UNIVERSITY OF BIRMINGHAM | SCHOOL OF CHEMICAL ENGINEERING

EngBAM

Healthcare Technologies

Teaching Resource

This resource has been designed to support the delivery of Chemistry content to an A Level Chemistry class. This pack contains a presentation, demonstration videos and an experiment that has been developed by the University of Birmingham School of Chemical Engineering with the aim of inspiring more students to pursue a career in STEM subjects. Linking A Level specification points to University undergraduate content, relevant industry examples and current research projects, it is hoped to further engage students with learning by highlighting how this knowledge is being applied in the industry.

This resource has been designed to be run in conjunction with the OCR A Chemistry PAG 6.1. However, the resource can be easily adapted for similar practicals from other exam boards. The accompanying PowerPoint presentation can be delivered in part of in full alongside the practical sessions to provide extra information, context and background to the activities being carried out during the practical session. Lesson Length: -

Key Specification Points:
OCR A Level Chemistry A:

- 1.1.1 Planning
  - (a) experimental design, including to solve problems set in a practical context
  - (b) identification of variables that must be controlled, where appropriate
  - (c) evaluation that an experimental method is appropriate to meet the expected outcomes.
- 1.1.2 Implementing
  - (a) how to use a wide range of practical apparatus and techniques correctly
  - (c) presenting observations and data in an appropriate format
- 1.1.4 Evaluation
  - (a) how to evaluate results and draw conclusions
  - (b) the identification of anomalies in experimental measurements
  - (c) the limitations in experimental procedures
  - (d) precision and accuracy of measurements and data, including margins of error, percentage errors and uncertainties in apparatus
  - (e) refining experimental design by suggestion of improvements to the procedures and apparatus.

- 4.2.3(a) the techniques and procedures for:
  - (i) use of Quickfit apparatus including for distillation and heating under reflux
  - (ii) preparation and purification of an organic liquid including: use of a separating funnel to remove an organic layer from an aqueous layer; drying with an anhydrous salt (e.g. MgSO4, CaCl2); redistillation
- 4.2.3(c) two-stage synthetic routes for preparing organic compounds.
- 6.2.5(a) the techniques and procedures used for the preparation and purification of organic solids involving use of a range of techniques including:
  - (i) organic preparation: use of Quickfit apparatus; distillation and heating under reflux
  - (ii) purification of an organic solid: filtration under reduced pressure; recrystallisation; measurement of melting points
- 6.2.5(c) multi-stage synthetic routes for preparing organic compounds.

Materials required:

From OCR A Specification Practical Endorsement information pack

- Eye protection
- Access to balance accurate to two decimal places
- Measuring cylinder ($10cm^3$)
- Measuring cylinder ($50cm^3$)
- Quick-fit apparatus:
  - Pear shaped flask ($50cm^3$)
  - Liebig condenser and tubing
  - Retort stand, boss and clamp
- Anti-bumping granules
- Water bath, electric heater or sand bath
- Beaker ($100cm^3$)
- Larger beaker to contain ice and water to cool the mixture
- Wash bottle with distilled / deionised water
- Dropping pipette
- Stirring rod
- Apparatus for filtration under reduced pressure
- Watchglass
- Sample tube and lid
- Glass marker pen

Practical Endorsement Experiment

Both the teachers and student learning packs for this experiment can be found under PAG 6 on the OCR exam board website (https://www.ocr.org.uk/qualifications/as-and-a-level/chemistry-a-h032-h432-from-2015/planning-and-teaching/). These packs contain all instruction on how to run the experiment and well as appropriate risk assessment guidance. Within this resource you will find teaching points and additional information that links this practical to the pharmaceutic industry as well as the role of a Chemical Engineer in this sector. The resource can be ran fully in parallel with the practical or can be delivered as an introductory or plenary activity.

Mentimeter

Throughout this resource there will be links to the online voting software mentimeter. This software allows for students to use their smartphones to respond to an onscreen prompt or question. The use of this tool encourages students to engage with the topic.

Slide Notes

- Slide 1 - Title Slide
  Pose the question 'Healthcare is just for Biologists, right?'. Use the linked mentimeter question (https://www.menti.com/1rcm6ewqjg) to gather the students response to this question. Students can also access the poll using the QR code on the title screen. Comment on this result and then move to the second the mentimeter question to ask the class to list all the different specialisms that are often required during the manufacture of pharmaceuticals.

- Slide 2 - Question Response
  Comment on the result of the polls. Then show the list of all the different specialisms which are involved in this area. Note that chemical engineers and chemists are highlighted in bold as this resources will focus on drug development from a chemists and chemical engineers viewpoint. Students may be surprised with the variety of disciplines needed to make medication.

- Slide 3 - Drug Development Process
  Define what a drug is. Highlight how complicated the process of trying to get a drug through clinical trials is. This process can take decades to complete to ensure that the drug is completely safe to be sold to the public. Due to the time and specialisms required to get a drug through clinical trials, the process can end costing around £500 million. Because of the high standards that medication needs to adhere to, the success rate of drugs making it all the way through to market is very low.

- Slide 4 - The Four Stages of Drug Development
  Draw students attention to the diagram on the right of the screen. This shows how many compounds are considered at each stage. This is designed to show the students that there is a very high level of failure during the drug development process. For one component to make it to the market, over 10,000 compounds may have been considered and rejected. Run through the different stages of drug development.

- Slide 5 - Drug Discovery
  Research into new drugs and treatments often start in research groups within universities. The first stage is to test these compounds to see if they have any therapeutic effect (if they actually treat the disease). For a drug to pass this stage it needs to be able to treat the disease in a safe usable manner that will meet all clinical and commercial requirements. Research during this stage will then focus on dosage, side effects, optimal level of delivery and how the medication will interact with other medication. This stage is crucial to find discover how safe the drug is and the best level of delivery to the patient.

- Slide 6 - Preclinical Research
  This stage is focuses on the safety of the drug and whether it is safe for human consumption. To find the toxicity of the drug a series of in vivo and in vitro methods will be used. In vivo methods use test the toxicity levels on animals, encourage a debate within the class on the ethics of testing medication on animals. In vitro techniques use laboratory tests to determine the toxicity of the drug. This is a relatively quick stage compared to other stages of drug development. The dosage and toxicity of the drug should be further explored during this stage, as well as the optimal delivery method.

- Slide 7 - Clinical Development
  This stage will explore how safety of the drug for human consumption. This is a key stage so will be split into a further four sub-stages to allow for more in depth research.

- Slide 8 - Clinical Development Phase 1
  This stage will focus on monitoring closely a small group of volunteers who are healthy or have the disease or condition. This stage lasts several months and is focused on finding the safest dosage. As a lot of the research into the safety of the drug has been completed during stage 2, the majority of drugs pass this phase.

- Slide 9 - Clinical Development Phase 2
  At this stage the study is expanded to several hundred subjects. The time period is also expanded to look at more of the side effects, efficiency and mid to long term impact of the treatment. At this point many of the unacceptable side effects are discovered so only 33% of compounds make it through this stage.

- Slide 10 - Clinical Development Phase 3
  Both the scope and time period of the study is expanded to thousands of subjects of up to 4 years. This phase will look at whether the treatment of the drug has been effective and if there is any long term adverse reactions to the treatment. Around 25-30% of compounds will pass this stage. At this stage the drug is deemed to be safe to be placed on the market.

- Slide 11 - Clinical Development Phase 4
  This is the last stage of the drug development process. After the drug has been approved, post-market safety monitoring will take place to ensure that there are no long term adverse reactions that have not been picked up during earlier trials. This stage will involve several thousands volunteers who have the disease or condition over many years to highlight any adverse reactions to the treatment.

- Slide 12 - Drug Survival Rate
  Emphasise to the class that as few as 1 in 5000 drugs will actually survive the entire development process to make it to the market.

- Slide 13 - How do we make drugs?
  Introduce the idea that medication is made from a complicated organic synthesis process. Introduce the techniques such as distillation, reflux etc. that are used during this synthesis process. Ask the students what challenges could be associated with scaling up the drug development process from test tube scale to industrial manufacture. Introduce the concept of the scale up of chemical processes being non-linear. Therefore, you cannot simply double the size of the test tube to produce double the amount.

- Slide 14 - Aspirin
  Start to introduce the drug the students will be making during the practical. Give an overview of aspirins uses and its synthetic pathway.

- Slide 15 - Synthesis of Aspirin
  At this stage introduce the PAG as well as the practical skills (found on the first page of this document) that the students will develop. Run through the five different stages that will be explored within this process as well as the different techniques required for each of them.

- Slide 16 - Preparation of 2-hydrobenzoic acid
  Complete stage 1 of PAG 6.1.

- Slide 17 - Stage 1 Techniques Reflux
  Cover how reflux works and the science behind this process. Relate the theory to the experimental equipment used within the class room.

- Slide 18 - Stage 1 Techniques in Industry
  Link to how reflux processes are carried out on a large scale in industry. Distillation columns are used in many industrial chemical processes, especially within the Petrochemical sector. The reflux ratio determines how much vapour is condensed and re-added to the column, and therefore the purity of the product.

- Slide 19 - Preparation of aspirin
  Complete stage 2 of PAG 6.2.

- Slide 20 - Stage 2 Techniques Crystallisation
  Crystallisation is the process in which a solid forms in a highly organised structure. Link to examples

of crystals students may be familiar with such as salt and sugar granules. Reinforce the point that the properties of the crystal highly depend on the conditions under which it was formed.

- Slide 21 - Recrystallisation
  Complete stage 3 of PAG 6.1.

- Slide 22 - Stage 3 Techniques Solubility
  Link the practical activity to learning about solubility that the students should already be familiar with. Emphasise the point that solvents will dissolve like solutes. Link back to the solvents that are being used during the practicals.

- Slide 23 - Chromatography
  Complete stage 4 of PAG 6.1.

- Slide 24 - Stage 4 Techniques TLC
  Explain the TLC process. Comment on the success of this analysis depending on the solvents used.

- Slide 25 - Stage 4 Industry Application
  Knowing that the drugs produced are of a high enough purity is crucial for the safety of the medication. Quality control checks need to occur during the manufacture of drugs to ensure sufficient purity. These can take place in the form of in line testing such as IR and mass spectrometery to highlight any foreign compounds that would indicate a low purity. However, this is easier to achieve during a batch process. If there is an issue with the quality of a sample of a batch then the entired batch can be disposed of. However, testing and removing impure tablets on a continuous production line becomes more difficult.

- Slide 26 - Melting point
  Complete stage 5 of PAG 6.1.

- Slide 27 - Stage 5 Techniques Melting Point
  This is another technique that can be used to test the purity of the drug. Note at what temperature the sample drug melts at and compare the difference to the known melting point in literature. The bigger the difference in melting temperature, the greater the impurity of the drug. Emphasise to students that drugs need to be as pure as possible, ask students what the consequences of impure medication may be.

- Slide 28 - Stage 5 Techniques Industry Application
  Note that in industry there are a series of purity tests that a drug will need to pass. These can include UV spectroscopy, sterility testing etc.

- Slide 29 - Tablet Making
  The students should now have completed the five stages of the synthesis of aspirin. They will have produced a small amount of impure aspirin. However, note that the students will be used to seeing medication tablet form and not in powder form.

- Slide 30 - Chemical Engineers Part
  Note that up to this point we have been focused on how a chemist would produce a small amount of the active ingredient. Now we will be looking at how a chemical engineer would take this powder to produce tablets.

- Slide 31 - Tablet Making
  The active ingredient (or in this case the powdered aspirin), only makes up a small micro-grams of the actual tablet. Ask the students what they think will make up the rest of the tablet.

- Slide 32 - Recipe to make a tablet
  Run through each of the parts that are required to make a tablet, and why they are required. Emphasise that all of these extra compounds also need to be safe to consume as well as non-toxic.

- Slide 33 - Tablet making process
  Run through the 7 stages of the tablet making process:

  1. Granulation machine:
     This ensures that all of the compounds are a uniform size.
  2. Mixing machine:
     Ensures a uniform distribution of powder.
  3. Drying machine:
     Removes any moisture from the mixture.
  4. Tablet press:
     Pushes the powder under pressure into a mould to produce a tablet.
  5. Encapsulating machine:
     This covers the tablet in a glucose coating to improve the taste as well as preserving the shape of the tablet.
  6. Punches:
     To remove the tablets from the presses.
  7. Packaging machines:
     These will fill boxes full of the tablets.

- Slide 34 - What properties should a tablet have? Use the last slide on the metimeter presentation previously linked to ask the students their opinions in a virtual mind map.

- Slide 35 - Desirable Properties for a tablet
  If the medication is not easy or pleasant to take, people simply won't take the medication they need. Therefore, producing an easy to swallow, small, pleasant tasting pill that will provide effective therapeutic treatment is essential for the success of the treatment as well as patient compliance with the medication.

- Slide 36 - Tablet making demonstration
  This short video looks at how a tablet may actually be made on a small scale.

- Slide 37 - Future of tablet technology
  This slide looks at how personalised medication could be the future of healthcare technologies. Highlight to students that each person will react to medication differently. This is often due to the function of the liver enzymes. Therefore, testing liver enzymes can help us to determine how the body will metabolise a drug, and therefore the drug dosage can be adjusted accordingly. Another option with personalised medication is 3D printing tablets. This allows for specific doses of multiple drugs to be contained within one tablet. This is very useful for very young or old patients as well as for those with complex health conditions. Again this can provide optimal dosage as well as reducing the number of tablets a patient may need to take.

- Slide 38 - Downsides to personalised medicine
  Ask the class what some potential downsides to personalised medicine are? Possible arguments include the cost to produce each tablet, the time taken to produce personalised tablets as well as the requirement for more expert staff and clinicians.

- Slide 39 - Chemical Engineers shaping the future of our health
  This slide looks at some of the projects currently being researched at the University of Birmingham. Reducing tissue scarring uses specifics molecules to regenerate cell behaviour to limit scarring. A gel can be added to the cornea and cured with UV light to help fight peripheral ulcerative keratitis instead of using superglue. Blood tests can be used to detect the presence of prostate cancer. Drug development to stop excessive tissue regeneration after limb amputation. Adding antibiotics to hip replacements using 3D printers to limit the chance of infection.

- Slide 40 - Development in drug trials
  This slide explores how growing cells on chips to replicate body parts can remove the need for animal testing during drug trials. The drug can then be added to this chip to see the effect on the body, eventually the aim is to link together chips to see the effect a drug would have on the entire body.

- Slide 41 - Metal 3D printing
  Research is being completed on 3D printing hip replacements. 3D printing metals is a more difficult process. However, it allows for antibiotics or bone stimulating drugs to be added into the hip replacement. This would limit the chance for infection and thus increase the chances of the operation being a success.

- Slide 42 - Questions
  Ask if the class has any questions on the session. Challenge the class to all tell you something new they learnt or quiz the class to consolidate their knowledge.

- Slide 43 - EngBAM
  This slide shows the QR code to the EngBAM website. Direct students to the student resource section of the website to find more helpful resources.