OCR
Oxford Cambridge and RSA

Tuesday 13 October 2020 – Morning

A Level Chemistry B (Salters)

H433/02 Scientific literacy in chemistry

Time allowed: 2 hours 15 minutes

You must have:
- a clean copy of the Advance Notice Article (inside this document)
- the Data Sheet for Chemistry B

You can use:
- a scientific or graphical calculator
- an HB pencil

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H433/02

Please write clearly in black ink. **Do not write in the barcodes.**

Centre number | | | | | | Candidate number | | | | |

First name(s) _____

Last name _____

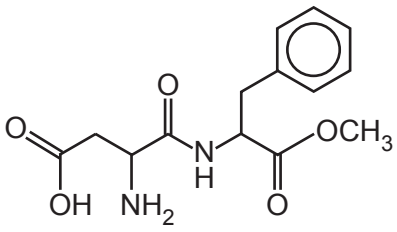
INSTRUCTIONS
- Use black ink. You can use an HB pencil, but only for graphs and diagrams.
- Write your answer to each question in the space provided. If you need extra space use the lined pages at the end of this booklet. The question numbers must be clearly shown.
- Answer **all** the questions.
- Where appropriate, your answer should be supported with working. Marks might be given for using a correct method, even if your answer is wrong.

INFORMATION
- The total mark for this paper is **100**.
- The marks for each question are shown in brackets **[ ]**.
- Quality of extended response will be assessed in questions marked with an asterisk (*).
- This document has **24** pages.

ADVICE
- Read each question carefully before you start your answer.

Answer **all** the questions.

1 Aspartame is a dipeptide that is used as an artificial sweetener. The structure of aspartame is shown in **Fig. 1.1**.

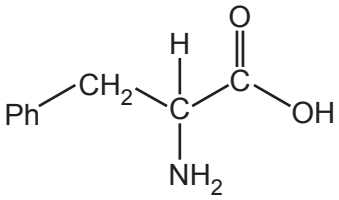


aspartame

Fig. 1.1

(a) Circle a secondary amide group on the structure of aspartame in **Fig. 1.1**. **[1]**

(b) Aspartame is hydrolysed by boiling with acid. One of the products is phenylalanine which is shown in **Fig. 1.2**. 'Ph' represents a benzene ring.



phenylalanine

Fig. 1.2

(i) Phenylalanine has a chiral centre. Draw the three dimensional formulae to show the enantiomers of phenylalanine.

mirror

[2]

(ii) Phenylalanine in solution exists mainly as a zwitterion.
Complete the diagram in **Fig. 1.3** to show the structure of this zwitterion.

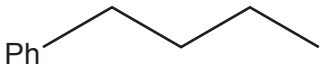


Fig. 1.3

[1]

(iii) A student says that acid hydrolysis of aspartame will only produce phenylalanine and one other amino acid.

Comment on the accuracy of this statement, giving the structures of any compounds you include in your answer.

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..... **[3]**

(c) Aspartame tastes sweet. One theory is that the sweetness is caused by hydrogen bonds forming between sweetener molecules and sweetness receptors in the body.

On the structure of aspartame in **Fig. 1.4** circle **all** the atoms that could hydrogen bond with a receptor.

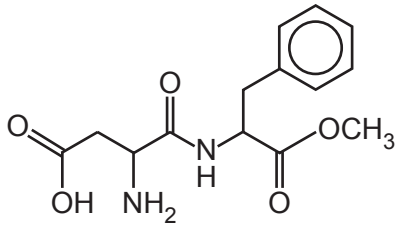

Fig. 1.4

[1]

(d) The enzyme pepsin catalyses the hydrolysis of protein chains. Some students read that pepsin breaks the peptide bonds adjacent to aromatic amino-acids, for example phenylalanine. This is because the active site is specific to benzene rings.

Suggest the type of bonds that form between a benzene ring and the active site.

..... **[1]**

(e) The students mix excess aspartame and pepsin in aqueous solution at room temperature. After 30 minutes they place a spot of the mixture on some chromatography paper.

(i) Describe the rest of their method, including how they could tell whether hydrolysis has occurred.

You may include a diagram in your answer.

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..... **[4]**

(ii) Other students boil the mixture of aspartame and pepsin to attempt to speed up the hydrolysis reaction.

State and explain whether or not this would work.

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..... **[1]**

(iii) Another student says that using a higher concentration of aspartame at room temperature will speed up the hydrolysis reaction.

Comment on this statement.

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..... **[2]**

2 Some students use a method based on an electrochemical cell to measure the concentration of silver ions in solution.

They set up a cell as shown in **Fig. 2.1**.

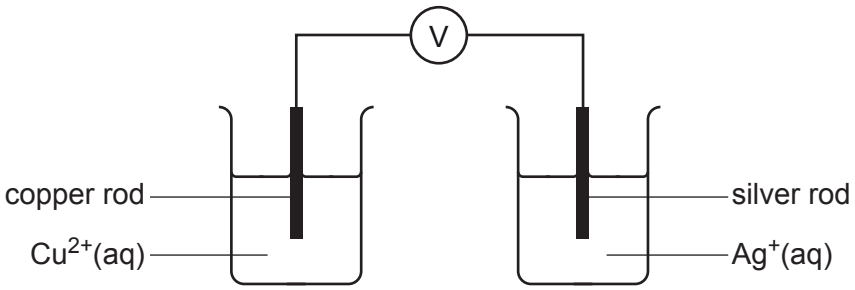

Fig. 2.1

(a) (i) There is something missing from the diagram.

State what it is and describe what it is made of.

.....

..... **[2]**

(ii) State **two** conditions necessary for the cell to measure electrode potentials under **standard** conditions.

1 .....

2 .....

[2]

(b) **Table 2.1** shows the electrode potential data for the cell in **Fig. 2.1**.

Half-equation	$E^{\ominus}$/V
$Cu^{2+}(aq) + 2e^{-} \rightleftharpoons Cu(s)$	+0.34
$Ag^{+}(aq) + e^{-} \rightleftharpoons Ag(s)$	+0.80

Table 2.1

Equation 2.1 shows the reaction that occurs when the standard cell delivers a current.

$2Ag^{+}(aq) + Cu(s) \longrightarrow Cu^{2+}(aq) + 2Ag(s)$ **Equation 2.1**

(i) Identify the oxidising agent in **equation 2.1**.

..... **[1]**

(ii) State and explain which way electrons flow in the wire when the standard cell is delivering a current.

.....

..... **[1]**

(c) Silver bromide, AgBr, is usually described as 'insoluble' but a small amount can dissolve in water.

The students have a saturated solution of AgBr. This contains as much AgBr as will dissolve. They place this saturated solution in the right-hand beaker of the cell in **Fig. 2.1**.

They measure the cell potential against a standard copper electrode. Their result is 0.09 V (with the same electrode polarity as in the standard cell in **(b)**).

The students are told that the relationship between their measured cell potential, E_{cell}, and the concentration of silver ions is given by:

$E_{cell} = E^{\ominus}_{cell} + 0.06 \log[Ag^+]$

Calculate the silver ion concentration in the saturated solution of AgBr.

$[Ag^+]$ = ... mol dm^{-3} **[4]**

(d) Some other students make another cell, using two different half cells as shown in **Table 2.2**.

Half-reaction	$E^{\ominus}$/V
$Cu^{2+}(aq) + 2e^- \rightleftharpoons Cu(s)$	+0.34
$2IO_3^-(aq) + 12\ H^+(aq) + 10e^- \rightleftharpoons I_2(aq) + 6H_2O(l)$	+1.19

Table 2.2

(i) Write an equation for the reaction that occurs when the cell delivers a current.

[2]

(ii) Draw a labelled diagram to show how the IO_3^-/I_2 electrode is made up.
You do **not** need to give concentrations.

[2]

(iii) The students are told that in a standard IO_3^-/I_2 electrode $[IO_3^-]^2 = [I_2]$.

They plan to prepare $40\,cm^3$ of the solution for the electrode by mixing $20\,cm^3$ of $0.08\,mol\,dm^{-3}$ $I_2(aq)$ with $20\,cm^3$ of $IO_3^-(aq)$.

Calculate the concentration of IO_3^- needed so that $[IO_3^-]^2 = [I_2]$.

$[IO_3^-]$ = ... $mol\,dm^{-3}$ **[3]**

3 'Monopotassium phosphate', KH_2PO_4, is added to fertilisers.
KH_2PO_4 acts as a buffer and supplies phosphorus.

(a) The $H_2PO_4^-$ ion has two OH groups.

Draw a 'dot-and-cross' diagram for this ion.

[2]

(b) KH_2PO_4 when used in fertilisers is said to be equivalent to 52% P_2O_5 and 34% K_2O by mass.

Show that the mole ratio of potassium to phosphorus in 52% P_2O_5 and 34% K_2O is the same as in KH_2PO_4.

[2]

(c) In a solution of KH_2PO_4, the equilibrium in **equation 3.1** occurs:

$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$ $\quad K_a = 6.2 \times 10^{-8}\,\text{mol dm}^{-3}$ **Equation 3.1**

(i) Identify the base in this reaction and explain your choice.

.....

..... **[1]**

(ii) Calculate the pK_a for the equilibrium in **equation 3.1**.

pK_a = ... **[1]**

Equation 3.1 is repeated again.

$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$ $\quad K_a = 6.2 \times 10^{-8}\,\text{mol dm}^{-3}$ **Equation 3.1**

(iii) Calculate the pH of a $1.0 \times 10^{-3}\,\text{mol dm}^{-3}$ solution of KH_2PO_4.

pH = ... **[2]**

(d) The acidity of KH_2PO_4 reduces the loss of ammonia from ammonium ions (NH_4^+) in a fertiliser.

Explain how this happens when the fertiliser is in solution.

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..... **[2]**

(e) A mixture of HPO_4^{2-} and $H_2PO_4^-$ ions in solution makes a 'phosphate buffer'.

Calculate the mass of KH_2PO_4 that must be added to $1.0\,\text{dm}^3$ of a $0.10\,\text{mol dm}^{-3}$ solution of HPO_4^{2-} to make a solution with a pH of 6.50.

The volume of the solution does not change when the solid is added.

mass of KH_2PO_4 = ... g **[4]**

Equation 3.1 is repeated again.

$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$ $\quad K_a = 6.2 \times 10^{-8}\,\text{mol dm}^{-3}$ **Equation 3.1**

(f) (i) A student says that a solution of HPO_4^{2-} alone will act as a buffer when acid is added. The student says that this is because the position of equilibrium in **equation 3.1** moves to the left to remove H^+ ions.

Discuss the student's statements.

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..... **[2]**

(ii) A student is doing calculations involving solutions of hydrochloric acid.

The student says that the concentration of hydrogen ions can be taken as the concentration of the acid.

Discuss this statement.

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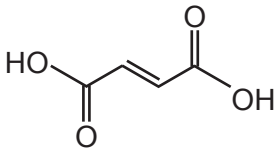
..... **[1]**

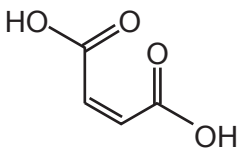
(iii) Calculate the **change** in pH when 1 drop ($0.05\,\text{cm}^3$) of $0.01\,\text{mol dm}^{-3}$ HC*l* is added to $1.0\,\text{dm}^3$ of water at pH 7.0.

pH change = ... **[2]**

4 'Fumaric acid' is used as an acidity regulator in food. 'Maleic acid' is a stereoisomer of fumaric acid. The structure of the two acids are shown in **Fig. 4.1.**



fumaric acid



maleic acid

Fig. 4.1

(a) (i) Describe chemical tests that can be carried out in a laboratory to identify the two functional groups in both acids.

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..... **[2]**

(ii) A solution has 2.32 g dm^{-3} of maleic acid.

Calculate the volume (in cm^3) of 2.0 mol dm^{-3} NaOH(aq) that would completely neutralise 250 cm^3 of the solution.

volume = ... cm^3 **[3]**

(b) (i) Give the **empirical** formula of both acids.

..... **[1]**

(ii) Give the systematic name for **maleic acid**.

..... **[2]**

(c) Explain why maleic acid and fumaric acid are different compounds.

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..... **[2]**

(d) The mass spectra of maleic and fumaric acid both have a peak at 71.
Suggest a reason for this.

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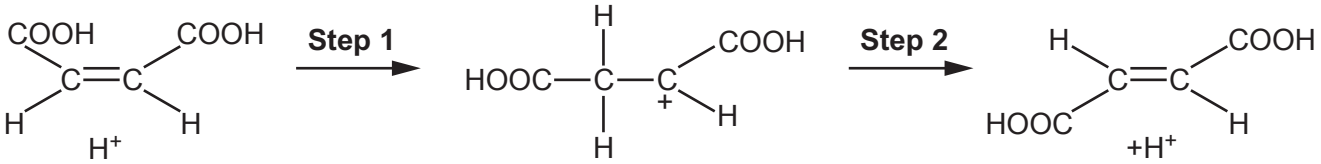
..... **[1]**

(e) Fumaric acid is made from maleic acid by an acid-catalysed isomerisation reaction.

A student suggests the mechanism shown in **Fig. 4.2** for the reaction.

(i) Draw 'curly arrows' on **Fig. 4.2** to complete the mechanism.



maleic acid **fumaric acid**

Fig. 4.2

[2]

(ii) Name the **type** of reaction that is occurring in **step 2**.

..... **[1]**

(iii) The student then reads that if $^{2}H^{+}$ ions are used for the isomerisation, then there isn't any ^{2}H found in the fumaric acid formed.

Does this support the student's mechanism in **Fig. 4.2**?

Explain your answer.

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..... **[2]**

(f) Maleic acid can be made from 'maleic anhydride', $C_4H_2O_3$.

Suggest a skeletal formula for maleic anhydride.

[1]

(g) Maleic anhydride can be made industrially by oxidising butane or benzene.

$C_4H_{10} + 3.5O_2 \longrightarrow C_4H_2O_3 + 4H_2O$ **Reaction 1**

$C_6H_6 + 4.5O_2 \longrightarrow C_4H_2O_3 + 2H_2O + 2CO_2$ **Reaction 2**

(i) Use calculated atom economies to suggest, with a reason, which reaction is used more.

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..... **[2]**

(ii) Suggest another reason why the reaction selected in **(g)(i)** is preferred.

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..... **[1]**

(iii) Calculate the maximum mass of maleic anhydride, $C_4H_2O_3$, (in kg) that could be made from 15 m^3 of butane (measured at RTP).

Give your answer to an **appropriate** number of significant figures.

mass of maleic anhydride = ... kg **[2]**

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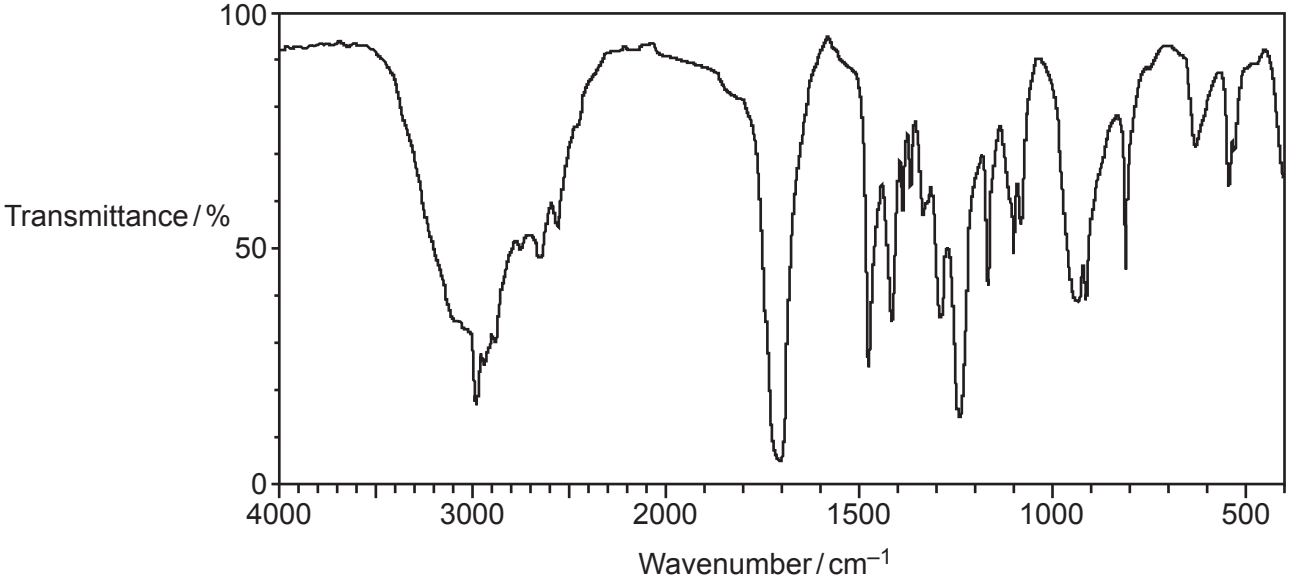
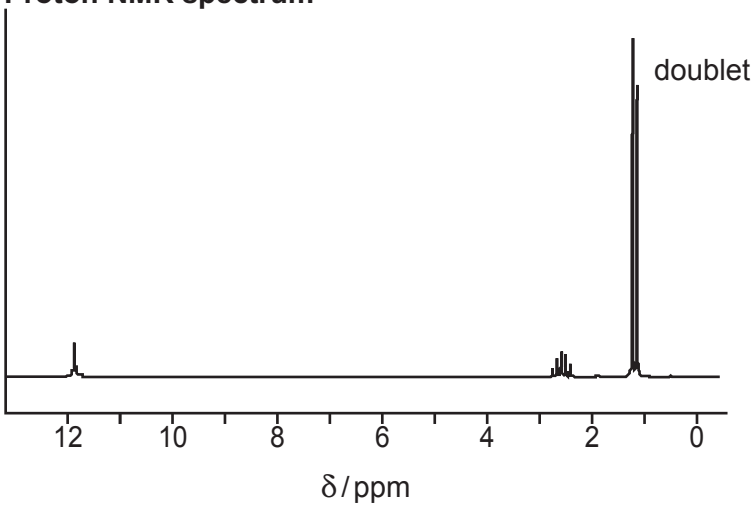
(h)* Compound **A** has spectra as shown below.

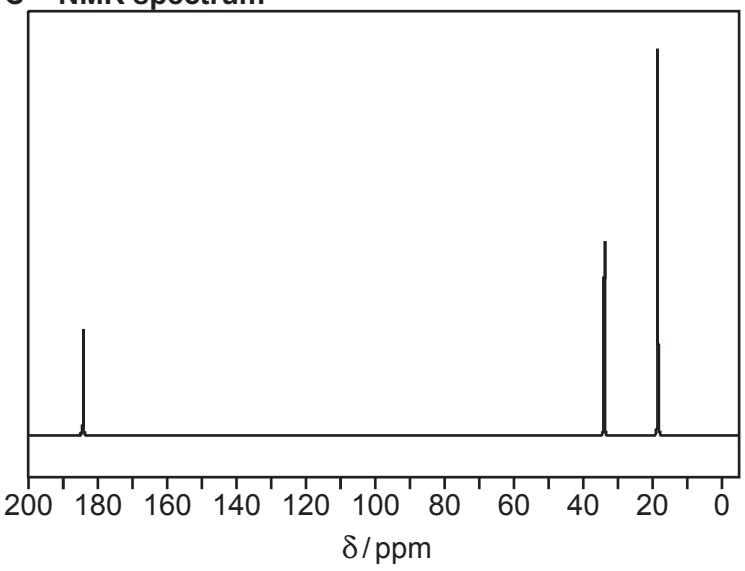
Infrared spectrum



Proton NMR spectrum



C^{13} NMR spectrum



You may do working on this page but it will not be marked

Compound **A** has four carbon atoms in its molecule.

Identify compound **A**, giving evidence from each spectrum. **[6]**

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Additional answer space if required

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5 This question refers to the Advance Notice Article 'Platinum metal complexes in medicine' that is included inside this document.

(a) Cisplatin is a neutral molecule.

(i) Explain why the oxidation state of the platinum in cisplatin is +2.

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..... **[1]**

(ii) Suggest the electronic configuration of the outermost sub-shell in a Pt^{2+} ion.

..... **[1]**

(iii) Is platinum a transition metal?

Give a reason.

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..... **[1]**

(b) Some ligands are described as bidentate.

Give the **full** structural formula of a bidentate ligand from a compound in the article.

[2]

(c) **Fig. 5.1** is a diagram from page 3 of the article. It shows a possible way in which a compound derived from cisplatin is thought to attach to a base in DNA. Two bonds have been labelled **B** and **C**.

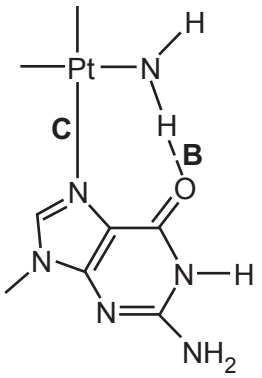

Fig. 5.1

(i) What is the name of the base in **Fig. 5.1**? Use the Data Sheet to help you.

..... **[1]**

(ii) What is the name of the type of bond at **B** in **Fig. 5.1**?

..... **[1]**

(iii) Name the type of bond at **C** in **Fig. 5.1** and describe how it is formed.

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..... **[2]**

(d) Satraplatin was designed to be taken by mouth as it is soluble.

(i) Name the shape of a satraplatin molecule around the Pt atom.

..... **[1]**

(ii) Give the co-ordination number of Pt in satraplatin.

..... **[1]**

(iii) Suggest, in terms of intermolecular bonds, why satraplatin is soluble whereas cisplatin is not.

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..... **[3]**

(e)* Give the **disadvantages** of using cisplatin as an anti-cancer drug and give examples of how newer platinum-based drugs attempt to overcome these disadvantages. **[6]**

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Additional answer space if required

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END OF QUESTION PAPER

ADDITIONAL ANSWER SPACE

If additional space is required, you should use the following lined page(s). The question number(s) must be clearly shown in the margin(s).

Oxford Cambridge and RSA

Tuesday 13 October 2020 – Morning

A Level Chemistry B (Salters)

H433/02 Scientific literacy in chemistry Advanced

Notice Article

Time allowed: 2 hours 15 minutes

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INSTRUCTIONS
- Do **not** send this Advanced Notice Article for marking. Keep it in the centre or recycle it.

INFORMATION
- This is a clean copy of the Advance Notice Article you have already seen.
- This document has **8** pages.

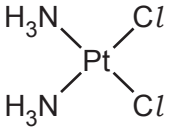
Platinum metal complexes in medicine

Adapted from an article in Chemistry World, 13 MARCH 2018, by Joseph Clarke.

The history of the surprisingly simple metal complex that is still the gold – or should that be platinum? – standard in cancer drugs.

This is the story of cisplatin, from the accidental discovery of its anti-tumour properties in 1965 to the related generations of platinum-based derivatives. It tells how one simple metal complex revolutionised the treatment of cancer in the latter half of the 20th century.

The original: Cisplatin



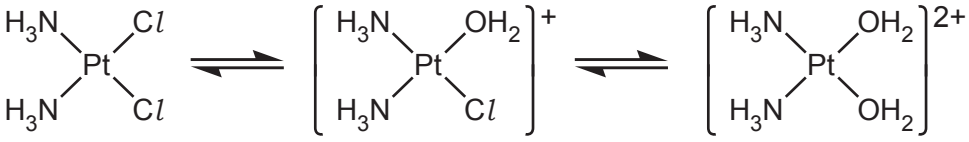
Cisplatin is an example of a metal complex. The name combines its stereoisomeric geometry, *cis*-, and the platinum metal at the heart of the complex, *-platin*. Its formula is cis-$PtCl_2(NH_3)_2$, with the platinum metal centre bonded to four ligands: two ammonia (NH_3) and two chloride (Cl^-) groups. What makes cisplatin special is the platinum metal, which enforces the adoption of a square planar geometry, meaning all four ligands are in the same plane as the metal centre. There are two possible stereoisomers that a $PtCl_2(NH_3)_2$ complex can adopt, cis and trans, which differ according to the geometric arrangement of the four ligands. Later investigations would show that the cis configuration is essential for the anti-tumour activity.

Cisplatin dates back to 1845, when it was originally known as Peyrone's chloride. The discovery of its anti-tumour properties was one of the greatest accidental discoveries in modern science.
In the early 1960s, physicist-turned-biologist Barnett Rosenberg at Michigan State University hypothesised that applied electric or magnetic fields might affect cell division. He tested the effect of an electric field on the growth of Escherichia coli bacteria. Luckily for him – and humanity – he used platinum electrodes. After turning on the field, Rosenberg noticed something odd about the bacteria. They were around 300 times longer than expected. The bacteria elongation was found to be caused, not by the presence of the field, but by the presence of two platinum-based complexes which had prevented bacterial cell division. One of which later became known as cisplatin.

Barnett Rosenberg and his colleagues showed for the first time that platinum-containing drugs disrupted cell division and could possibly be used in the treatment of certain types of cancer. If cisplatin inhibited cell division seen in the bacteria, would it have a similar effect on tumour cells? Rosenberg set about testing his hypothesis. Results published in Nature in 1969 showed that cisplatin caused marked tumour regression in mice. The first steps towards an effective metal-based treatment for cancer had begun.

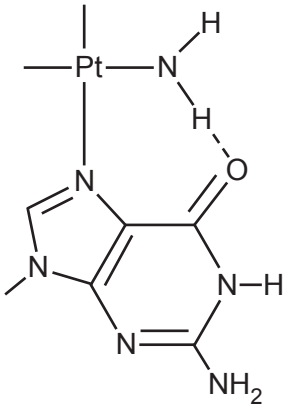
The story of cisplatin continued through the 1970s, with the drug entering clinical trials in 1971 before being made commercially available in 1978. As with any pharmaceutical discovery, shortcomings had to be addressed relating to how the drug was administered, but this was a major advance in a field that saw survival rates of many cancers increase. Typically prescribed for ovarian, lung and stomach cancer, it was actually in the treatment of testicular cancer that survival rates saw the largest improvement, from 10% to upwards of 85%. Cisplatin is still used, both as an anti-cancer treatment, and as the 'gold standard' of cancer drugs against which all newly proposed drugs are measured.
The advent of more powerful research-enabling technologies and the scientific community's increased knowledge of cellular processes have resulted in refined understanding of the mechanisms behind cisplatin's anti-tumour properties. Following an intravenous injection of cisplatin – which is the only way to administer the treatment – cisplatin is transported around the body in its neutral, relatively unreactive form.

For cisplatin to be reactive, it first must be activated. Following entry into a cell, this is achieved through water replacing its chloride ligands.



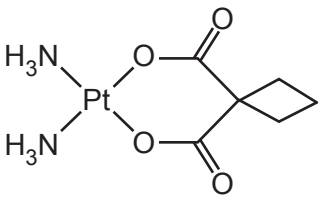
The complex becomes positively charged, which facilitates the interaction with the negatively charged DNA backbone. This leads to covalent binding with specific sites on the DNA base pairs through an exchange of the weakly bound water ligands. There are several possible methods of binding, forming complexes known as cisplatin–DNA adducts that distort the helical structure. It is this irreversible binding to DNA that is thought to disrupt the normally routine DNA repair and cell division cycle, leading to controlled cell death, known as apoptosis.

The diagram shows a possible way in which a compound derived from cisplatin is thought to attach to a base in DNA.

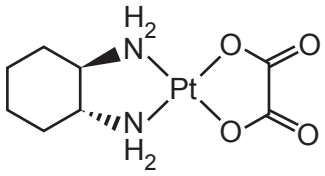


Side-effects and the second-generation platinum drugs.
Cisplatin is not a flawless medication. Early in clinical trials, side-effects became apparent. The most major of these was the toxicity, particularly damaging to the kidneys, gastrointestinal tract and nervous system. The cause is the indiscriminate nature in which cisplatin, and other platinum-based cancer treatments, target all cells, healthy and tumorous. Other problems with the administration of the drug meant that alternative cisplatin derivatives were sought.

The square-planar properties responsible for the directed DNA binding meant platinum metal complexes remained attractive. The task was to find a complex either as active as cisplatin while eliminating the most serious side-effects, or that had increased potency – a drug's effectiveness – allowing for a lower dose administration, effectively reducing the severity of the side-effects.
The second generation of platinum drugs, below, offered improved side-effects over cisplatin.



carboplatin



oxaliplatin

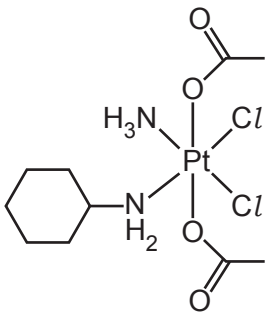
Thus began the renaissance of inorganic chemistry and decades of academic-industrial research in metallic chemistry. Multiple analogues of cisplatin were tested, whereby the ligands were altered and tested. The most successful of these was carboplatin, which gained FDA (Food and Drugs Administration) approval in 1989. Carboplatin offered a dramatic reduction in toxicity, but at a reduced activity.

Oxaliplatin was approved by the FDA in 2004. However, it is an inconvenient part of drug development that most platinum complexes screened end up not being developed.

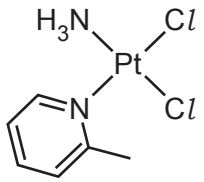
Resistance and the third generation of platinum drugs.
Following the development of carboplatin and its commercial availability, researchers' attention shifted to types of cancer that weren't so responsive to cisplatin. In addition, certain cancers that had previously been treated by cisplatin had developed cisplatin-resistance and the tumours had recurred. The search now began to identify a new platinum complex that could treat such cancers. Thus began the third generation of cisplatin drugs.

There are three major mechanisms by which a cell can be resistant to cisplatin. First, the mode of entry of cisplatin into a cell can be prevented or slowed. Alternatively, the modes of cell exit are accelerated, removing cisplatin before it can interact with a cell's DNA. Finally, the cancer cells themselves can evolve to improve the methods of DNA repair, meaning damage caused by cisplatin is repaired and cell apoptosis is not triggered. Owing to the similar mechanism of DNA binding between cisplatin and the second-generation platinum metal complexes, cell lines resistant to cisplatin were also resistant to drugs such as carboplatin. Thus, a platinum-based complex was sought with a different structure that would be active in cisplatin-resistant cells.

Two such third generation of platinum drugs that showed activity in cisplatin-resistant cells are known as satraplatin and picoplatin.



satraplatin



picoplatin

Satraplatin, with ethanoate ligands, was originally developed as an orally administered drug, more desirable than the intravenous injection necessary for cisplatin and carboplatin. More importantly, during clinical trials satraplatin was found to remain active in cells that had developed cisplatin-resistance. Satraplatin never made it to market, with the FDA putting its approval process on hold in 2007.
Picoplatin was the final platinum metal complex developed. It also showed activity in cisplatin-resistant cancers due to the steric bulk of an alternative nitrogen-based ligand. However, despite promising clinical trials, the drug never became commercially available.

The new renaissance of pharmaceutical research.
Platinum metal complexes were revolutionary innovations for an era when cancer research was in its early days. Cisplatin and its metal complex derivatives are still essential therapies to this day, being offered to patients around the world.

Other therapies will eventually surpass cisplatin as cancer treatment, because of their better targeting capabilities showing reduced side-effects, due to their increased specificity towards cancer cells. Innovative treatments such as antibody drug conjugates that deliver a cytotoxic treatment directly to a targeted cell and light-focused treatments involving bursts of directed lasers are some of the potential next-generation anti-cancer therapies. Shifting away from indiscriminately cytotoxic small-molecule treatments will reduce side effects benefitting the patient and may relegate cisplatin and its analogues to the past. But we should never forget the impact this one simple metal complex has had on modern medicine.

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