation, particularly UVB (which damages DNA, proteins, lipids, and membranes), and dissipates it as heat.

Hippopotamuses produce sweat that not only helps them to control their body temperature, but is red and orange in colour. The red pigment contains an antibiotic, while the orange pigment absorbs UV rays - therefore the two chemicals work together to protect them from both bacterial infections and sun damage.

Hippos produce red-orange sweat which is a natural sunscreen and antibiotic combined!

New Method of Harvesting 'green' Sunscreen Ingredient [3]

Some of the most widely-used sunscreen filters such as octinoxate (for UVB) and oxybenzone (UVA) are both potent SPF filters, however these particular filters can enter into marine life and cause harm - it can accumulate in coral tissue, which induces bleaching, damages DNA, and deforms young coral. It can also impair growth and photosynthesis in green algae, which is the most important producer in marine ecosystems.

In 2018, at the College of Pharmacy at the University of Florida, scientists discovered a method of harvesting a UV‐absorbing amino acid called shinorine, produced by cyanobacteria and macroalgae (both are marine microorganisms). The scientists mined the genes responsible for the synthesis of shinorine from cyanobacteria, and then inserted these genes into Synechocystis (another strain of cyanobacteria). Synechocystis was used as it grows quickly and is easy for scientists to modify its genes. At the end, the yield of shinorine (produced by per gram of cyanobacteria) was similar to the yield of the conventially used method of harvesting it from red algae. However, the method of using red algae has a very long processing time and the algae itself can

Biosynthesis of sunscreen

By Eleanor Gao

take as long as a year to grow.

This new method is not only more efficient, but a great advancement in shinorine and cyanobacterial research.

The Impact of Ozone Depletion

It is also important to know that ozone depletion can have a very harmful effect on entire marine ecosystems and the natural sunscreen compounds produced by organisms can not shield them from strong and intense UV radiation completely. Small organisms like plankton and algae are among the most severely affected by UV radiation, however they are the most important primary producers, and are at the lowest trophic level of the aquatic food web. Although they produce their own natural sunscreen, they still have a maximum tolerance of UV radiation, and if even some were to die, less food would be available for fish, shrimps, and crab.

In Antarctica, most of the organisms have a low tolerance for UV radiation since during most of the year hardly any sunlight reaches the continent. However, due to the reduced layer of ozone, UVB radiation has been able to penetrate the atmosphere with a higher intensity and has reduced the plankton populations by at least 6%.

References

[1] https://www.biologyonline.com/dictionary/biosynthesis

[2] https://www.nationalgeographic.com/animals/article/150815-animals-sunscreen-health□science-hippos?loggedin=true&rnd=1688835643490

[3] https://news.ufl.edu/articles/2018/02/researchers-discover-method-for□harvesting-green-sunscreen-ingredient

Psychedelics

By Varshita Yettapu

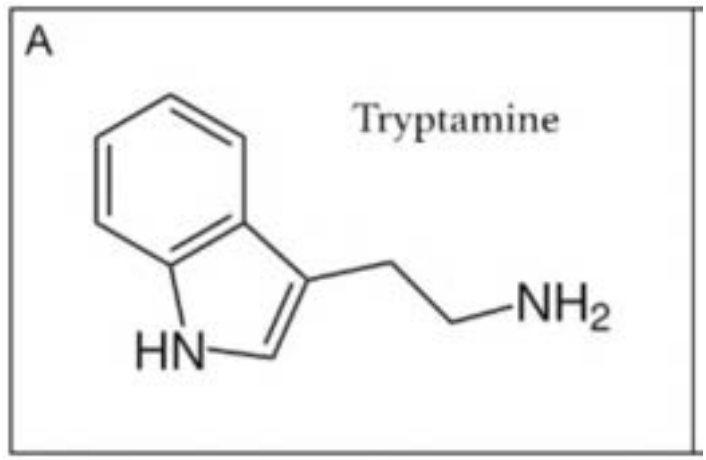
What are psychedelics?

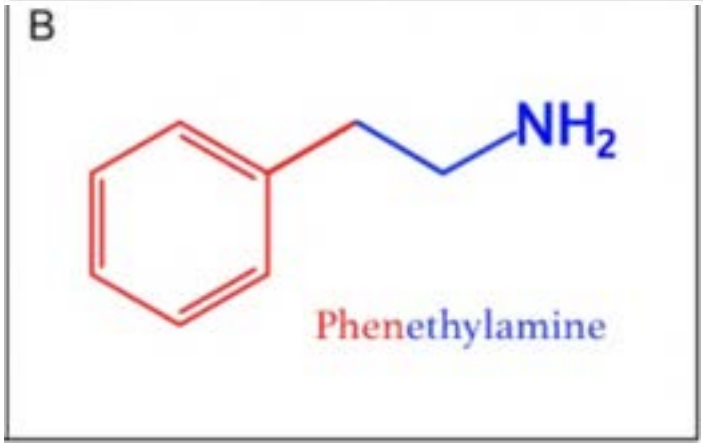
Psychedelics are a category of hallucinogenic drugs whose primary effect is to trigger non – ordinary mental states to change/ enhance sensory perceptions, thought processes and energy levels.

A very common example is Psilocybin, also known as “magic mushrooms”. This works by activating serotonin receptors in the prefrontal cortex – affecting mood, cognition and perception. Research on this for the treatment of mental disorders, such as depression, is still in the early stages.

The two main classes:

- Tryptamines – called this due to their ring system, derived from the amino acid tryptophan (Image A)
- Phenethylamine – named this due to the phenyl group attached to the ethylamine group (Image B)





Psychedelics

By Varshita Yettapu

In relation to our consciousness:

We have a neurotransmitter called 5 – hyrdoxytryptamine, also known as serotonin – a primary neurotransmitter used by neurons in regions of the brain regulating mood, cognitions, reward learning and memory. Neurons related to this are called “serotonergic”.

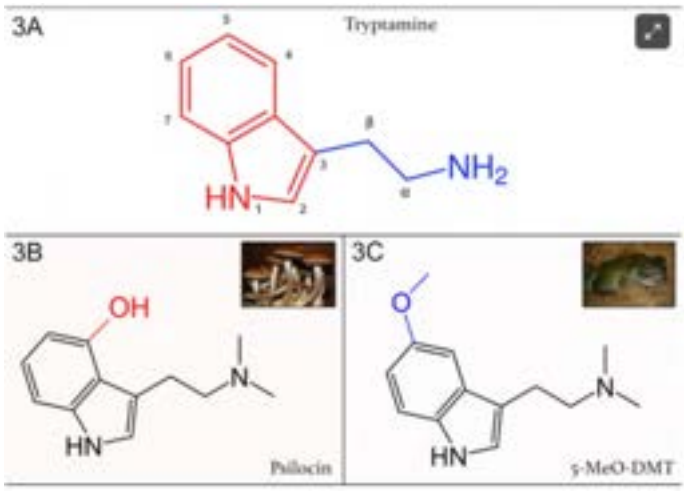
When a serotonergic neuron receives a signal, it releases serotonin which then binds to complementary receptors on neighboring neurons to effectively spread the signal. Countless numbers of serotonin receptors attach to a wider range of neuron types that are spread across the regions of the brain. Tryptamines primarily activate a receptor called serotonin HT21 receptor, as well as others to a lesser degree – Psilocin (a tryptamine) has the power to do this since it looks very similar to serotonin.

Modification to tryptamine molecules:

Modifying the chemical compound at the 6 and 7 position – hallucinogen activity is decreased and so molecules with this modification are rarely used for recreational purposes. Adding a hydroxyl group (OH) at position 4 or a methoxy group at position 5 increases the potency above other substitutions at these positions. Figure below shows this, where Psilocin from magic mushrooms (3B) is very similar to 5 – MeO- DMT found in the Sonoran Desert Toad (3C) but produces very different psychedelic experiences. A fun fact – the 5 – MeO- DMT found on the Sonoran Desert Toad was first unknowingly used for “toad smoking”, with this poison dried into crystals and smoked through a pipe to give an intense experience.

Adding a methyl group to the amine group and the alpha – carbon on the phenethylamine group does two things – 1) increases the ability for the molecule to cross the blood brin barrier and 2) prevents molecules from being degraded by enzymes in our stomach. These both factors increase the effect of the drug by increasing the amount it can reach to the receptors in our brain.

Note: Potency refers to amount of substance needed to induce the desired effect.



Psychedelics

By Varshita Yettapu

Current news on the topic

Jon Kelly, psychiatrist and clinal lecturer at Trinity College Dublin, collaborates with the largest clinical trial of psilocybin in combination with psychotherapy for treatment – resistant depression.

They found that a single dose would improve depression symptoms and could potentially be harnessed across different stages of therapy to improve patient outcomes. Some of the beneficial effects of psychedelic – assisted psychotherapy was meditated through the microbiota – gut – brain axis (also known as enteric nervous system).

DISCLAIMER: This is still fairly new research that, while has potential, would still require a thorough medical examination before being prescribed.

Various signaling molecules involving neurotransmitters (like serotonin and tryptamine), hormones and immunomodulatory factors form the basis of this information exchange highway – which the gut microbiota contributes to.

These key pathways would likely influence behavior – creating an endogenous psychedelic system against depression.

References:

https://www.medicalnewstoday.com/articles/308850

https://www.verywellmind.com/types-of-psychedelic-drug-22073

https://www.bbc.co.uk/news/health-56745139

https://www.newyorker.com/magazine/2022/03/28/the-pied-piper-of-psychedelic-toads

https://www.the-scientist.com/features/natural-high-endogenous-psychedelics-in-the-gut-and-brain-71301#:~:text=Psychedelics%20are%20evolutionarily%20ancient%20compounds,to%20know%20how%20and%20why.

CONTENT WARNING: Tumours

Anti-NMDAR encephalitis: "Brain on Fire" disease

By Warda Amir

Anti-NMDA-receptor encephalitis is an autoimmune disease where the immune system essentially attacks the brain, causing inflammation. It is often misdiagnosed as other neurological disorders or psychiatric illnesses due to the similarity of its symptoms to a range of other diseases. Although this is a rare disease affecting 1 out of 1.5 million people per year, anti-NMDAR encephalitis is the best known and most common autoimmune encephalitis.

History and discovery

Anti-NMDA receptor encephalitis was first discovered by Dr. Josep Dalmau and his colleagues at the University of Pennsylvania in 2007, when he identified 12 female patients presenting with prominent neuropsychiatric symptoms. In all 12 patients, the neurological symptoms preceded the diagnosis of ovarian teratomas, leading to the belief that these neurological symptoms were due to paraneoplastic syndrome.

Paraneoplastic syndromes of the nervous system occur when cancer-fighting agents of the immune system also attack parts of the brain, spinal cord, peripheral nerves or muscle.

What was interesting, however, was that all these patients also had similar antibodies in their cerebrospinal fluid (CSF) acting against specific areas of the brain, mainly the hippocampus.

Using the patient's CSF to test on rats, Dr Dalmau confirmed that the hippocampus seemed to be more affected than the rest of the brain. But why? After further investigation using genetic engineering to ensure only certain receptors were being synthesised, the team discovered that the antibodies in these patients were acting against NMDA receptors in the hippocampus. This makes sense, as NMDA receptors are in high volume in the hippocampus. This led to the conclusion that NMDA-receptor-seeking antibodies were the cause of the neuropsychiatric symptoms.

Since then, however, there have been many cases of anti-NMDA-receptor encephalitis that have not been accompanied by a teratoma, suggesting that there may be another cause. As is the case with most autoimmune diseases, this cause has yet to be discovered.

CONTENT WARNING: Tumours

Anti-NMDAR encephalitis: "Brain on Fire" disease

By Warda Amir

Diagnosis

Anti-NMDA receptor encephalitis is often first identified through clinical symptoms. Diagnosis is confirmed through lab testing of cerebral spinal fluid (CSF) or blood serum for anti-NMDA receptor autoantibodies.

Symptoms

Anti-NMDAR encephalitis usually evolves through several stages:

- Flu-like prodromal syndromes (I.e. early signs)
- Psychotic stage
- Unresponsiveness with hypoventilation
- Autonomic instability and dyskinesia (involuntary erratic movements)
- Catatonia

The prodromal phase is suggestive of a viral flu-like illness, in which fever and fatigue may be prominent. This phase varies in duration and may also involve upper respiratory or gastrointestinal symptoms. This is followed by the psychotic phase, in which delusions, hallucinations, paranoia, and agitation may be shown. During this phase, anti-NMDAR encephalitis is often misdiagnosed as a primary psychotic or substance-induced disorder. Following this is often the progression to a state in which impaired attention, dyskinesias, seizures and eventually catatonia may develop. In addition, significant autonomic instability, with wide-ranging fluctuations in body temperature, blood pressure, respiratory rate, and cardiac rhythm, may occur.

These phases can vary on a case-by-case basis. Remarkably, it has been found that even those who have progressed to what is considered the last stage (catatonia) can make a full recovery.

But how do these autoantibodies cause all these symptoms? The N-methyl-D-aspartate (NMDA) receptor is a receptor of glutamate, the primary excitatory neurotransmitter in the human brain. It plays an integral role in synaptic plasticity, which is a neuronal mechanism believed to be the basis of memory formation. This condition is mediated by autoantibodies that target NMDA receptors in the brain.

Autoantibodies are antibodies that react with self-antigens. This leads to an abnormal immune response that attacks your own cells, contributing to the development of autoantibody (autoimmune) diseases.

CONTENT WARNING: Tumours

Anti-NMDAR encephalitis: "Brain on Fire" disease

By Warda Amir

While the exact pathophysiology of this disease is still debated, 2 mechanisms have been suggested:

- The first is the diffusion of autoantibodies from the blood across a disrupted blood-brain barrier (BBB).This filter, separating the CNS from the circulatory system, normally prevents larger or harmful molecules from entering the brain. Many reasons for such a collapse have been suggested, with the most likely answer being the effects of acute inflammation of the nervous system. Likewise, the involvement of corticotropin releasing hormone on mast cells in acute stress has been shown to facilitate BBB penetration.

- The second is intrathecal production (production of antibodies in the intrathecal space). Dalmau et al. demonstrated that 53 out of 58 patients with the condition had at least partially preserved BBBs, whilst having a high concentration of antibodies in their CSF. Furthermore, cyclophosphamide and rituximab, drugs used to eliminate dysfunctional immune cells, have been shown to be successful second-line treatments. These destroy excess antibody-producing cells in the thecal sac, thus alleviating the symptoms.

Treatments

Early diagnosis and subsequent treatment can be beneficial, though many patients who have been diagnosed quite late in the progression of the disease have still managed to recover well!

The first-line therapies for this disease focus on immunosuppression, and include corticosteroids, immunoglobulin infusion (IVIG), and plasmapheresis (PLEX).

Corticosteroids work by mimicking the effects of a hormone called cortisol, which is naturally produced by your body in times of stress. They suppress the multiple inflammatory genes that are activated, mainly by reversing histone acetylation (a type of epigenetic modification which generally increases gene expression) of activated inflammatory genes through binding of liganded glucocorticoid receptors (GR) to coactivators and recruitment of histone deacetylase-2 (HDAC2) to the activated transcription complex. Basically, it turns the inflammatory genes 'off', or (more accurately), reduces the expression of these genes. This ultimately lowers the inflammation caused by the anti-NMDAR antibodies.

CONTENT WARNING: Tumours

Anti-NMDAR encephalitis: "Brain on Fire" disease

By Warda Amir

IVIG is a product made up of human antibodies that can be given intravenously (through a vein). It is prepared from the blood donated by thousands of people, to make a super-concentrated and very diverse collection of antibodies. IVIG contains a high concentration of normal antibodies that can compete with and neutralize these autoantibodies. By binding to and neutralizing the autoantibodies, IVIG helps reduce their harmful effects and minimize tissue damage. IVIG also regulates the activity of immune cells, such as T cells and B cells. IVIG therapy prevents the proliferation of B-cells that produce autoantibodies. It also suppresses the production of pro-inflammatory cytokines (molecules involved in promoting inflammation) and enhances the production of anti-inflammatory cytokines, which helps to reduce inflammation.

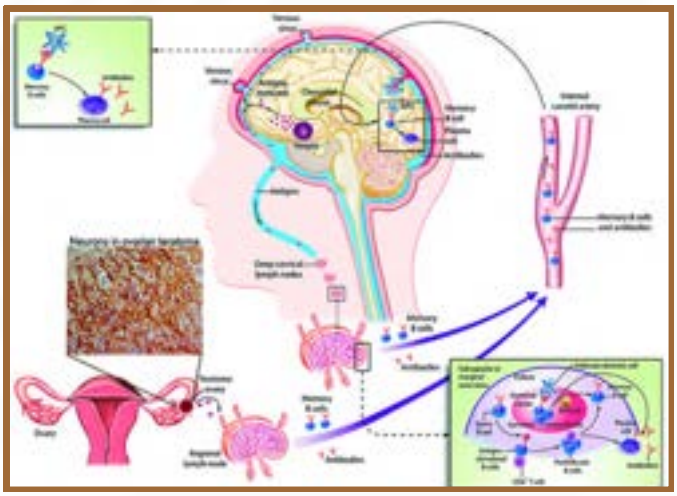
Plasmapheresis (or plasma exchange) is a process involving the following steps:

1. Whole blood is withdrawn from a large vein
2. A machine separates the liquid portion of blood (plasma) from the red and white blood cells.
3. The cells are transfused back along with a plasma replacement fluid.

This works by essentially removing the harmful autoantibodies from the blood.

Unfortunately, only approximately half of the patients would respond to first-line therapy. Rituximab (monoclonal antibodies), cyclophosphamide (a type of chemotherapy), azathioprine (immunosuppressive), and mycophenolate mofetil (immunosuppressive) have been used as second-line therapies.

Recovery is slow and typically occurs in REVERSE of symptom onset. The most severe symptoms typically resolve first while the cognitive, behavioral, and memory problems take longer to resolve. Most patients will make a full recovery within two years of disease onset



How does sleep affect our body?

By Sheza Amir

Many people nowadays tend to have a sleep deficiency, often because of work or school. However, sleep deficiency is linked to many chronic health problems including heart disease, kidney disease, high blood pressure, diabetes, stroke, obesity and depression. A study examining the associations of sleep duration and sleep disturbances with healthy and chronic disease-free life expectancy between ages 50 and 75 shows that sleeping 7–8.5 hours and having no sleep disturbances between ages 50 to 75 are associated with longer healthy and chronic disease–free LE.

What most people don't know is that a lack of sleep causes numerous negative effects on their cognitive and mental health, to name a few:

- Slower thought process
- Weaker memory
- Inability to focus/concentrate
- Slowed reaction time
- Irritability
- Lessened ability to cope with stress

There's a close relationship between sleep and mental health. Living with a mental health problem can affect how well you sleep, and a lack of sleep can have a negative impact on your mental health. The sleep cycle above demonstrates this.

How does sleep affect our brain?

According to a study conducted at the University of Oslo in Norway, it was found that people with disrupted sleep had a smaller brain volume. The grey matter of the human brain makes up the majority of its weight and volume may shrink over time. Over 147 Norwegian adults were studied and those with worse sleep habits had a decrease in brain volume.

How does sleep affect our body?

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The decrease in brain volume was confined to specific areas of the brain. The parts of the brain which were impacted are responsible for aspects of reasoning, planning, memory, and problem solving.
The average age of the participants in the study was 54 years old and the participants were rescanned around 3.5 years later. Participants who slept poorly saw a decrease in brain size, no matter their age, but those over 60 had the highest losses.

Research from the NIH shows poor sleep quality was associated with reduced volume within the superior frontal cortex and a greater rate of atrophy across the frontal, temporal, and parietal cortices. Each of these lobes is responsible for processing different types of information. This could explain why people who have a lack of sleep have a slower thought process.
However, this question still remains: **Is the volume decrease a result of poor sleep or is poor sleep the result of a volume decrease?**

BEE VENOM & ITS EFFECT ON CANCER CELLS

By Harini Saseetharan

Contains mention of cancer

A study conducted in Australia in 2020 1, found that bee venom had a significant effect on the growth of cancerous tumours. The laboratory experiment was conducted at the Harry Perkins Institute of Medical research in Western Australia by a group of scientists.

The study involved 312 honeybees and bumblebees. The venom was extracted from them, and it was surprisingly found to be effective at destroying specific types of cancer cells and inhibited the growth of the cancerous cells. This included a specific type of breast cancer: hormone receptor positive, HER2-encriched and triple-negative breast cancer.

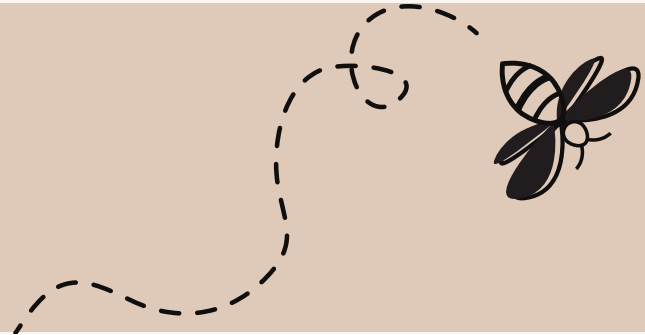
A peptide called melittin present in bee venom was tested on the cancer cells. They also tested a synthetic version of the peptide and found that it mirrored the anti-cancer effects of the honeybee venom.

A meta-analysis of several other studies 2 consisted of bee venom being injected into breast cancer cells in 6 studies, whereas melittin or synthetic melittin was given to breast cancer cells in 7 studies.

Of these studies, 3 studies compared the results of melittin and bee venom. The components of bee venom and bee venom itself is known to cause toxic effects such as apoptosis of cancer cells. The experimental results of the studies confirmed that breast cancer cells were more effectively eliminated in the experimental group than in the control group. One study reported that the effect of melittin was greater than that of bee venom, and another showed that the effect of bee venom was due to melittin.

Melittin

·One of the smallest proteins known to fold spontaneously
·Consists of 26 amino acids, mostly with hydrophobic or uncharged side chains
·Induces the lysis of erythrocyte plasma membranes
·Contains 6 positive charges and no negative charges
·Makes up around 50% of honeybee venom



BEE VENOM & ITS EFFECT ON CANCER CELLS

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Cancer, specifically breast cancer, is one of the most common cancers. It is the 5th leading cause of cancer mortality worldwide in 2020. Whilst the survival rate has increased due to treatments for breast cancer, being 5 years, the quality of life has decreased for people with breast cancer due to the side effects of chemotherapy. Chemotherapy is usually an essential treatment for preventing recurrence by disrupting mitosis or DNA replication. Many patients who undergo chemotherapy suffer from leukemia and edema.

According to these study and others which followed after, bee venom has the potential of preventing and treating breast cancer in the future. As well as this, it has the potential of treating similar cancers of the same type in the future, which has not yet been studied.

References

1 - https://www.biopharma-reporter.com/Article/2020/09/07/Honeybee-venom-kills-aggressive-breast-cancer-cells-study

2 - Of these studies, 3 studies compared the results of melittin and bee venom. The components of bee venom and bee venom itself is known to cause toxic effects such as apoptosis of cancer cells. The experimental results of the studies confirmed that breast cancer cells were more effectively eliminated in the experimental group than in the control group. One study reported that the effect of melittin was greater than that of bee venom, and another showed that the effect of bee venom was due to melittin.

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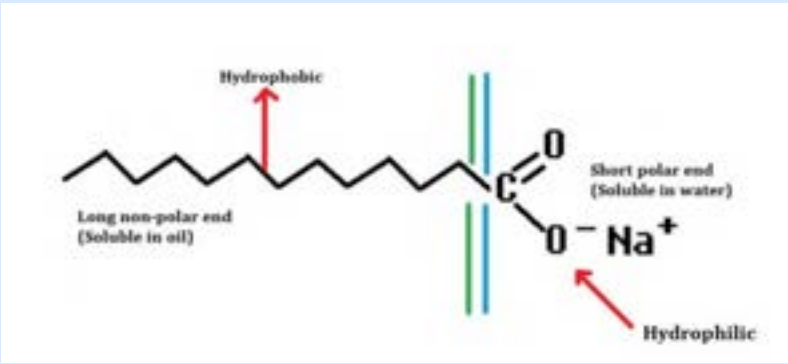
THE SECRET BEHIND SOAP

By Vera

The importance of soap has been understood since at least 2800 BCE, when it was first made using animal fat, water and ashes to clean pottery and other possessions important to the Babylonians [1]. But how is it so effective at cleaning and disinfecting just about anything?

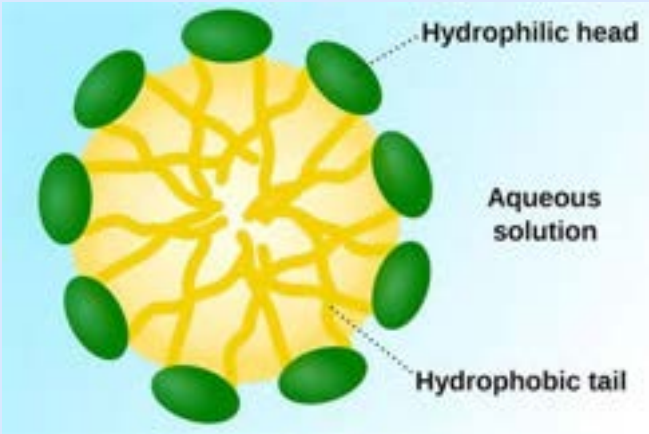
The manufacture of soap [2]

Nowadays, a base such as NaOH or KOH is used instead of ashes and although animal fats are still usually used, they can also be swapped out for plant oils such as cocoa butter. The base is used to catalyse the hydrolysis (splitting apart) of the ester bond between glycerol and the hydrocarbon chain making up the fatty acids. As a result, a negative carboxylate ion (with the functional group COO-) coming from the hydrocarbon chain forms a strong electrostatic attraction with the positive Na+ or K+ ion: this is a carboxylate salt. The resulting compound has a non-polar, hydrophobic hydrocarbon tail, but also a charged, hydrophilic head. Its strange amphipathic property- that's similar to the phospholipids in our cells' membranes- is the key to its special ability.



Mechanism of soaps [3]

Normally, grease or oil is not able to be washed away with water as these non-polar hydrocarbon molecules do not interact with polar water molecules. Oily sebum released by sebaceous glands in your skin also retains dirt or dust that you encounter throughout the course of your day. However, when soap is dissolved in water the hydrophobic fatty acid tails of the carboxylate soap are able to interact with the oil through van der Waals forces. The 'soap molecules' surround the oil and dirt and trap it in structures called micelles. Since the heads of the carboxylate salts are charged and so hydrophilic, they face out of the micelle and interact with water molecules through hydrogen bonding. The micelles are able to remain dissolved in water and be washed off, clearing your hands or your clothes from grease.



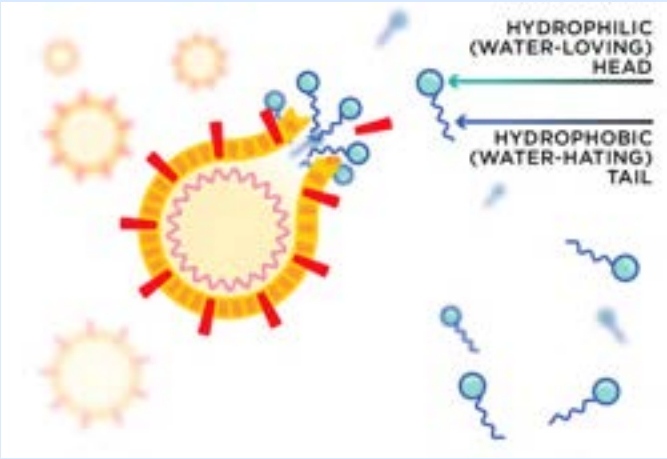
Micelle formed by soap molecules (carboxylate salts). Accessed from https://www.thoughtco.com/how-dos-soap-clean-606146

THE SECRET BEHIND SOAP

By Vera

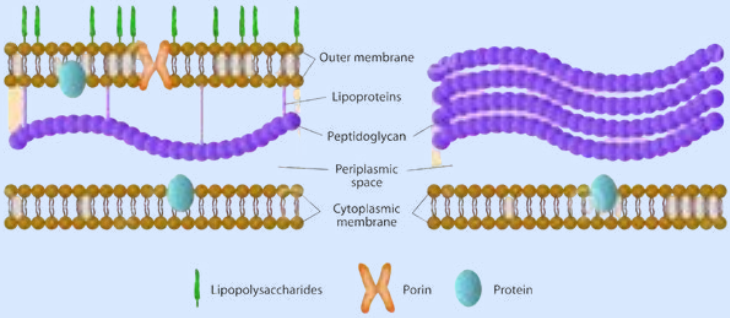
Soap vs germs [4]

So, soap gets rid of grease stains by emulsifying fat droplets inside micelles, but how does it act on viruses and bacteria? Soap has two mechanisms of action against these organisms. The first is piercing their membranes so they release their contents into the soapy water. For example, viruses have a phospholipid bilayer which encases its contents, made up of phospholipids. Phospholipids are similar to carboxylate salts in soap, in that they have a hydrophilic head (a charged phosphate group) and hydrophobic tails (2 fatty acid chains). This similarity is the cause of the virus' downfall: the hydrophobic ends of carboxylate salts are attracted to the hydrophobic tails in the virus' phospholipid bilayer and wedge themselves into it, splitting the membrane. The genetic material needed for the virus to replicate is released into the water, leaving it unable to attack host cells.



Carboxylate salts can disrupt a virus' phospholipid bilayer. Accessed from https://www.science.org.au/curious/people-medicine/hand-sanitiser-or-soap-making-informed-choice-covid-19

However, bacteria are less susceptible to this mode of attack since they contain a peptidoglycan cell wall that soap molecules cannot penetrate. This is especially true for gram-positive bacteria, which have a much thicker peptidoglycan wall compared to gram-negative ones.



Bacteria have different plasma membrane structures. Accessed from https://byjus.com/biology/difference-between-gram-positive-and-gram-negative-bacteria/

Soap is still able to remove these microorganisms via its second mechanism of action that works in the same way as previously mentioned with fat droplets. Hydrophobic ends of carboxylate salts surround the viruses, bacteria or fungi and enclose them in micelles that are then washed away by water. Overall, soap is incredibly effective at protecting us from communicable diseases caused by pathogens, and in fact a 2011 study found that handwashing with water and soap reduced the presence of pathogenic bacteria on the volunteers' hands by 8% [5]. It is worth noting that it takes around 20 seconds for micelles to properly form around bacteria or viruses, hence the recommendation to wash your hands for at

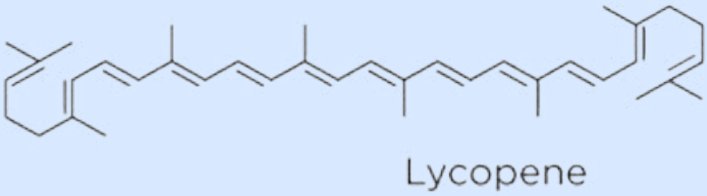
THE SECRET BEHIND SOAP

By Vera

least 20 seconds to fully profit from the protection offered by soap.

Soap vs plastic [6]

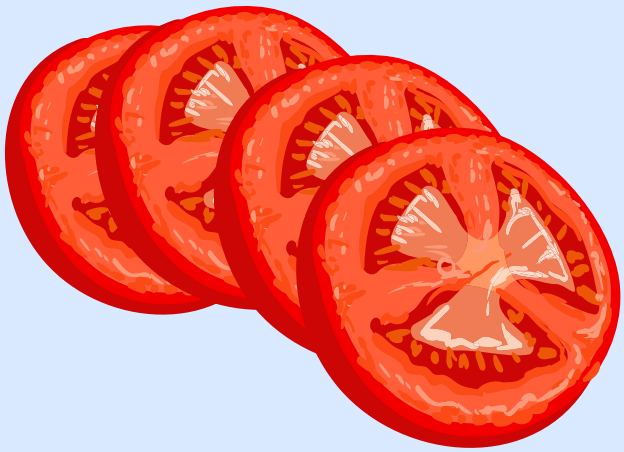
Although soap is usually very effective at de-greasing a variety of different objects, it is less effective at doing this on plastics compared to glass or metal objects. This is because plastics are non-polar polymers which therefore attract non-polar lipid molecules through van der Waals attractions. As a result, there is a sort of 'tug-of-war' between the plastic and the hydrophobic parts of carboxylate salts to try and dissolve the fats, which are attracted to both non-polar substances. This doesn't occur with glass or metallic surfaces as they contain polar silicon oxides and polar metallic ions respectively that don't attract non-polar grease. The staining of plastic containers with tomato sauce happens for a similar reason as the red pigment in tomatoes, lycopene, is also hydrophobic so it buries itself deep into the plastic polymer of a container [7].

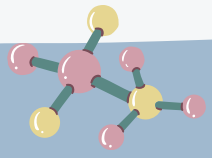


Lycopene

References

[1] http://www.soaphistory.net/soap-history/
[2] https://www.youtube.com/watch?v=wTuRmwSkuzQ
[3] https://www.worldofmolecules.com/3D/how-does-soap-work.html
[4] https://www.qub.ac.uk/coronavirus/analysis-commentary/how-soap-kills-covid-19-virus/
[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3037063/#:~:text=Handwashing%20with%20water%20alone%20reduced,depend%20on%20the%20bacteria%20species
[6] https://davidson.weizmann.ac.il/en/online/askexpert/chemistry/why-does-soap-easily-remove-fats-metalware-and-glassware-not-plastic-tom
[7] https://www.sciencefocus.com/science/why-does-bolognese-sauce-stain-my-plastic-containers

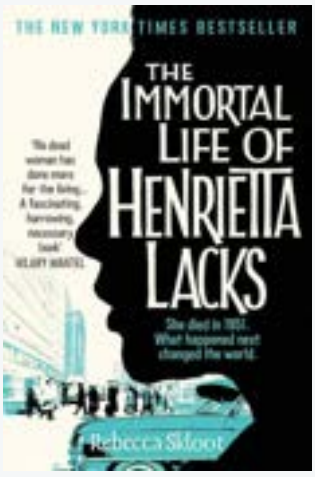




FURTHER READING...

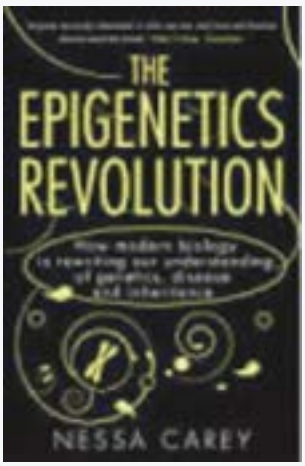
Here are some of our favourite resources for learning more about science and the world around us from reliable sources. Please feel free to share any books, podcasts, websites etc... that you like by reaching out to one of us via Teams or email, so we can include these in the next edition (or in our Weekly Recommendations)!
We hope you enjoy:

Haniah:



This is an insightful and impactful read: an exploration of not only biology but also medicine, ethics, class and race issues that were especially prevalent in 1950s America. Henrietta Lacks was a poor black tobacco farmer, diagnosed in 1951 with cervical cancer and had her tumour cells taken from her – without her knowledge or consent. They then became the world's first immortal cells grown in culture, used in various vital advancements such as developing the polio vaccine; uncovering secrets of cancer, viruses, and the atom bomb's effects. Her cells were bought and sold by the millions, yet Henrietta Lacks remained unknown, buried in an unmarked grave. I highly recommend this novel as it doesn't contain any difficult scientific concepts or processes but instead focuses on Henrietta's emotional story and her HeLa cells.

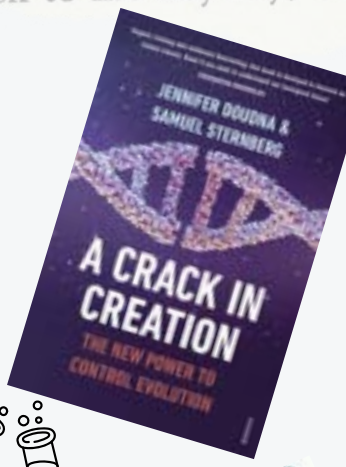
https://www.smithsonianmag.com/science-nature/henrietta-lacks-immortal-cells-6421299/



If you are interested in further details about iPS cells or just in general biochemistry, I highly recommend this book. Epigenetics is the set of modifications to our genetic material that changes the ways genes are switched on or off but which don't alter the genes themselves.These can be caused by your behaviours and environment which affect the way your genes work. They do not alter which protein is made but affect gene expression to turn genes "on" or "off"

Vera:

‘A Crack in Creation’ by Jennifer Doudna and Samuel Sternberg is not only a story about the discovery of CRISPR (the breakthrough discovery that won inventors Doudna and Charpentier a Nobel Prize in 2020) but about scientific research more generally. It captures how these scientists went from studying bacterial immune responses to coming up with the most effective and cheapest way of editing organisms’ genomes , which has allowed biomedical research to become a more accessible and prosperous area of science. Not only does it clearly explain how CRISPR works, but it tackles important ethical questions that go hand-in-hand with genetics research.

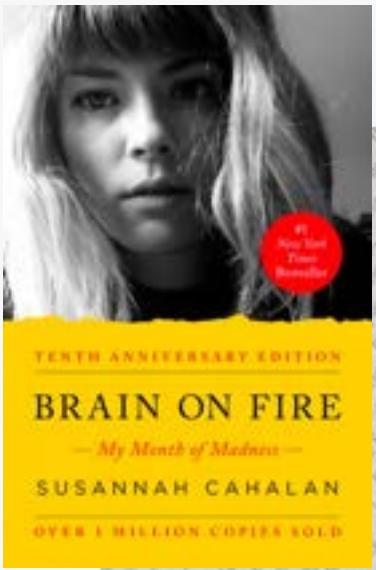


If you’re looking to unwind after a busy day, but also want to learn some microbiology- you’re in luck! ‘Journey to the Microcosmos’ on YouTube explores the lives of microscopic organisms that you otherwise would’ve never known about, all accompanied with relaxing music and beautiful visuals. It almost feels like you’re watching a David Attenborough documentary, but instead of lions attacking zebras it’s *Bursaria* hunting down a yummy *Paramecium*.

To extend your super-curricular knowledge of science, you can visit *https://myheplus.com/* which is a resource made by Cambridge students to encourage secondary school pupils to go beyond the curriculum. There’s a huge variety of subjects and subtopics within them; each contain extra information, questions to test your thinking and answers. Some examples of topics covered are: epigenetics, neuroscience, chirality and chromatography.

Warda:

“Brain on Fire” by Susannah Cahalan is a gripping memoir that details Susanah’s struggles with a rare autoimmune disease of the brain. This book actually inspired me to write my article on her disease. Many of her memories from what she refers to as her ‘month of madness’ have been lost, and we are taken on a captivating journey as Susanah discovers who she was and who she is now. She openly discusses the many challenges she faces even after being diagnosed with this rare condition. This book not only shows you the emotional and social impacts of the disease, but also details the more medical and scientific side. For example, the reconstructive nature of memory is explored, with case studies such as HM and psychologists such as Dr Elizabeth Loftus mentioned (both of which will be familiar to anyone studying A-Level psychology). This book not only details a riveting medical mystery, but also shows the tale of a strong young women bouncing back from a terrible disease. Susanah is now trying to spread more awareness of this condition to try and reduce the number of people ‘slipping through the cracks’ and being misdiagnosed.

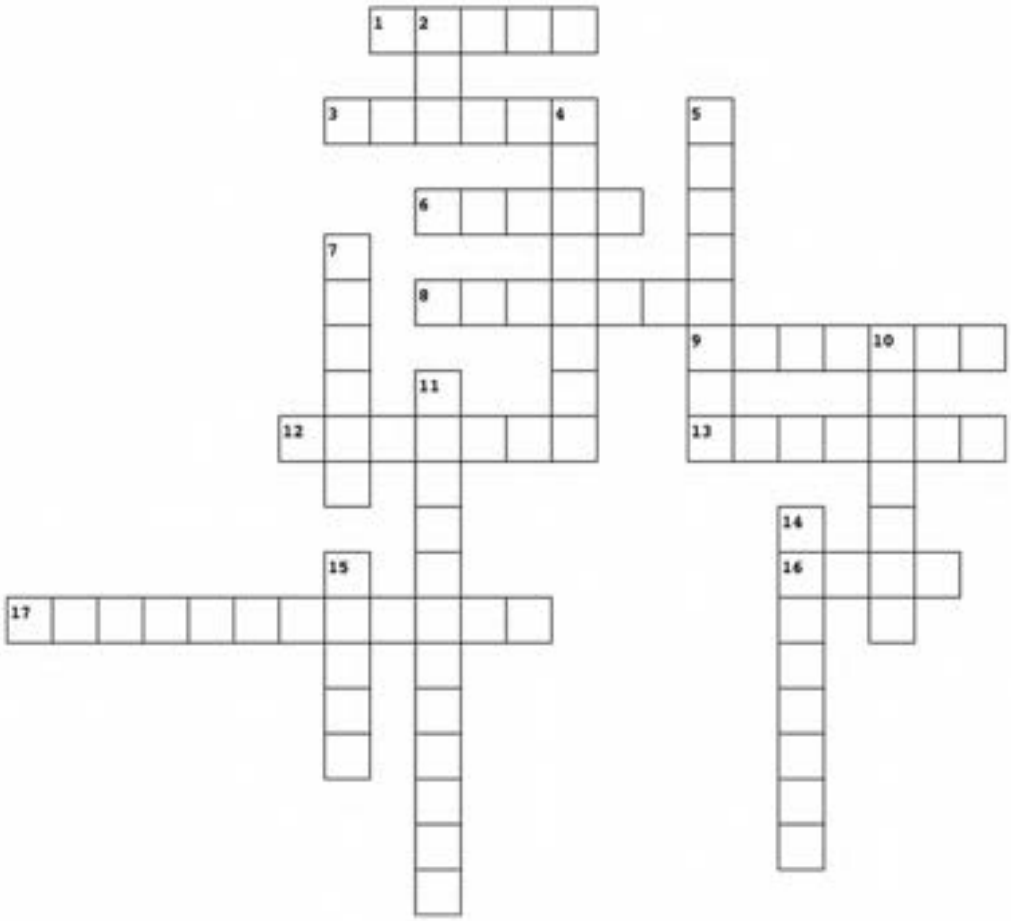


**“Someone once asked, "If you could take it all back, would you?"
At the time I didn't know. Now I do. I wouldn't take that terrible experience back for anything in the world. Too much light has come out of my darkness.”**

If you want to keep yourself up-to-date on the current advancements in the world of science, I would recommend Science Daily. Their articles are short and relatively easy to read, but very informative and thorough, with links for further reading if you are interested. They talk about everything, from genetics to stars to particle chemistry, so there is definitely something for everyone!

Podcasts are always great to listen to as they are easy to enjoy; you can listen to them at home in the comfort of your own bed or when you're travelling on the bus and just need something to do. The 'BBC Earth Podcast' is hosted by zoologists Rutendo Shackleton and Sebastian Echeverri, and each episode features special guests including the world’s most respected scientists and naturalists, stars of film and television and more! The Guardian also has their own bi-weekly science podcast called 'Science Weekly', which is always interesting to listen to.

PUZZLES!



Across

1. organ which produces bile

3. the entire set of genetic material of a cell or organism

6. the vascular tissue in plants which transports water and dissolved minerals

8. the covalent bond formed between two amino acids

9. tiny air sacs in the lungs

12. basic unit of structure in the kidney

13. biological catalysts

16. a chemical species that donates protons

17. a compound of hydrogen and carbon

Down

2. a charged atom

4. negatively charged subatomic particle

5. the enzyme that breaks down proteins

7. a solution that resists changes in pH

10. the movement of water particles from an area of high concentration to an area of low concentration

11. the site of photosynthesis

14. cells without a true nucleus

15. a collection of tissues that work together to perform a particular function

Think you've solved it? Email one of the BioChemSoc Presidents with your completed crossword and we'll let you know how you did!

PUZZLES!

I R A N L I E Y O G H P S I L O C Y B I N O
I A R A P P T N H R A A G R A R N D I I I B
S N C S Y I A D R E N A L I N E O Y O E A A
I N G E L D A T E O D G R O G T S R I S R I
T E O O I S E I O U X R I H G N A I S I O D
I O P X E R S A S O P R B R O E C S N E M B
L L E I I N I O I R Y N O S A T N G O B A T
A R A A T D L C A G S I S Y L O C Y L G T L
H O Y P A O A E T A A T O S Y P I Y S I I A
P I D R I S R T G R O S M I E I S S L C C T
E N I I P A T A I Y N A E T T T B R D H S R
C E S B G U U R Y O H L C N A O N I A I D I
N E I A X L E L C D N E I I I T T C I E G U
E A L D R T N S A S N T S E S L I B E S L M
I G G C L O R O T P E C E R C A R L S U L A
E M O L E P R E A S L T G L E S M E L O U O
A T D C A G R U L T R T L A D I B L B O X I
I E A O A O A M Y E O I A R C R O D N R C O
E O P N I T E A S O S S N T S T L T C N N S
S I O D N S U U T L S T A P A S D T D S E I
T I N C E P O I N A E D I S B I R I T B M R
D N R I C Y R M L L I O A S X D O E I I R O

HALOGEN
PSILOCYBIN
RIBOSOME
ELASTIN
NEUTRALISE
ADRENALINE
GADUSOL
CATALYST
AROMATIC
GLYCOLYSIS
MOLE
ENCEPHALITIS
TOTIPOTENT
RECEPTOR
ANALGESIC
OXIDATION

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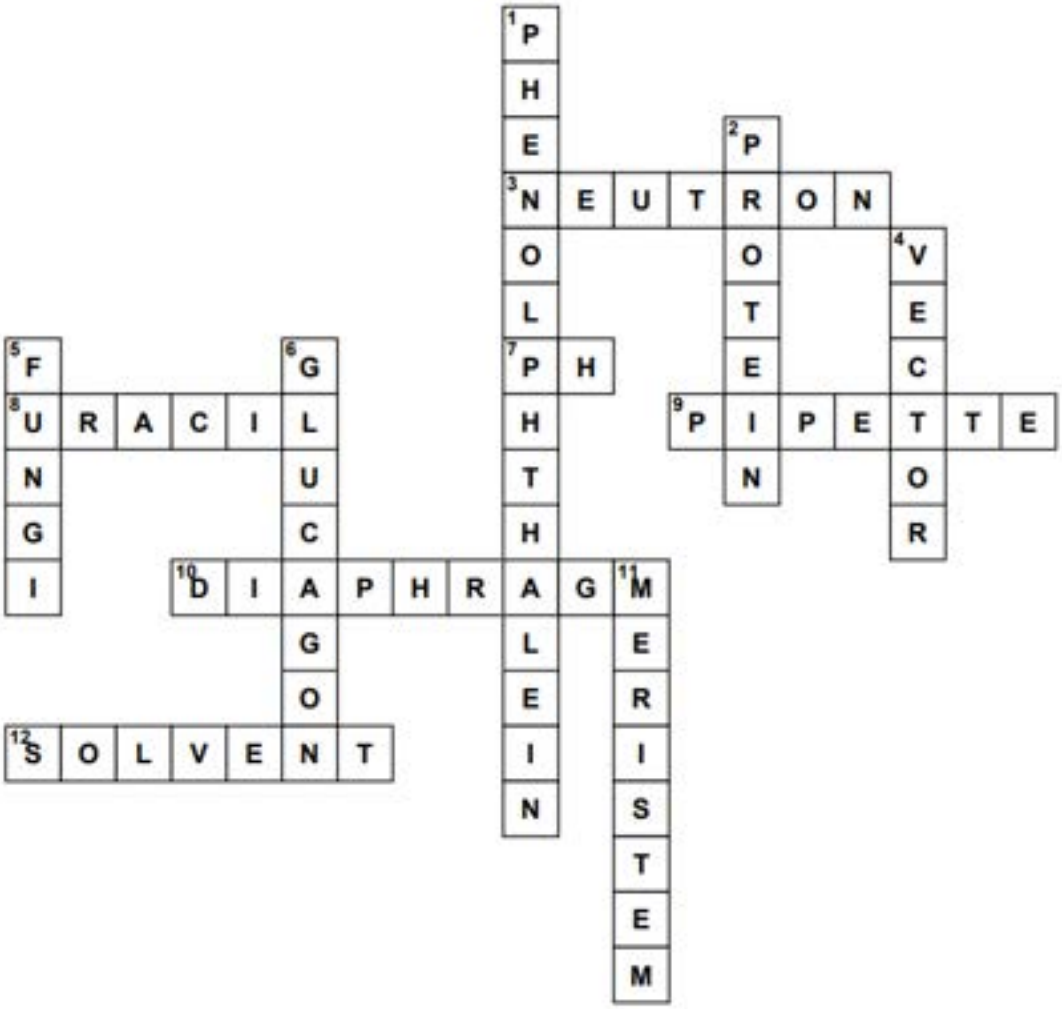
ANSWERS FROM THE LAST EDITION



ANSWERS FROM THE LAST EDITION