The periodic table of medicine

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Abstract In this article we discuss the chemistry, pharmacology and therapeutics of a range of medicines that contain in their formulation a key element from the periodic table. The elements we discuss may be in their ionic or atomic form, or may be integral to the functioning of a much larger drug molecule, but in each case we explore how that element's fundamental chemistry can be exploited to treat a number of life-threatening or quality-of-life-threatening diseases.

If we examine cells at the greatest level of detail, that of individual atoms and molecules, what we find is that life is nothing more than a tightly regulated and highly complex chemical reaction (more accurately, a series of reactions), one in which the chemical machinery of the cell(s) provides the organism with the best opportunity to replicate its DNA and pass its genetic material on to a new generation. All we are is unwitting machines attempting to pass on our genes to the next generation.

Understanding that life really all boils down to chemistry is a key concept in medicine, pharmacology (the study of how drugs work) and pharmacy. Many diseases are caused by a disruption to a chemical process in the cell and can be corrected or manipulated by administering another chemical (a drug), in the form of a medicine, to restore the patient's biochemistry.

Most drugs are small organic compounds that interact with targets such as receptors, ion channels and enzymes. In recent years, however, we have seen an explosion in the development of larger, more complicated biological compounds, such as monoclonal antibodies, that are used to treat previously untreatable diseases. At the other end of the spectrum are elemental atoms and ions, which also have an important therapeutic role. In this special edition of *School Science Review* which celebrates the anniversary of Mendeleev's periodic table, we have picked out several important elements that are used in health care to treat, diagnose or prevent disease (Table 1). We discuss in detail how and why some of these chemicals are used in medicine and pharmacy, and relate this back, where possible, to the basic chemical properties of that element.

Elements used in medicine and pharmacy

Outlined in Table 1 is a list of elements that appear in medicines which are used to treat, prevent or diagnose a wide variety of diseases. Most of these medicines* have been used therapeutically for decades, and, despite their chemical simplicity, some of these agents can be used to save a patient's life in an emergency situation. We have chosen several of these medicines to discuss in more detail below, as they have some very interesting chemistry and pharmacology. For the sake of simplicity, these are addressed alphabetically.

Aluminium

Aluminium warrants a passing nod since it is used in styptic pencils, which are used to treat shaving grazes; its salts can also be used to treat heartburn and diarrhoea. For some time in the 1980s, it was thought that aluminium in cooking pans caused dementia; this theory was later debunked. Aluminium has, however, been implicated in dialysis-associated encephalopathy, whereby patients on dialysis machines developed disproportionately high rates of dementia and died prematurely. The cause of this was identified as the aluminium in the dialysis machine attaching to transferrin, which acted as a Trojan horse allowing the aluminium into the brain.

Barium

Barium meals in the form of barium-sulfate-containing comestibles are given to patients with suspected obstructions in their gastrointestinal tract since barium is opaque to X-rays and does not react with stomach acid.

Bismuth

Bismuth is used in antacids that treat indigestion and, latterly, stomach ulcers, since it acts on the mucous membrane of the stomach, which prevents the stomach from digesting itself. The common names for this

* When even the simplest chemical entity is formulated into a product to treat, diagnose or prevent disease, it is classed as a medicine.

Table 1 Summary of relevant elements and their uses

Element	Indication (what it's used to treat)
Aluminium	• Aluminium salts can be used to treat heartburn and diarrhoea • In a styptic pencil to seal wounds
Barium	• Barium meals to diagnose gastrointestinal obstructions
Bismuth	• Treating stomach acid and stomach ulcers
Boron	• Treating tumours via boron neutron capture therapy
Calcium	• Calcium salts can be taken orally to treat/prevent osteoporosis • Calcium gluconate solution can be used intravenously to prevent abnormal heart rhythms in patients who have elevated blood potassium concentrations • Oral calcium carbonate can be used to bind to phosphate ions in food, preventing their absorption. This can be useful in patients who have severe kidney disease who tend have large amounts of phosphate in their blood because their kidneys are unable to excrete it.
Carbon	• Activated charcoal is used to treat poisoning and drug overdoses • Used in PET imaging
Fluorine	• Radioactive fluorine is used in medical imaging • Fluoride ions are used in dentistry to prevent dental caries
Gadolinium	• Gadolinium is used in the diagnostic technique neutron radiography
Gold	• Gold salts can be used to slow the progression of rheumatoid arthritis (chrysotherapy)
Helium	• Helium allows us to use diagnostic techniques that require very low temperatures, such as magnetic resonance imaging (MRI)
Iodine	• Radioactive iodine can be used to treat thyroid cancer
Iridium	• $^{192}_{77}Ir$ is used in radiation therapy
Iron	• Used to treat anaemia (low levels of haemoglobin in the blood)
Lanthanum	• Used to treat excess phosphate in blood which causes kidney hyperphosphataemia
Lithium	• Used to treat psychiatric conditions such as biopolar disorder
Magnesium	• Used in Milk of Magnesia for constipation and indigestion • A solution of magnesium sulfate is used intravenously to prevent or treat seizures (abnormal electrical activity in the brain) in patients who have high blood pressure associated with pregnancy, and also to aid breathing in patients with severe asthma (inflammation of the airways) • Orally, magnesium salts can be used to treat constipation
Nitrogen	• Liquid nitrogen is used to cryogenically freeze tissue • Nitrous oxide, N_2O, is used as an anaesthetic ('laughing gas')
Oxygen	• Can be administered via a face mask to patients who have severe respiratory problems (such as a chest infection)
Phosphorus	• Bis-phosphonates are used in treating bone-ravaging diseases and also for SPECT imaging with $^{99m}_{43}Tc$
Platinum	• Used to treat cancers such as ovary, breast and testicular
Potassium	• A solution of potassium chloride is used intravenously to prevent abnormal heart rhythms in patients who have a low blood concentration of potassium
Samarium	• $^{153}_{62}Sm$ is used as a radiopharmaceutical
Selenium	• Selenium supplements are used to address low sperm count and depression
Silicon	• Polymers of silicon are used to manufacture silicone breast implants
Sodium	• A solution of 0.9% sodium chloride is used intravenously to restore perfusion of organs in patients who are severely dehydrated or in shock (e.g. septic shock, hypovolaemic shock)
Strontium	• $^{87m}_{38}Sr$ is used in diagnostic research and $^{89}_{38}Sr$ is used as a β-emitting radiopharmaceutical
Technetium	• Used in medical imaging
Titanium	• Replacing or repairing bone
Xenon	• Can be used to anaesthetise patients during surgery

treatment include De-Nol®, which contains bismuth subcitrate potassium or bismuth tripotassium dicitrate, and Pepto Bismol®, the name of which alludes to the bismuth within.

Boron

Boron is used in boron neutron capture therapy in which the patient is given a ${}^{10}_{5}$B-containing compound that is selectively taken up by the brain, after which it is bombarded with neutrons. The ${}^{10}_{5}$B absorbs neutrons to become unstable ${}^{11}_{5}$B that then undergoes decay to lithium while emitting an α particle that kills tumour cells.

$$ {}^{11}_{5}B \rightarrow {}^{4}_{2}\alpha + {}^{7}_{3}Li $$

Calcium

Calcium supplements are used to combat osteoporosis, a progressive condition that affects predominantly post-menopausal women, smokers, patients with chronic kidney disease, and those on long-term corticosteroids.

Carbon

Life on Earth is, of course, carbon based. From time to time it is postulated that silicon-based life could potentially exist since silicon, being directly below carbon in the periodic table, shares some of its properties. Sadly, this is not the case for one very obvious and simple reason, and one less obvious but equally simple reason. Carbon-based life is possible partly because of the ability of carbon to *catenate*, that is, to form effectively limitless chains, rings and multiple bonds and other such molecular scaffolds which then, in turn, confer the ability to form three-dimensional shapes of molecules. No other element catenates to the extent that carbon does. This leads to the ability for carbon-based lifeforms to utilise enzymes, hormones and other biomolecules to act as locks-and-keys and the use of structural molecules to form organs and tissues. Silicon cannot catenate to anything like the extent that carbon can, mainly owing to its size and lesser degree of flexibility. This is one explanation for why carbon-based life is ubiquitous (rather than an explanation for why silicon-based life is not). The reason for the latter is again based on the different properties of carbon and silicon.

Carbon-based life respires (oxidises) glucose (a high-energy molecule) into water and carbon dioxide (low-energy molecules). Water and carbon dioxide are at the end of an oxidation chain, which means that they cannot be further oxidised and are relatively unreactive in this regard, which is why they are ideal fire extinguishants.

$$ C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O $$

Crucially, the end products water and carbon dioxide are gas or liquid/vapour and can be breathed out.

The analogous equation for a silicon equivalent (silane) would be:

$$ SiH_4 + 3O_2 \rightarrow SiO_2 + 2H_2O $$

While water is a common byproduct to both reactions, the silicon dioxide (i.e. sand) can't be breathed out because it's a solid. Breathing solids isn't viable to life since they cannot flow or be moved about efficiently or with anything like the ease that gases or liquids can.

So, life as we know it is based around the element carbon. It is no surprise, therefore, that the vast majority of drug molecules that are used in clinical practice consist of chains or rings of carbon atoms, with various functional groups added here and there.

Space and time do not allow us to give a broad description of the uses of carbon in medicine, so we will confine our discussion to an elegant use that is often overlooked in such a discussion.

Carbon has four important isotopes, three natural and one synthetic (Table 2). There appears to be a pleasing symmetry about the numbers associated with Table 2. The most stable and ubiquitous isotope of carbon is ${}^{12}_{6}$C, which has a numerical elegance about it since the mass number (the total of protons plus neutrons) is 12, which is double the atomic number (the number of protons only) of 6. ${}^{13}_{6}$C seems to be somewhat awkwardly top-heavy, ${}^{14}_{6}$C seems even more top-heavy and ${}^{11}_{6}$C seems to be bottom-heavy. It is the property of the ratio of neutrons to protons that is exploited for carbon to be used in positron emission tomography (PET) imaging.

Table 2 Properties of the isotopes of carbon

Isotope	Mode of decay	Relative abundance	Half-life	Decay equation
${}^{11}_{6}$C	Positron β^+	Synthetic	20 minutes	${}^{11}_{6}C \rightarrow {}^{0}_{+1}\beta + {}^{11}_{5}B$
${}^{12}_{6}$C	Stable	98.9%	Stable	–
${}^{13}_{6}$C	Stable	1.1%	Stable	–
${}^{14}_{6}$C	Beta particle (electron) β^-	1 ppt*	5730 years	${}^{14}_{6}C \rightarrow {}^{0}_{-1}\beta + {}^{14}_{7}N$

* In science and engineering, the parts-per notation is a set of pseudo-units to describe small values of miscellaneous dimensionless quantities, such as mole fraction or mass fraction. Since these fractions are quantity-per-quantity measures, they are pure numbers with no associated units of measurement. Commonly used are ppm (parts per million, e.g. for mg kg^{-1}) and ppb (parts per billion, e.g. for µg kg^{-1}) and ppt (parts per trillion, e.g. ng kg^{-1}).

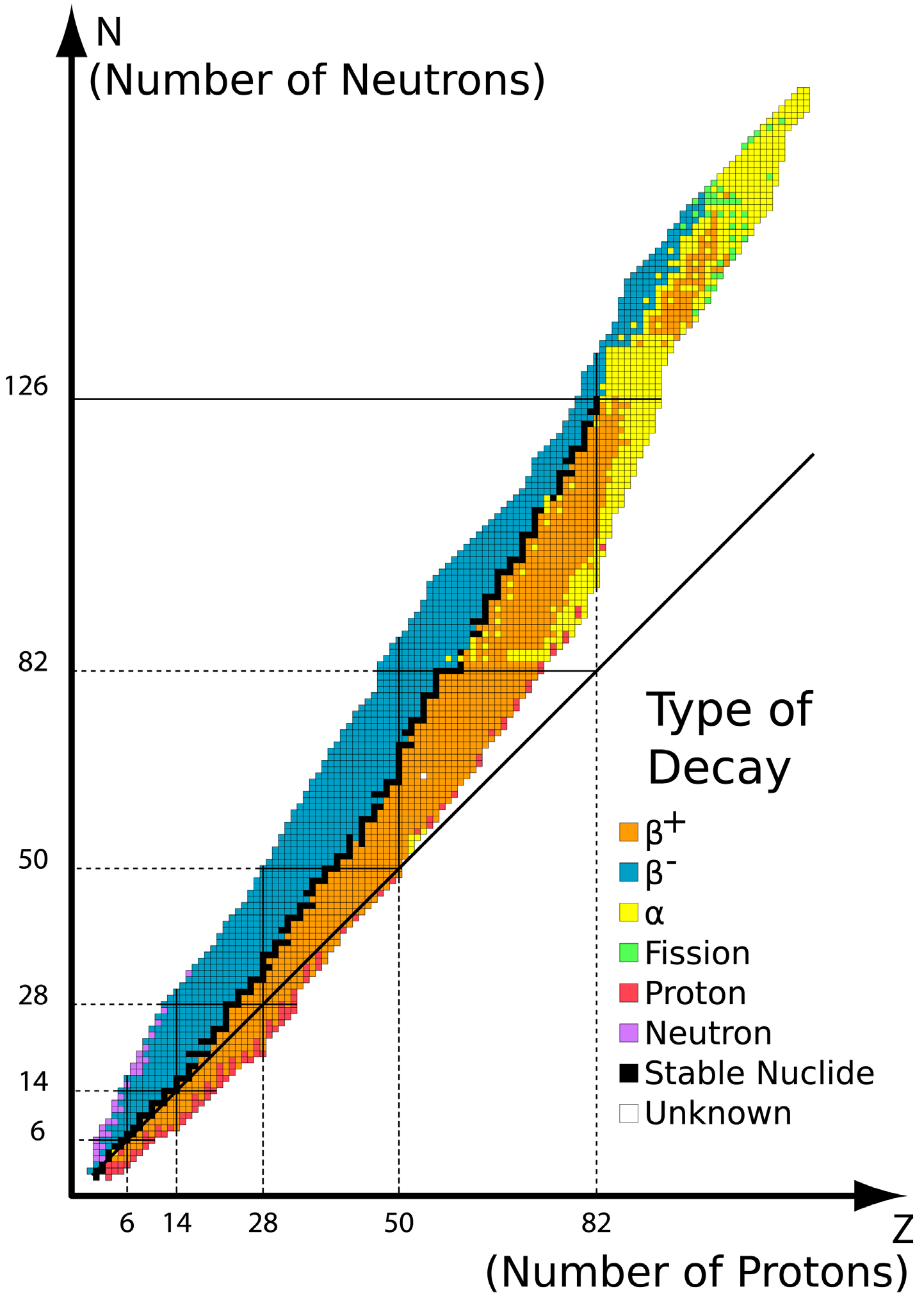

Figure 1 Chart of the nuclides showing the ratio of protons to neutrons, with a black 'Island of Stability' in a 'Sea of Instability'; image by Napy1kenobi (derivative work by Sjlegg), reproduced under a CC BY-SA 3.0 licence (https://commons.wikimedia.org/w/index.php?curid=6703703)

The 'Island of Stability' in the 'Sea of Instability' is shown in Figure 1; the stepped black line shows the theoretical (and actual) nuclides that have the ideal n:p ratio. Above this line the nuclides have too many neutrons (or, if you prefer, too few protons) whereas below the line the nuclides have too few neutrons (or, if you prefer, too many protons) and, in either case, they need to make a nuclear adjustment to counteract this. Such an example is $^{14}_{6}C$, which has 8 neutrons and 6 protons (an n:p ratio of 1.33:1). It therefore lies above the Island of Stability in the blue section of Figure 1. To get the n:p ratio nearer to the ideal 1:1 ratio, a neutron decays into a proton (and a beta particle to balance the charges), leaving the daughter nuclide of $^{14}_{7}N$ with an n:p ratio of 1:1. It is this property that is exploited in carbon dating: all living tissue will have a $^{14}_{6}C/^{12}_{6}C$ ratio that matches that of its surroundings. However, once it dies, the ratio will reduce as the $^{14}_{6}C$ continues to decay (and isn't replaced as it is during life). By calculating how many half-lives have elapsed, the age of the artefact can be calculated.

The overall equation is:

$$^{14}_{6}C \rightarrow {}^{0}_{-1}\beta + {}^{14}_{7}N$$

What actually happens in the nucleus is:

$$^{1}_{0}n \rightarrow {}^{1}_{1}p + {}^{0}_{-1}\beta$$

Figure 1 shows a graph of the ratio of protons to neutrons for all known isotopes. For elements below atomic number 20, the ideal neutron to proton ratio is 1:1; each neutron is able to dilute the repulsive force among the protons and the nuclide is stable. It is therefore no surprise that lower stable nuclides have a 1:1 n:p ratio. Some examples of this stable 1:1 n:p ratio include $^{32}_{16}S$, $^{16}_{8}O$ and $^{4}_{2}He$. Above atomic number 20, more and more neutrons are required to dilute the repulsive force of each proton, which is why the n:p ratio starts increasing. The heaviest stable nuclide is $^{209}_{83}Bi$ with an n:p ratio of 1.52:1. All nuclides above $^{209}_{83}Bi$ are radioactive since above this mass no amount of neutrons can dilute the proton–proton repulsion sufficiently.

$^{11}_{6}C$ finds itself on the opposite side of the Island of Stability compared with $^{14}_{6}C$ inasmuch as it has 5 neutrons and 6 protons and thus an n:p ratio of 0.833:1. It therefore lies below the Island of Stability (in the orange section). It addresses this imbalance within the nucleus by causing a proton to decay into a neutron (the exact opposite process to $^{14}_{6}C$) and a daughter nuclide of $^{11}_{5}B$ that has an n:p ratio of 1.2:1.

The overall equation is:

$$^{11}_{6}C \rightarrow {}^{0}_{+1}\beta + {}^{11}_{5}B$$

What actually happens in the nucleus is:

$$^{1}_{1}p \rightarrow {}^{0}_{+1}\beta + {}^{1}_{0}n$$

The apparent impossibility of a neutron being able to decay into a proton and a proton being able to 'decay' (back) into a neutron may have occurred to you. What makes this possible is the existence of the unshown neutrino or antineutrino particle, which balances the fundamental particle books.

It is the ${}^{0}_{+1}\beta$ particle, a *positron*, which is exploited in PET imaging. A positron is an antimatter electron. Antimatter can exist just as easily as matter; in fact, in the first fractions of a second after the Big Bang, there were almost equal amounts of matter and antimatter. As any *Star Trek* connoisseur will immediately point out, matter and antimatter annihilate each other and in so doing provide energy: the matter Yin meets the antimatter Yang and they are mutually annihilated (not dissimilar to a debit and an equal credit on a bank ledger). Luckily for us, the universe was formed anisotropically (i.e. having a physical property that has a different value when measured in different directions), in that there were approximately a billion and one particles of matter to each billion particles of antimatter, and, once the billion had annihilated the billion, the odd single particle of matter left was all the matter in the universe now.

The mass of any matter/antimatter collision disappears, but, due to the law of conservation of energy, in the case of a ${}^{0}_{+1}\beta/{}^{0}_{-1}\beta$ annihilation, since both particles had been travelling when they collided, the kinetic energy has to be accounted for. This happens in the form of two gamma rays (${}^{0}_{0}\gamma$) with a particular energy signature (512 keV) that are emitted at 180° to the collision.

PET imaging works as an imaging modality by injecting the patient with a PET imaging agent, a ligand carrying a positron emitter, that will be selectively taken up by the tissue or organ of interest. The emitted positrons annihilate surrounding electrons, producing characteristic 512 keV gamma rays which can be detected by a gamma camera that surrounds the patient, and an image of the tissue or organ of choice can be rendered (Figure 2).

$${}^{0}_{+1}\beta + {}^{0}_{-1}\beta \rightarrow {}^{0}_{0}\gamma$$

${}^{11}_{6}$C can be used as a PET imaging agent in the form of a ${}^{11}_{6}$C-labelled biomolecule since it will be taken up by most tissues or organs and has a convenient half-life of 20 minutes. Too short a half-life and the activity has gone before the imaging agent reaches the patient on its way from the cyclotron, too long a half-life and the patient is exposed to gamma radiation for longer than necessary.

The ${}^{11}_{6}$C-labelled compound needs to interact or bind with the target tissue or organ of interest where it annihilates and releases its gamma radiation before it is excreted. Another element used to label carrier molecule agents for selective imaging is the next element, fluorine.

Fluorine

The isotope of fluorine that is of particular use in PET imaging for tumours is fluorine-18, ${}^{18}_{9}$F, which has an n : p ratio of 1 : 1 and therefore, curiously, seems to be an exception to the 1 : 1 n : p rule in that it is radioactive. The half-life of ${}^{18}_{9}$F is 110 minutes, which makes it ideal for patient administration. It is particularly useful for imaging tumours in the form of 18-FDG (18-fluorodeoxyglucose). The challenge when trying to image tumours (and indeed treat them) is that they are simply the body's own cells which don't know when to stop growing. In order to image or treat them, one needs to find some way of differentiating them from normal cells. This is no simple matter, and explains why many cancer therapies are painful and such an ordeal. One of the ways in which cancer cells can be differentiated is their speed of reproduction and consumption of glucose. The former is exploited in chemotherapy, where a cytotoxic agent kills fast-reproducing cells more quickly than it kills cells reproducing at normal speed. The selectivity is not complete, so patients often experience damage to healthy, quickly reproducing cells such as hair. Cancer cells also selectively take up glucose faster than normal cells, which is why 18-FDG is used. The cancer cells

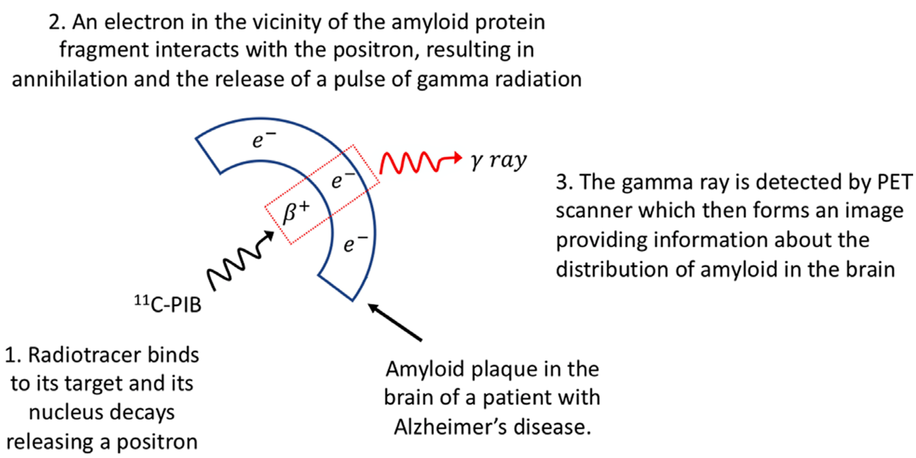

Figure 2 The use of radioactive ligands (radiotracers) in medicine provides images of diseased tissues and organs. In the scenario pictured here, the radiotracer ^{11}C-PIB is injected into a patient where it binds preferentially to amyloid plaques in the human brain. The nucleus of the ^{11}C atom in the compound decays over time to release a positron. This positron annihilates with electrons that are in the vicinity of the amyloid plaque, releasing a pulse of gamma radiation in the process. This pulse is detected in a PET scanner, and an image of the brain with amyloid pathology is reconstructed.

take up more 18-FDG than normal cells and the concentration of the positron-emitting $^{18}_{9}F$ is higher in the cancer cells, which means they show up in greater contrast. Figure 3 shows multimodality imaging, which is the current protocol whereby two modalities are used simultaneously. This is because each modality 'looks' at different things. PET observes function, i.e. things happening, whereas magnetic resonance imaging (MRI) or computed tomography (CT) image structure or anatomy.

As a further example, we are able to see lower rates of glucose metabolism in the brains of a patient with AIDS-induced dementia (Figure 4).

On the other hand, increased glucose metabolism can be seen in parts of the body in cases of cancer. Another radiotracer, ^{11}C-PIB (*N*-methyl-[^{11}C]-2-(4′-methylaminophenyl)-6-hydroxy-benzothiazole), is a thioflavin derivative that binds to extracellular amyloid plaques. Amyloid plaques are proteinaceous deposits that accumulate in patients with Alzheimer's disease, which makes this technique a valuable diagnostic and research tool in patients with this particular disease.

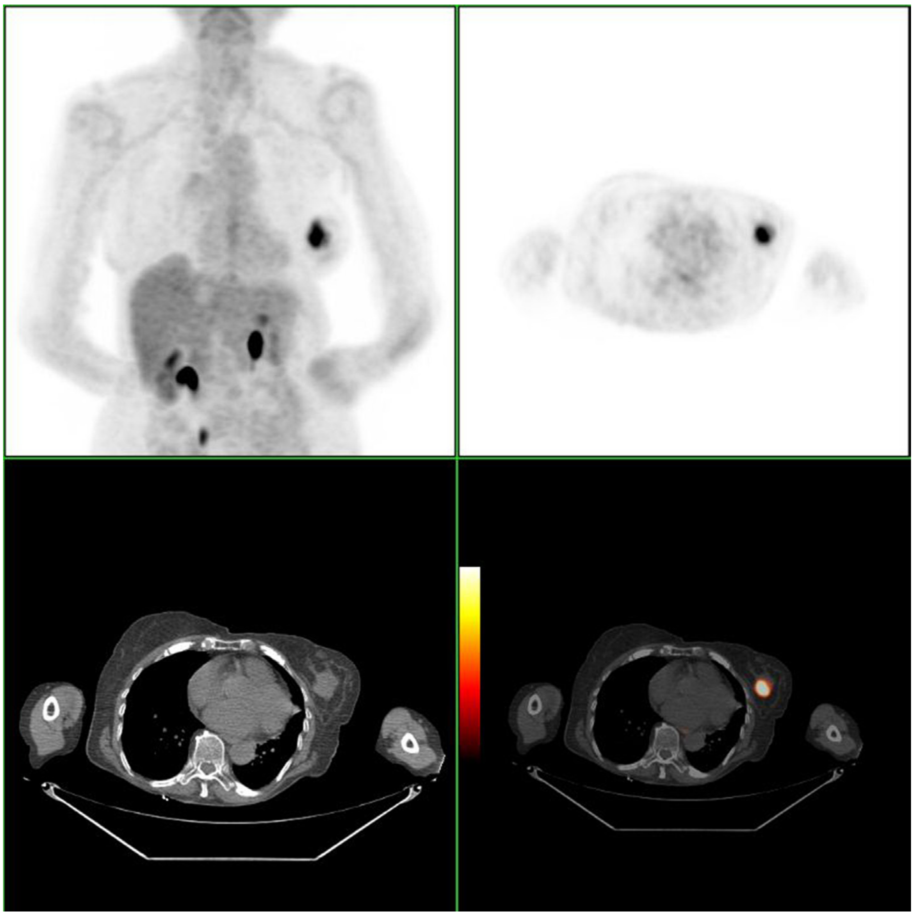

Figure 3 PET/CT study of breast cancer. The top two images are the 18-FDG PET images. In the top left image, which is taken from behind the patient, you can clearly see the dark 'hot spot' that indicates cancer in their right breast. The black spots lower down the patient are the kidneys, which are indicated as the 18-FDG is renally excreted. The top right image is an axial image and the cancer is again clearly visible. The bottom left image is CT, a modality that uses low-energy X-rays. You can clearly see the bed upon which the patient is lying. The bottom right image is a composite of both the PET and the CT images, with the cancer shown clearly. Attribution: Hg6996 [CC BY-SA 3.0].

Fluorine is also used as an additive in toothpaste since it converts tooth enamel (hydroxyapatite, $Ca_5(PO_4)_3(OH)$) into the more acid-resistant fluoroapatite ($Ca_5(PO_4)_3F$).

Gadolinium

Gadolinium is used in neutron radiography, a process whereby a neutron is produced which results in an image that is recorded on photographic film. The normal modality involves a gadolinium conversion screen that converts neutrons into high-energy electrons; these expose X-ray film, producing the image. Gadolinium is also used as a contrast agent in MRI to make images brighter.

Gold

Somewhat surprisingly, gold is used in medicine in chrysotherapy to treat rheumatoid arthritis.

Helium

While not directly used as a medicine, helium allows us to use diagnostic techniques that require very low temperatures such as MRI. This is thanks to its very low boiling point (4.2 K, −269 °C). It is the lowest 'convenient' laboratory temperature attainable.

Iodine

The only human requirement for iodine is in the production of thyroxine by the thyroid gland. This means that iodine is exclusively taken up by this gland. Cancer of the thyroid is treated with radioactive iodine for this reason, and iodine was historically used to treat goitre.

Iridium

$^{192}_{77}Ir$ is used in radiation therapy.

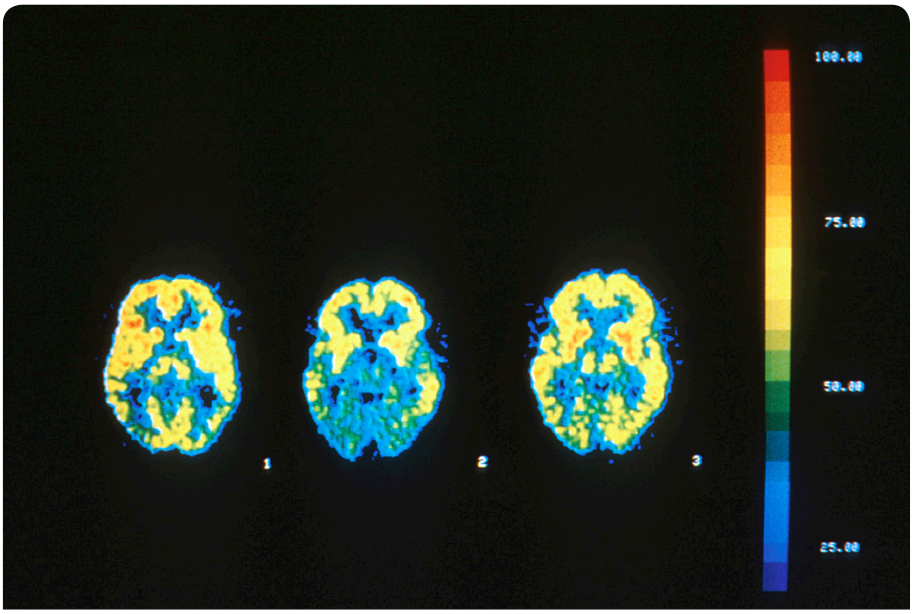

Figure 4 18-FDG PET scans of a patient with AIDS-induced dementia. 18-FDG PET scans at the level of the basal ganglia of a normal control (1), and of a patient with AIDS-induced dementia before treatment with AZT (2) and the same patient after treatment with AZT (3). In (1) there is a normal homogeneous pattern of glucose metabolism across the relevant brain areas. At the onset of treatment with AZT (2), there is an abnormal heterogeneous pattern of glucose metabolism across the relevant brain areas. Thirteen weeks after treatment with AZT, the abnormal pattern has partly resolved (3). All images are scaled from zero to 100% of the maximum activity within the slice (scale shown on right of figure). Image, in the public domain, from the National Cancer Institute, an agency of the National Institutes of Health in the USA.

Iron

Iron, in its Fe^{2+} ferrous form, is an essential element in mammalian physiology. Because of its electronic configuration and size, the Fe^{2+} is able to form complexes with multiple charged chemical species, a process called chelation. Nature has utilised this property by incorporating a ferrous ion into haem. The ferrous ion chelates four nitrogen atoms in the haem structure, ensuring that the ion is held tight at its centre. The haem molecule is then incorporated into several different proteins found throughout the body. In the liver and the gastrointestinal tract, haem is found in a complex with enzymes, cytochrome oxidases, that help to break down toxins through oxidation and reduction reactions. In red blood cells, haem is found in a complex with globin molecules, forming haemoglobin. The haem molecule is able to attach to these proteins through a fifth chelation interaction between the ferrous ion and an amino acid on the globin protein chain. There is still room, however, for the ferrous ion to chelate with one final molecule, molecular oxygen, O_2, which in the case of the cytochrome oxidases allows the oxidation/reduction reactions to take place and in the case of haemoglobin allows the transportation of oxygen around the body (Figure 5).

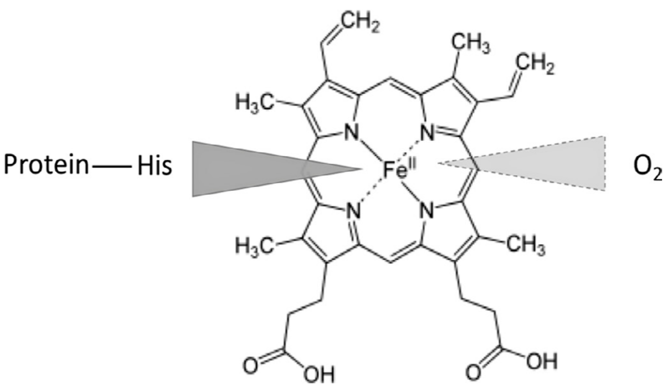

Figure 5 The chelation of Fe^{2+} by haem in haemoglobin. The Fe^{2+} ion sits within the haem molecule and coordinates to four nitrogen atoms. It also coordinates to a nitrogen atom contained within the imidazole ring of a histidine side chain that is part of the globin protein surrounding the haem molecule. The sixth and final coordination site is with molecular oxygen.

The human body typically stores around 4–5 g of iron. A reduction in total body iron, because of poor diet, gastrointestinal infections such as hookworm, or acute blood loss, for example, can lead to a reduction in the haemoglobin content of red blood cells. This condition is called microcytic anaemia (small cells), which if untreated can be life-threatening. Treatment of microcytic anaemia involves identifying the cause of the low haemoglobin concentration, in conjunction with supplementation with ferrous salts, such as ferrous sulfate ($Fe^{2+}SO_4^{2-}$). Iron, in its ferrous form, is well absorbed from the gastrointestinal tract. However, the Fe^{2+} ions can become oxidised to their Fe^{3+} ferric form, which is very poorly absorbed. To prevent this from occurring, patients are advised to take their iron salts with orange juice, which contains an antioxidant, ensuring the iron stays in its more absorbable Fe^{2+} form.

Lanthanum

In chronic kidney disease, normal homeostatic function of the kidney is disrupted. One of these functions is to excrete phosphate, and so blood phosphate levels can be elevated in people with kidney disease. To normalise these, patients are prescribed lanthanum compounds that either chelate or form insoluble ionic complexes with phosphate ions in the gut when taken orally.

Lithium

Lithium is a very soft white alkali metal that can be cut with a blunt knife. In its ionic form, Li^+, it was first used as a medicine in psychiatry in Denmark in the mid-19th century, but it was not until nearly 100 years later (1949) that an Australian doctor, John Cade, used Li^+ salts to treat mania (which is a condition that affects a patient's mood). Coincidently, Australia is one of the major producers of mined lithium.

We are still trying to establish exactly how Li^+ works as a mood stabiliser, but it may work by interfering with the uptake of an important chemical that is released from nerve cells (a neurotransmitter) in the brain (glutamate); too much glutamate can cause mania and too little can cause depression (Dixon and Hokin, 1998). Li^+ is now being used as a treatment in depression and schizoaffective disorder, and in exciting developments, scientists are investigating whether Li^+ has a role in conditions such as Parkinson's disease, Alzheimer's disease and Huntington's chorea (Lazzara and Kim, 2015).

Magnesium

Magnesium is used in Milk of Magnesia for constipation and indigestion.

Nitrogen

Liquid nitrogen is a convenient way of obtaining relatively low temperatures owing to its boiling point of −196 °C. Sperm cells are stored in such a way. Nitrous oxide, N_2O, also known as 'laughing gas', is used as an anaesthetic.

Oxygen

Oxygen is used to supplement normal air: 30% oxygen can be administered via a face mask to patients who have severe respiratory problems (such as a chest infection). Interestingly, excess oxygen can be harmful – premature babies kept in oxygen-rich incubators sometimes became blind until this was realised.

Phosphorus

Bis-phosphonates are used in treating bone-ravaging diseases and also for SPECT imaging (single-photon emission computed tomography) with technetium-99m.

Platinum

Platinum is a rare, precious metal that is most notable for its use in jewellery. It is very unreactive and highly

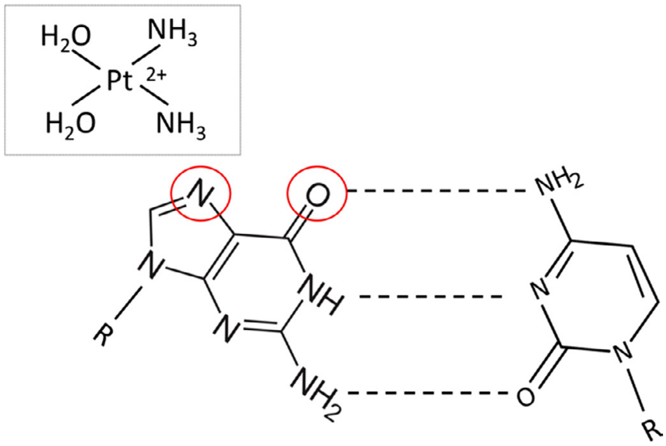

Figure 6 The mechanism and structure of cisplatin, an anticancer drug which, when inside the cancer cell, reacts with water to form the charged platinum compound shown. This compound act as an electrophile and targets electron-rich atoms such as the nitrogen and oxygen atoms on guanine bases in DNA that are ringed in red. This interaction disrupts the hydrogen bonding of the double helix and thus disrupts DNA replication.

resistant to corrosion, which makes it ideal for use as electrodes in engineering. However, in a series of experiments in the 1960s that investigated whether electrical currents can inhibit bacterial growth, it was found that it was not the current but an electrolysis product from the platinum electrode that halted bacterial division (Rosenberg, Vancamp and Krigas, 1965). It was later confirmed that this product was cisplatin, an anticancer drug that is now used to treat many different types of cancer, including ovarian and testicular cancer.

Cancer is disease in which the signals that regulate cell division inside the cell have been disrupted, usually by a mutation in the DNA, resulting in uncontrolled cell growth. Anticancer drugs work in a multitude of ways, but one common mechanism is to interact with a cell's DNA to prevent it from replicating effectively. Cisplatin, whose chemical name is *cis*-diammoniadichloroplatinum, works in such a way. When administered to patients as a treatment for cancer, cisplatin (which is uncharged) undergoes a chemical transformation whereby the two chlorine atoms that are attached to the platinum atom are replaced by two water molecules, resulting in a compound with an overall valency of 2+ (Dasari and Tchounwou, 2014; Patrick, 2005). This positively charged molecule, termed an electrophile, targets negatively charged molecules (nucleophiles) inside the cell. The DNA molecule, which is made up of nucleotide bases, is a good nucleophile. The charged cisplatin molecule reacts with nitrogen atoms in some of the DNA bases and forms chemical bonds between the strands of DNA, preventing transcription and replication (Dasari and Tchounwou, 2014), thereby stopping the cancer cells from dividing (Figure 6).

Potassium

Potassium is found in the human body in its ionic form, K^+. The majority of potassium ions are located inside cells, making the intracellular concentration of this particular ion very high. In comparison, the concentration of K^+ in the blood and in the fluids that bathe cells is relatively low. The reason why there is a difference in the concentration of K^+ inside and outside of cells is because of the activity of a protein in the membrane of all cells called the sodium/potassium ATPase transporter. This transporter uses energy to pump $3 \times K^+$ out of the cell, in exchange for $2 \times Na^+$. This leads to a concentration, and electrical, gradient across the cell membrane, where the membrane voltage (or potential) is more negative on the inside compared with the outside. This electrical and concentration gradient forms the basis of nerve impulses and muscle contractions (action potentials). The role that K^+ plays in this process is key. During a muscle contraction or nerve impulse, the electrical gradient across the membrane of the muscle or nerve cell becomes positive. Immediately following this depolarisation, the cell needs to be rapidly reset to a negative voltage. To do this, these particular cells open specialised protein pores, potassium channels, which are located in the cell membrane. When they are open, these channels allow K^+ ions to flow down their concentration gradient (i.e. from the inside, to the outside of the cell). As they do so, the positive charge that they carry flows out of the cell, and the voltage across the membrane is reset (Figure 7).

Sometimes we find that the concentration of K^+ in a patient's bloodstream is very low, or alternatively very high, and this can lead to problems with muscle contractions and nerve impulses. The reason is that the driving force which allows potassium ions to move out of the cell to reset the membrane voltage is disrupted. The most dangerous consequence of an out-of-range K^+ concentration in the bloodstream is the development of an abnormal heart rhythm. This can be treated by correcting the patient's K^+ blood concentration by either administering K^+, in the form of a KCl infusion into the vein, if the concentration is too low, or administering another drug, such as insulin, to help lower the K^+ concentration if it is too high.

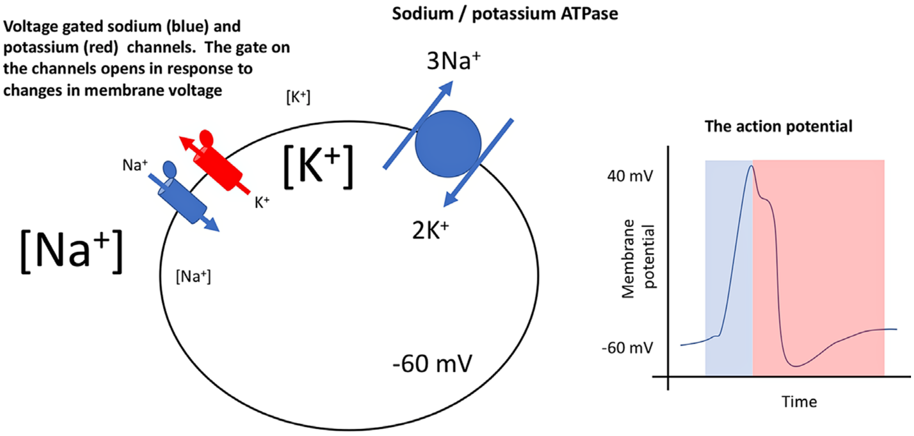

Figure 7 The action potential, which in excitable cells is made possible because of the function of the sodium/potassium ATPase transporter. This pump sets both the electrical and chemical gradient across the cell membrane. In response to a slight change in the membrane potential, voltage-gated sodium channels open (the blue-shaded area), which allows Na^+ to flow down its electrical and chemical gradient into the cell. This influx of positive charge depolarises the cell (makes the membrane potential more positive). These channels close very quickly, while voltage-gated potassium channels begin to open. These allow potassium ions to flow along their concentration and electrical gradient out of the cell (note that the inside of the cell is now positive). This flow of positive charge out of the cell repolarises the membrane (the red-shaded area). Disruption of the concentration gradient of ions by changes to the extracellular concentrations of Na^+, Ca^{2+} and most notably K^+ can result in abnormal electrical activity in the cells.

Samarium

${}^{153}_{62}Sm$ is used as a radiopharmaceutical.

Selenium

Low selenium levels are associated with low sperm counts or faulty/lazy sperm cells since some key enzymes that are important for their function require selenium. Selenium supplements are a way of addressing this matter, but this is a good example of nature giving with one hand and taking with another. An excess of selenium is dealt with by the body by excreting it as dimethyl selenide $(CH_3)_2Se$, which makes doggy-poop smell like Chanel №5 in comparison. So you may end up with sperm that can swim 100 metres in record-breaking time, but your chances of fertilising anyone's eggs with them are non-existent since no one will let you near them (Emsley, 2004). A more successful approach to raising your selenium levels lies in the consumption of Brazil nuts, which are selenium rich, with each nut containing the daily recommended allowance.

Silicon

Polymers of silicon are used to manufacture silicone breast implants.

Sodium

Saline drips are solutions of sodium chloride.

Strontium

${}^{87m}_{38}Sr$ is used in diagnostic research and ${}^{89}_{38}Sr$ is used as a β-emitting radiopharmaceutical. ${}^{90}_{38}Sr$ is found in radioactive fallout and is often the cause of leukaemia since it is a bone-seeker, with the body mistaking it for calcium since it is in the same group. The ${}^{90}_{38}Sr$ is incorporated into the bone where it emits β-particles, which then cause damage and mutations to the nearby bone marrow. This was very prevalent in the years after the Chernobyl disaster.

Technetium

Technetium in the form ${}^{99m}_{43}Tc$ has been described as one of medicine's gifts from God. It is an excellent imaging agent, emitting a signature gamma ray, and is used in SPECT imaging with a carrier such as MDP (methylene diorthophosphonate). It is relatively easily made by bombarding ${}^{98}_{42}Mo$ with neutrons to form ${}^{99}_{42}Mo$. ${}^{99m}_{43}Tc$ has an almost perfect half-life of 6 hours, meaning that 94% of it will have decayed to ${}^{99}_{43}Tc$ within 24 hours.

Titanium

Sam Kean tells the story of how titanium was found to be a perfect material for strengthening or replacing bone in his book *The Disappearing Spoon* (Kean, 2011). The following is a summary of his story. In 1952, Per-Ingvar Brånemark was studying the mechanism of cell production in bone marrow by drilling holes in the femurs of live rabbits. He covered the holes with a window of titanium, which was transparent to strong light. When he was finished with the rabbits, he noticed that the titanium window had become interchelated with the bone. By trial and error, he worked out that titanium 'fools' the body into thinking it is part of the body and the titanium becomes attached to bone cells. It is now used for dental implants, hip replacements and prosthetic digits.

Xenon

Xenon can be used as a general anaesthetic. The curious factor concerning general anaesthetics is the widely disparate structures they have. They include diethyl ether (CH_3CH_2–O–CH_2CH_3), chloroform ($CHCl_3$), nitrous oxide (N_2O) and halothane ($CF_3CHClBr$). Their modes of action aren't completely understood but appear to be connected to the fact that they are all lipophilic and therefore affect the brain, which is of course a very fatty tissue.

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