Learn Chemistry

Molecules against Malaria: Design of a Structure Activity Relationship Study of Antimalarial 4-Aminoquinolines

Student Guide

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Context/Problem-Based Learning (C/PBL)

A C/PBL approach aims to increase students' engagement with a subject by designing courses based upon real-life applications of the principles, techniques and experiments that they encounter during their undergraduate careers. These real world contexts are presented in the form of problem scenarios which are ill-defined and have a number of satisfactory solutions. Learners work collaboratively to solve problems and acquire new knowledge and then present the outcomes or product. This approach encourages students to take control of their learning, gain deeper understanding and provides the opportunity to develop valuable transferable skills such as communication, team work and problem solving. Academic staff adopt the role of facilitator or guide during the process.

About This Resource

This resource is designed to introduce you to the activities that make up the early stages of drug discovery and development. It focuses on antimalarial 4-aminoquinolines (4-AQs) and involves an introduction to malaria, its causes, societal impact and the need for new drugs. It then presents an overview of 4-AQs, their mode of action, structure activity relationships (SARs) and pharmacokinetics. The resource differs from a traditional lecture course by employing Context/Problem-Based Learning (C/PBL) as a teaching methodology. The context of the resource asks you to adopt the role of a medicinal chemist working for the GHO (Global Health Organisation) in the Tropical Diseases Research Centre. You are asked to prepare a research proposal of not more than 2000 words to seek funding for a SAR study which aims to find new and much needed antimalarial 4-AQs.

You will work in groups of 3-5 and your tutor will guide you through a number of Workshops that will allow you to perform the overall task in a stepwise manner over a number of weeks. Descriptions of each Workshop and clear guidelines are provided in this document which you should read carefully. By the final Workshop, you and your group will be ready to submit your research proposal and you will present your findings to the class.

How is the Resource Delivered?

The resource is designed to be delivered as a continuously assessed module. Together with the Hybrid Workshops, independent study and writing-up time, it is intended that this resource requires a total of 50 learning hours (24 contact hours plus 26 hours of self study).[#] As such, it represents approximately 2.5 European Transfer Credit System (ECTS) or 5 UK credits of work or 1.5 US credits. A schedule for delivery of the Antimalarial Workshops is outlined in Table 1.

[#]This time includes 10 hours of contact time used for Hybrid Workshops which aim to introduce some of the underlying concepts and fundamental principles of medicinal chemistry. However, if you have already had some instruction in medicinal chemistry or pharmacology, these may not be needed and your tutor will inform you accordingly. The learning outcomes of the hybrid workshops are given in Appendix 8 as the authors have identified these outcomes as the prior knowledge that you will need to tackle the Antimalarial Workshops with confidence.

Table 1: Content and Schedule of Delivery for the Antimalarial Workshops

Workshop #, content and work to do between Workshops	Activities
Workshop 1:	**Module induction** Your tutor will present an introduction outlining the context and associated problem, group work, learning outcomes and assessment of the module. You will be divided into groups.
• Introduction to the Workshops and context.	**Introduction** You will be given time to read and discuss the Chemistry World article that reviews aspects of the context (Malaria No More, V.Gill, Chemistry World, April 2008, 50-55). You can use this article and your own research to answer the following questions: • What is malaria? • What is the impact of malaria in a global context? • The malaria parasite and its lifecycle. • Chloroquine and its mode of action. • Problems with the use of chloroquine and the need for new drugs. • Drug resistance.
• Abstract writing. **Between workshops:** **Have a group meeting (this should happen every week), read the Student Guide and prepare a half-page summary of research performed.**	**Preparing an Abstract** You are required to prepare an abstract based on the article. You will: work in a group (applies to this and all subsequent Workshops) to: • Select the information you think should be included in the scientific abstract. • Feed back and as a class agree on the key points to be included in the abstract and the order in which those points should appear. • Compare and contrast a sample abstract of the article provided to the class version. • Compare and contrast the style used in the popular press to that used in the Chemistry World article. • Suggest the changes to be made to the abstract if it was aimed at a lay audience. Guidelines for preparing abstracts are provided in Appendix 1.

Workshop #, content and work to do between Workshops	Activities
Workshop 2: • Tools to support the project - using a wiki.	You will be shown how to use a wiki and how it can be used to assess your individual contribution to group work. Your wiki will be used to generate your final research proposal and / or presentation. • Set up the wiki according to the proposal guidelines. Include a page for Group Planning and Communication with sub-headings / links to pages for submitted work, project planning & meetings and a bibliography. • Begin generating your wiki by uploading content researched over the previous week. • Use this content to begin preparing the research proposal and continue it on an ongoing basis. Guidelines for using a wiki are given in Appendix 2. In addition, you should read the guidelines given in Appendix 7 which provide information on avoiding plagiarism.
• The relationship between chemical structure and biological activity. **Between workshops:** **Hold a group meeting, continue to populate the wiki.**	In the second part of the Workshop, you will be asked to use the information provided to: • Determine how changes in the structure of compounds affect their activity, and therefore identify a likely / probable pharmacophore of 4-aminoquinolines (4-AQs). • Suggest likely drug target interactions and the mode of action 4-AQs, such as chloroquine. • Determine groups that can be varied in order to investigate the structure-activity relationship (SAR) of 4-AQs with a view to developing more potent analogues. • Critically evaluate the biological data that you have been given.

Workshop #, content and work to do between Workshops	Activities
Workshop 3: Design of a structure activity relationship study. **Between workshops:** **Hold a group meeting, continue to populate the wiki, read about pharmacokinetics.**	You will be asked to use the information provided to design a logical SAR study which will require you to: • Select and / or recognise the desired properties of a lead compound. • Propose molecular modifications of the lead to give target compounds (new 4-AQs). • Give synthetic route(s) to the target compounds from commercially available starting materials (sourced using an online chemical catalogue). • Select a suitable bioassay(s). • Populate your wiki with your findings. Full explanations of decisions based on information provided and that found in your own independent research is required.
Workshop 4: • Pharmacokinetics. • Timelines **Between workshops:** **Hold a group meeting, continue to populate the wiki, submit memo and drug-likeness sheets. Produce / submit Gantt chart.** **Read relevant texts: Parallel synthesis and high throughput screening.**	You will be asked to: • Research relevant information about drug metabolism (objectives and the transformations that may take place). • Predict metabolism of the target compounds and note how this will impact on the design of the SAR study. • Complete the 'drug-likeness sheet' by entering the physiochemical properties of the target compounds and predict their oral availability. • Prepare a memo summarising the above. • Plan the time that it will take to carry out the proposed SAR study and show graphically in the form of a Gantt chart. • Estimate the time involved in taking a lead compound from the bench to clinical use with reference to text books and / or journal articles. A sample Gantt chart is provided in Appendix 3. **Note that a rough draft of your proposal is due in, or shortly after, the next Workshop.** A checklist of the proposal content is given in Appendix 4.

Workshop #, content and work to do between Workshops	Activities
Workshop 5: Parallel synthesis and high throughput screening. **Submit draft proposal and work in progress summary.** **Hold a group meeting, continue to edit the wiki.**	You will be asked to: • Critically assess the impact of parallel synthesis and high throughput screening on your proposed SAR study by identifying the advantages and disadvantages associated with their application. • If appropriate, propose the application of any other tools commonly used by a medicinal chemist. • Produce a memo justifying and / or requesting the use of these or other tools in the proposed SAR study. You should have time to assess your progress to date, identifying sections of the proposal that require work; • Prepare a work in progress summary (less than one page) of tasks complete, tasks to do and persons responsible. • Consult with tutor if there are any issues / problems that need to be addressed / clarified.
Workshop 6: Clinic for formative feedback **Amend proposal according to feedback.** **Work on the final stages of the proposal: check for coherence, structure and formatting.** **Hold a group meeting. Practise the presentation.**	This session is a 'clinic' where you will: • Receive feedback on your draft research proposal and work in progress summary. • Act upon the feedback provided to improve your wiki in advance of the final workshop and submission. • Discuss any queries or problems encountered with the tutor. • Start to prepare your presentation. Guidelines for oral presentations are given in Appendix 5.
Workshop 7: Oral presentation and submission of final report **Submit reflective piece. Submit proposal.**	You will be asked to: • Give a presentation to peers summarising the proposal and answer any questions from the tutor and other students. • You will also receive general oral and / or written feedback from your tutor. • Discuss any final queries or problems encountered with the tutor. • At the end of this workshop you will be given a deadline for the submission of your final proposal (printed from your wiki) and an individual reflective piece. Guidelines for the reflective piece are given in Appendix 6.

Assessment

The assessment components (Table 2) will mean that each group maintains and contributes to a wiki, gives a group presentation and submits a final group report in the form of a research proposal in keeping with the context. An individual reflective piece is also required. Therefore the assessment focuses on:

1. Contribution to the group project (most conveniently monitored using a wiki).
2. The group presentation.
3. The group research proposal.
4. An individual reflective piece.

Assessment components and a guideline for the weighting of the assessment are provided in Table 2.

Table 2: Assessment components and suggested weightings

Activity	Basis of Delivery	% Marks Allocation
Participation during Workshops[#]	Individual	15
Contribution to wiki[#]	Individual	30
Presentation[#]	Group	10
Research proposal (Generated directly from the wiki. Criteria are content, accuracy, structure, clarity, and reasoning.)	Group	35
Reflective piece	Individual	10

[#]*A proportion of these marks may be awarded by peer assessment by other group / class members (e.g. frequency and quality of contributions inside and outside of the classroom, both online and face-to-face). Clear guidelines will be provided by your tutor at the appropriate stage of the module if this is the case.*

A Word about Wikis

A wiki is an excellent tool to facilitate group learning while allowing the tutor to monitor and assess individual contributions. Your tutor will demonstrate how this is done in Workshop 2. It is important that you understand that your final research proposal is generated directly from your wiki (by converting it to PDF or printing). Extensive guidelines concerning the use of wikis are provided in the Appendices to this Guide.

Feedback on an individual and on a group level will be provided throughout the module via your group wiki, during the Workshops and on the tasks/assignments that you are asked to complete. You will also receive feedback on a draft of your research proposal which must be submitted in advance of Workshop 6.

Group Work and Organisation

The resource is designed so that you work together in small groups to complete the tasks associated with each Workshop. Once your group has been assigned, it is recommended you move so that you are sitting close enough to other group members to allow conversation without the need for raised voices, and that you return to the same group at the beginning of each Workshop.

Throughout the module, handouts and further information will be distributed as required for each Workshop. In addition to your group wiki, your tutor may use a Virtual Learning Environment (VLE or equivalent) to support this module and will advise you of this at the start of the module.

Groups will be allocated at the start of Workshop 1 and you may decide to choose a name and design a logo. As a group, you must discuss and decide how to deal with the tasks set during each Workshop, assigning individual responsibility where appropriate. A list of actions should be compiled before you leave each Workshop (i.e. things that must be done before the next Workshop). Name the people responsible for completing each action and arrange a time when the group will have a short meeting to review the group's progress before the next Workshop. You will need to meet regularly outside of the classroom to ensure that you are making good progress.

There are 3 roles that must be assigned to group members each week on a rotating basis: Chair, Reporter and Editor. The Chair will prepare the agenda for meetings, will lead/run the group meeting/discussions, listen with an open mind to all group members, and ensure that everyone in the group has the opportunity to contribute. The Reporter should prepare a summary of the action items arising from discussions and meetings and must post these on the group wiki before the next Workshop. The Editor will review the wiki content to ensure a consistent style, coherency and an overall structure; he / she will also liaise with authors when changes or additions to content are required. You should adopt each role at least once during the Workshops and should remember to nominate these roles at the start of each new Workshop (note than an Editor is not required until Workshop 2).

A good overview on effective group work is presented in Chapter 3 of "Study and Communication Skills for the Chemical Sciences"; Overton, T., Johnson, S., Scott, J.; Oxford University Press (2011).

Learning Outcomes

On completion of this module the learner will be able to do the following, within the context provided:

- To explain the principles of drug action.
- To identify drug targets and drug-target interactions.
- To discuss how the structure of a drug can be altered (by chemical modification of a lead compound or de novo synthesis of analogues) and explain how such changes may affect activity.
- To differentiate between various compounds in terms of the possible effect of functional groups on binding interactions and physiochemical properties.
- To explain the importance of considering drug metabolism and the physicochemical properties of drugs in the early stages of drug design, including the use of Lipinski's rule of 5 and alternatives to predict oral availability.
- To propose synthetic routes (by chemical modification of a lead compound or de novo synthesis of analogues) to a new drug.
- To interpret IC_{50} data in order to determine the effectiveness of a compound in the context of SAR studies and to critically evaluate the use of data reported in the literature.
- To be aware of the need for and types of assays used for the biological evaluation of compounds in the context of SAR studies.
- To describe the stages of drug discovery and development, and be aware of the timelines involved.
- To critically evaluate the use of high throughput screening and parallel synthesis as tools in the development of new drugs.
- To be aware of the issues of drug resistance and the problems it causes.
- To gain an appreciation of the importance of the study of medicinal chemistry and how it impacts on everyday lives.

Transferable Skills Development

C/PBL activities require the application of key skills and you will be required to reflect upon the development of these skills at the end of the project (see Reflective Piece, Workshop 7 and Guidelines in Appendix 6). The transferable skills that will be developed over the course of the Workshops are:

- Problem solving: Learners work in groups to address the brief presented in the context scenario.
- Team work: Learners work in teams to complete the tasks assigned, using a wiki to facilitate collaboration and meeting between Workshops to review progress.
- Information technology skills: learners use a wiki to collaborate and develop their ability to use word-processing, presentation, chemical drawing and database software.
- Professional skills: Learners adopt a professional role and construct a report in the form of a 'research proposal' in keeping with the context. This requires adherence to a strict word limit and incorporation of relevant information only. Learners are also required to adhere to deadlines.
- Independent learning: Learners can justify decisions, assumptions and conclusions made with reference to supporting documents and literature in order to produce a logical and clearly reasoned scientific proposal.
- Communication: Learners will be able to produce an abstract for a scientific and lay audience and grant proposal and be aware of the requirements to use the appropriate language and terminology in each case.
- Information retrieval and literacy: Learners must find and use relevant information in order to complete the research proposal.
- Metacognition: Learners reflect on the process involved in preparing the group proposal, the extent to which the stated learning outcomes were met and to which their transferable skills were developed.

Recommended Texts and Useful Reference Materials:

One or more of the following text books may be helpful:

- An Introduction to Medicinal Chemistry, G. Patrick, 4th edition, Oxford University Press, Oxford, England (2009).

  This text is aimed at undergraduates and graduates with a basic grounding in chemistry. It builds on the history of drug development, but does not assume much background knowledge. Section A covers the basic principles and techniques of medicinal chemistry, while section B focuses on a selection of specific topic areas such as antibacterial agents and opium analgesics.

- Medicinal Chemistry: An Introduction, G. Thomas, 2nd edition, Wiley and Sons, Chichester, England (2007).

  This introduction to medicinal chemistry focuses on the interdisciplinary nature of rational drug discovery, organising the chapters by biochemical and pharmaceutical fields rather than by drug classes. Topics covered include physicochemical considerations regarding drug candidate bioavailability, approaches to identifying lead compounds, quantitative structure−activity relationships in drug design, combinatorial syntheses and high-throughput screening, membrane theory, receptors and messengers, enzymes as targets, and pharmacokinetic modelling/metabolism.

Additional text books that may be useful include:

- In Quest of Tomorrow's Medicines, Drews, J., Springer Verlag, New York (2003).
- The Rise and Fall of Modern Medicine, Le Fanu, J., Carol and Graf Publishing (2001).
- Foye's Principles of Medicinal Chemistry, 6th edition, Lemke, T.L., Williams, D.A., Lippincott, Williams and Wilkins, Philadelphia (2007).
- The Organic Chemistry of Drug Design and Action, 2nd edition, Silverman, R.B., Academic press, San Diego (2004).
- Drug Discovery: Past, Present and Future, Sneader, W., John Wiley and Sons, Chichester (2004).
- The Practice of Medicinal Chemistry, 3rd edition, Wermuth, C.G. Academic Press London (2008).

Online resources:

- Medicines for Malaria Venture website: http://www.mmv.org/

  MMV, is a not-for-profit public-private partnership, established in 1999 with the mission to reduce the burden of malaria in disease-endemic countries by discovering, developing and facilitating delivery of new, effective and affordable antimalarial drugs. The website's "information for scientists" section provides useful background information on the drug development process

- Roll Back Malaria Partnership website: http://www.rbm.who.int/

  The RBM Partnership is the global framework to implement coordinated action against malaria. It was launched in 1998 by WHO, UNICEF, UNDP and the World Bank, in an effort to provide a coordinated global response to the disease. RBM's overall strategy aims to reduce malaria morbidity and mortality by reaching universal coverage and strengthening health systems. The website provides access to a number of publications, photos, audio public service announcements and video clips about malaria, produced by its partners.

- World Health Organisation website: http://www.who.int/topics/malaria/en/

  The WHO malaria topic area provides an overview of the disease, including its symptoms, treatment and impact on society, and access to more detailed resources for research purposes.

- World Health Organisation website, World Malaria Report 2011: http://www.who.int/malaria/world_malaria_report_2011/en/index.html

The *World Malaria Report 2011* summarizes information received from 106 malaria-endemic countries and a range of other sources.

- YouTube video about the AntiMal Consortium: http://youtu.be/RWST6Iq4VcI

  AntiMal (http://www.antimal.eu/) is an integrated project comprising leading groups of malaria researchers with expertise in malaria biology, chemotherapy and drug development. The aim is to exploit new scientific and political opportunities to secure the development of a portfolio of viable novel antimalarial drugs. The video provides an overview of the history of malaria treatment, the lifecycle of the disease and the challenges of research into new treatments.

- Malaria Atlas Project: http://www.map.ox.ac.uk/

  The Malaria Atlas Project aims to disseminate free, accurate and up-to-date information on malaria and associated topics, organised on a geographical basis. This should give students a clear image of the areas most affected by malaria.

- ChemSpider, The free chemical database: http://www.chemspider.com/

  This database provides access to over 26 million structures, properties and associated information.

- DrugBank, Open Data Drug and Drug Target Database: http://www.drugbank.ca/

  The DrugBank is a bioinformatics and cheminformatics resource that combines detailed drug (i.e. chemical, pharmacological and pharmaceutical) data with comprehensive drug target (i.e. sequence, structure, and pathway) information. The database contains 6711 drug entries including 1447 FDA-approved small molecule drugs, 131 FDA-approved biotech (protein/peptide) drugs, 85 nutraceuticals and 5080 experimental drugs.

- New Scientist 'Why we mustn't let malaria defences crumble', 22/06/09, http://www.newscientist.com/article/mg20227136.200-why-we-mustnt-let-malaria-defences-crumble.html (requires subscription to access full content)

  The article discusses issues surrounding the evolving resistance of malaria parasites to drugs and the importance of combinatorial treatment methods to prevent this occurring.

Workshop Content

In the following section, a detailed description of the content of each Workshop and student tasks are provided.

The tutor may wish to edit this section to suit his / her student group.

Workshop 1: Introduction to the Context and Abstract Writing

Duration: All Workshops will take approximately. 2 hours to complete

Part 1: Introduction to the Context and Problem (Approximately. 40 minutes)

This introduction will give an outline of the overall activity, protocols for assessment, module timeline, desired learning outcomes, and will allow group allocation and distribution of Student Guide and handouts.

You will be asked to adopt the role of a member of a medicinal chemistry research team and asked to prepare an application for a funding for a research programme entitled Molecules against Malaria. When introducing the activity, your tutor will distribute a Memo (#1) and a Call for Funding that contains much of the information that you will need to begin your research.

Part 2: Writing an Abstract (Approximately. 1 hour)

In part 2 of this introductory session, the importance of an effective abstract will be examined. This is to ensure that you have a clear understanding of how to compose an abstract in preparation for the research proposal. Guidelines for preparing abstracts are provided in the Appendices of this Guide.

You will be required to read a Chemistry World article which is accessible online (Malaria No More, V. Gill, Chemistry World, April 2008, 50-55, see http://www.rsc.org/images/MALARIA_tcm18-116487.pdf or http://www.rsc.org/chemistryworld/Issues/2008/April/MalariaNoMore.asp). This article expands on many aspects of the context introduced above, discussing malaria in terms of cause, global impact and the efforts to eliminate it, an overview of the life cycle of the parasite, the stage in this life cycle where antimalarial 4-AQs (such as chloroquine) are effective, an overview of the mode of action of chloroquine, and the problem of chloroquine resistance.

In summary, you will use the Chemistry World article provided (Malaria No More, V. Gill, Chemistry World, April 2008, 50-55) to discuss and determine the important information that should be included in an abstract. In groups, you will select the relevant information for inclusion in the abstract from the article which will be presented to and critiqued by the class. Following a class discussion, a sample abstract (provided as a handout) will be critiqued. As a class, you will be asked to discuss amendments to the abstract to suit a lay audience instead of an audience with a science education. Amendments should be justified and discussed.

Tasks to Students to Complete During Workshop 1:

- Start group work: Move to sit close to other group members, select a name and logo (if required). Nominate the Chair and Reporter.
- Read and understand the article on malaria provided. Discuss any new terms with group members and the tutor. The tutor may direct you to an appropriate reference source.
- Highlight or prepare a list of the main points to be included in the abstract.
- As a group, feed back to the class some of the highlighted points. Once all the points have been recorded on the board, decide if any points should be excluded, if any are missing and the order in which they should be presented in an abstract.
- Critique the sample abstract provided, comparing it to the abstract planned by the class. Note its length.
- If time, read the newspaper articles provided and discuss the differences in the style of writing between the articles.
- As a class, consider how the abstract could be modified to suit a lay audience.
- Provide an e-mail address to the tutor so that the wiki for your group can be set up before Workshop 2.

- Arrange a time when the group will have a short meeting to review progress before the next Workshop.

Tasks to Complete Before Workshop 2:

- Review all the material distributed in Workshop 1 including the Student Guide and in particular the assessment criteria and activity schedule provided. Review Memo (#1) and the Call for Funding provided and ensure you understand the overall brief.
- Meet as a group to review progress and assign tasks.
- Carry out research as part of your group on areas relevant to the grant proposal, both by looking at some of the suggested references and conducting your own search using keywords you have selected on a scientific database.
- Individually, you should save a typed summary of the research carried out (approximately half a page) in advance of the next Workshop and have it available to add to the group wiki.

You should note that keywords for your search can be obtained from the article used in this Workshop. Consult your library website for guidelines on carrying out this search or read Section 4 on Information Retrieval in Key Skills for Scientists, Royal Society of Chemistry, 2009 (http://www.rsc.org/images/Updated_Skills_2010_tcm18-193493.pdf) and Chapter 5 of "Study and Communication Skills for the Chemical Sciences"; Overton, T., Johnson, S., Scott, J.; Oxford University Press (2011).

Desired Learning Outcomes from Workshop 1:

On completion of this Workshop you should be able to:

- Understand the context based scenario and be aware of how the module will be assessed.
- Gain an awareness of the global impact of malaria and empathise with populations that live with the threat of this disease.
- Recall the life cycle of the malaria parasite that causes the disease and the relevance of this to developing new antimalarial drugs.
- Identify chloroquine and its proposed mode of action.
- Be aware of the issue of chloroquine resistance and the problems it causes.
- Construct an abstract and assess the relevance of information within articles.
- Gain an awareness of the need for scientists to communicate with a lay audience and discuss how this may be achieved.

Workshop 2: Tools to Support the Project and the Relationship between Chemical Structure and Biological Activity.

Part 1: Introduction to Using a Wiki as a Tool to Support and Assess the Workshops (Approximately. 30-40 mins)

This workshop will explore the uses and versatility of wikis, and sets out protocols for the wiki based project. Guidelines are provided in the Appendices to this Guide on how to use a wiki. All members of your group will have received invitations to your wiki by e-mail. Uploading files and editing page details can be practiced at this stage.

Most wikis allow conversion of the document to PDF form. In this manner, your wikis can form the final proposal and you may not be required to produce another, separate document. It is important that during, or very soon after, this Workshop your group set up the wiki appropriately, correctly identifying the page headings in line with the required content of the final proposal. You can begin to populate it over the next few Workshops.

Part 2: The Relationship between Structure and Activity (Approximately. 1 hour)

You will be provided with a section of a report (Part A: 4-AQ and Related Antimalarials) summarising some of the important information that can be found in the literature regarding antimalarial 4-AQs. The report will include the structures of 4-AQs that are currently in clinical use or that have reached clinical trials and also of analogues investigated during previous SAR (structure activity relationship) studies. From the information provided you will be required to:

- Identify a possible/likely pharmacophore.
- Suggest likely drug target and binding interactions.
- Give a detailed description of the mode of action of 4-aminoquinolines.
- Suggest how 4-aminoquinolines could be chemically modified in a SAR study while still retaining the pharmacophore.
- Discuss the nature and reliability of the biological data provided.

Tasks to Complete During Workshop 2:

- Select the Chair, Recorder and Editor.
- Use the proposal guidelines provided in Workshop 1 to identify headings for the pages of the wiki and set it up accordingly. When adding pages to the wiki it is important that you remember that they should be aligned with the sections of the final proposal that you have been asked to produce (see Call for Funding). It is likely that the wiki that you are using has the facility to be converted to a PDF or Word format allowing you to produce your final assignment (the proposal) directly from your wiki.
- Include a wiki page for Group Planning and Communication with sub-headings / links to pages for submitted work, project planning & meetings, and a bibliography.
- Upload files and link them to the appropriate wiki pages where necessary. Begin compiling a bibliography (on the wiki) and continue to add to it throughout the project (see wiki guidelines). You must write a brief comment on everything that you upload stating what it is and why it is relevant, so that other members of the group can keep track of each individual contribution and group progress. You can also begin to write the first draft of the proposal by adding your work directly to the wiki pages.
- Identify a likely pharmacophore of 4-AQ antimalarials based on the structures and activities of existing drugs and analogues.
- Identify the part or parts of the compounds that could be altered while still retaining the pharmacophore.

- Identify and describe the proposed mode of action of 4-AQ antimalarials, identifying the drug target.
- Suggest likely drug target interactions.
- Incorporate this information into the appropriate section of the wiki (if possible during class time).
- Compile a list of actions, people responsible for each action and the dates due in order to complete all of the tasks associated with this Workshop.
- Arrange a time when the group will have a short meeting to review progress before the next Workshop.

Tasks to Complete Before Workshop 3:

- Meet as a group and review progress on the actions assigned. Post a short summary of the meeting (date, time, those present and action items resulting).
- Continue to carry out research as part of the group on areas relevant to the grant proposal.
- Continue to update and edit the wiki by uploading files, posting summaries and responding to contributions from other group members. Remember to add brief comments to explain why particular files and links uploaded are relevant.

Desired Learning Outcomes from Workshop 2:

On completion of this session you should be able to:

- Log in and edit a wiki page, upload files and add comments.
- Collaborate with other members of a group using the wiki and organise a list of actions for the group's activity.
- Explain how the wiki will contribute to the overall assessment of the project.
- Give an overview of the structures and mode of action of clinically useful 4-aminoquinoline antimalarial drugs.
- Identify attributes of a pharmacophore and explain how chloroquine and related antimalarials interact with their target, identifying relevant binding interactions.
- Explain the outcome of previous SAR studies.
- Critically evaluate the reliability/limitations of biological data used.

Workshop 3: Designing and Planning a SAR Study

Selection of a lead compound, appropriate biological assay(s) and the synthetic routes to new compounds.

Overview:

In this Workshop, you will design your SAR study. At the start of this Workshop you will be presented with Part B of the Report: 4-AQs and Related Antimalarials and an Internal Memo (#3). They outline the synthetic routes to a number of 4-AQs and describe a number of biological assays that can be used.

You will be asked to select, or will be assigned, a compound and to decide how it can be modified to produce new analogues (your target compounds). You will propose synthetic route(s) to your target compounds and select the appropriate biological assay or assays. If you have not used a chemical catalogue and/or a structure based search engine before, your tutor will arrange a demonstration. This will allow you to ensure that you start your synthetic sequence with commercially available starting materials.

There is a lot to do during and after this Workshop, so you must be organised and work hard. However, there will be time to add to and amend your work / wiki in later Workshops and no new material or tasks will be introduced after Workshop 5.

Tasks to Complete During Workshop 3:

- Assign this week's Chair, Recorder and Editor.
- Read Internal Memo #3 and Part B of the Report.
- If you have not been assigned a lead compound by the tutor, the first task is to select a lead compound and provide reasons for the selection. If possible, the structure of the lead compound and a justification for the selection should be uploaded onto the wiki during the Workshop.
- In Workshop 2, you identified the part or parts of 4-AQs that could be altered while still retaining the pharmacophore. Using this information and Part B of the report provided, discuss possible chemical modifications that can be made to the lead compound in order to produce novel 4-AQs (your target compounds).
- Propose structures of target compounds for the SAR study and discuss these with the tutor. Your tutor will tell you how many analogues you should design.
- Suggest synthetic route(s) to the target compounds ensuring, where possible, that they begin from commercially available starting materials.
- Discuss the biological assays described and select one or more. Consider the cost and time as part of your discussions. You must justify the selection in your final proposal.
- Incorporate this information into the appropriate section of the wiki (if possible during class time).
- Compile a list of actions, people responsible for each action and the dates due in order to complete all the tasks associated with this Workshop.
- Arrange a time when the group will have a short meeting to review progress before the next Workshop.

Tasks to Complete Before Workshop 4:

- Read the pharmacokinetics section of the recommended text(s).
- Meet as a group and review progress on the actions assigned. Post a short summary of the meeting (date, time, those present and action items resulting).
- Continue to carry out research as part of the group on areas relevant to the grant proposal.

- Continue to update and edit the wiki by uploading files, posting summaries drafting sections of the proposal and responding to contributions from other group members. Remember to add brief comments to explain why particular files and links uploaded are relevant.

Desired Learning Outcomes from Workshop 3:

On completion of this session you should be able to:

- Recall the mode of action of the lead compound.
- Explain what is meant by the term ‘SAR’ and describe the steps involved in carrying out an SAR study.
- Explain what is meant by the term ‘lead compound’.
- Suggest suitable molecular modifications of the lead compound and propose synthetic route(s) for achieving these.
- Discuss the importance of selecting a suitable bioassay for a SAR study.
- Use a chemical catalogue to source commercially available materials.

Workshop 4: Pharmacokinetics and Timelines for the Drug Discovery and Development Process.

Part 1: Pharmacokinetics (Approximately. 1 hour)

You should have read the appropriate section on pharmacokinetics in the recommended text in advance of this Workshop. In this Workshop, you will be provided with Part C of the Report (4-AQs and Related Antimalarials) summarising the pharmacokinetics of known 4-AQ antimalarials (in particular chloroquine and amodiaquine). You will also receive an Internal Memo (#4) requesting information about the possible metabolism of your target compounds and predicting whether they will be orally available.

The information concerning the pharmacokinetics of the target compounds should be summarised in the form of an internal memo to the GHO Pharmacology Team and emailed or delivered in hardcopy to the tutor with the completed worksheets for each compound. Relevant material should also be incorporated into the appropriate section of the group wiki.

Part 2: Timelines (Approximately. 40 mins)

You will also be asked to produce a Gantt chart as a tool for planning and presenting the timeline for the SAR study. The information required to produce the chart can be obtained from Report Part B (Antimalarial Workshop 3). Finally, you are asked to estimate the time it would take to bring a successful target compound from 'bench to bedside'.

Tasks to Complete During Workshop 4:

- Select this week's Chair, Recorder and Editor.
- Read the report provided.
- Complete the templates provided for 'Analysis of Drug-Likeness' for each target compound. You must identify the functional groups, HBD, HBA and rotatable bonds in the structures.
- Apply Lipinski's rule of 5 to the target compounds identifying any violations. Use an online (or other) drug-likeness calculator to obtain c Log P.
- Use an online (or other) calculator to determine the PSA of the target compounds.
- Predict the oral availability of the target compounds based on the above analyses.
- Using the information provided and that obtained from your own reading, suggest the route(s) by which the target compounds will be metabolised.
- Prepare a memo (no more than one page) summarising the predicted pharmacokinetics and any additional information that is relevant and submit it to the tutor with the completed 'Analysis of Drug-Likeness' sheets.
- ***This stage should only be carried out if there is time (your tutor will advise):*** You may wish to modify the proposed SAR study on the basis of the findings. You must also propose associated changes to the synthetic route. Proposed changes and justifications must be made by the beginning of Workshop 7.
- Produce a Gantt chart to show the time that it will take to carry out the proposed SAR study. An example of a Gantt chart is provided in the Appendices to this Guide.
- Estimate the time that it would take to take for one of the target compounds to enter clinical use assuming it was successful in all steps of the drug development process. Provide a brief explanation for the answer, citing the references used.
- Assign tasks to group members ensuring that all of the information and decisions from this Workshop will be uploaded to and recorded accurately on the wiki in the appropriate section before the next Workshop (bearing in mind that this information will form a large part of the final research proposal).

Tasks to Complete Before Workshop 5:

- Meet as a group and review progress on the actions assigned. Post a short summary of the meeting (date, time, those present and action items resulting).
- Complete the pharmacokinetics section of your wiki/proposal and upload your Gantt chart to your wiki if you have not already done so.
- Continue to carry out research as part of your group on areas relevant to the grant proposal.
- Continue to update and edit the wiki by uploading files, posting summaries and responding to contributions from other group members. Remember to add brief comments to explain why particular files and links uploaded are relevant.
- Read the appropriate sections of the recommended text in advance of the next Workshop concerning the use of parallel synthesis and high throughput screening in the drug discovery process (your tutor will advise).

Note that the first draft of the proposal should be nearing completion. While there will be an additional task in Workshop 5, there will also be time to review the wiki/first draft of the proposal and address any areas of concern. The draft proposal will be submitted during or shortly after Workshop 5.

Desired Learning Outcomes from Workshop 4:

On completion of this session you should be able to:

- Discuss the effect of the study of pharmacokinetics on the early stages of the drug discovery.
- Apply Lipinski's Rule of 5 and the use of PSA/no. of rotatable bond to estimate oral availability of a drug.
- Explain what is meant by the term drug metabolism and describe how 4-aminoquinoline antimalarials are metabolised.
- Plan the time required for a small scale SAR study using a Gantt chart to show the timeline.
- Be aware of the typical stages of the drug discovery and development process and the time that it takes to develop a new drug.

Workshop 5: Parallel Synthesis and High Throughput Screening

Part 1: Parallel Synthesis and High Throughput Screening Evaluation (Approximately. 1 hour)

In this Workshop, you will be asked to consider the impacts (both positive and negative) that parallel synthesis and high throughput screening (HTS) could have on the proposed SAR study. You will receive an Internal Memo (#5) from Prof. Woodward and attached is a letter from Inspired Pharmaceuticals Ltd which describes a high throughput method reported to be suitable for screening antimalarial 4-AQs. You will be asked to produce a memo to Prof. Woodward indicating, with reasons, whether or not you will use parallel synthesis and HTS in your SAR study.

Part 2: Reviewing Progress and Completing Tasks (Approximately. 40 mins)

The additional contact time is available to allow you to consult with the tutor, review progress to date, identify any weaknesses or tasks that are not yet complete and to address feedback.

You will be given a deadline for submission of the draft research proposal, which will be during or shortly after this Workshop.

Tasks to Complete During Workshop 5:

- Select the Chair, Recorder and Editor.
- Read the information provided.
- Using the information provided and any you obtained from your own reading (i.e. the recommended text(s)), critically evaluate the impact of parallel synthesis and HTS on the SAR study. In order to do this, you must consider both the positive and negative aspects of their application.
- Write a memo (no more than one page) stating whether or not these tools will be employed in your study, ensuring that a brief summary of the discussions and a justification is given (i.e. stating both advantages and disadvantages regardless of your final decision). Upload the memo onto the wiki during the class, if possible.
- If there are other tools that would be of use in the current study, access to these may be requested in the memo. A brief justification for their use must also be given.
- As a group, review the work to date and identify any weaknesses or areas that need further work. Use the checklist provided in the Appendices to this Guide.
- Act on feedback provided from previous Workshops.
- Take a note of the submission date and format for the draft research proposal.
- Compile a list of actions, people responsible for each action and the dates due in order to complete all of the tasks associated with this Workshop and with completion of the draft of the proposal.
- Arrange a time when the group will have a short meeting to review progress before the next Workshop.
- Assign tasks to group members ensuring that the memo is uploaded onto the wiki and that the appropriate sections of the wiki are updated.

Tasks to Complete Before Workshop 6:

- Submit a work in progress summary (maximum one page) listing the areas of your research proposal that have been addressed and those which are not complete with details on who is responsible and due dates. Any clarifications required or queries that you have should also be noted. Upload a copy onto your wiki.
- Submit a draft proposal by the deadline in the format requested. It is important that you meet this deadline to provide your tutor with sufficient time to review the draft and provide feedback.

- Meet as a group and review progress on the actions assigned. Post a short summary of the meeting (date, time, those present and action items resulting).
- Continue to carry out research as part of the group on areas relevant to the grant proposal. Note that updates made after submission of the draft will not be reviewed by your tutor.
- Continue to update and edit the wiki by uploading files, posting summaries and responding to contributions from other group members ensuring that they meet the deadline. Remember to add brief comments to explain why particular files and links uploaded are relevant.

Desired Learning Outcomes from Workshop 5:

On completion of this session you should be able to:

- Describe what is meant by HTS and parallel synthesis.
- Critically evaluate, by discussing the advantages and disadvantages, the use of HTS and parallel synthesis in SAR studies.
- Identify any other appropriate tools for a SAR study.
- Work effectively as a group to assess progress to date, identify areas of the proposal that require work and plan the final stages of the project.

Workshop 6: Clinic for Formative Feedback

Overview:

This clinic is designed to allow you to obtain feedback from your tutor on the work to date. Clarification on delivery aspects and protocols for assessment will be reiterated. Question time will be assigned to your group and you should ensure that you are up to date with the work load and expectations. A brief discussion about presentations (and peer assessment if appropriate) will take place. If there is sufficient time, you should begin preparations for your presentation for Workshop 7.

The main aims of this Workshop are:

1. To answer any queries on the assignment and activities, and to discuss any issues raised.
2. To provide you with formative feedback (as an entire class and to each group) on which areas of the report you need to work on and which ones have been addressed satisfactorily.
3. Identify the tasks remaining and plan for when they will be achieved.

At the end of this Workshop, you should receive a deadline for the submission of the final research proposal.

Tasks to Complete During Workshop 6:

- Act on feedback provided and ask questions if anything is not clear.
- Review work as a group and identify any tasks that need to be completed.
- Complete any outstanding tasks.
- Plan and begin preparations for the presentation. If using a PowerPoint format, guidelines for the presentation of slides are provided in the Appendices to this Guide.

Tasks to Complete Before Workshop 7:

- Meet as a group to finalise and practice the final presentation. Practise it several times as a "dry run" and ensure it meets the time requirement. Students do not need to post full minutes, but should post a list on the wiki stating who attended the meeting and the tasks completed at the meeting.
- Continue to update and edit the wiki by uploading files, posting summaries, redrafting sections of the proposal and responding to contributions from other group members ensuring that they meet the deadline given by the tutor.
- The structure, coherence and consistency of style and formatting of the final proposal are important considerations at this stage.
- If the abstracts were not submitted with the draft proposal, they now need attention.

Desired Learning Outcomes from Workshop 6:

On completion of this session and the related independent learning hours you should be able to:

- Clarify the expectations for the final Workshop.
- Communicate effectively when receiving formative feedback to ensure that the maximum benefit is obtained.
- Work effectively as a group to:
    - Discuss your thoughts in relation to completion of the assignment.
    - Act on constructive criticism and suggestions.
    - Prioritise the remaining work to be done.
    - Prepare an informative and visually engaging presentation.
    - Identify problems and questions that relate to the assignment and related activities.

Workshop 7: Final Presentations and Feedback

Overview:

This Workshop is designed to allow each group to present their research proposals to the class. Each group will be allocated an identical time period to complete the oral presentation and to answer questions from the class and the tutor.

You will:

1. Present your group's work, to your peers and tutor, summarising your grant proposal and recommendations, and answering any questions they may have.
2. Obtain feedback from your tutor.
3. Learn about alternative approaches to the project from the other presentations, and provide a supportive audience and constructive feedback to your peers.

Tasks for Students to Complete During Workshop 5:

- Give an oral presentation.
- Peer-assess the oral presentations of the other groups in the class, if required (your tutor will advise).
- Ensure you have discussed and arranged submission of the final proposal including the abstracts.
- Complete resource evaluation forms (optional).

Remaining Tasks:

- Incorporation of feedback from the presentation into the final proposal.
- Final editing and completion of group's grant proposal. REMINDER: The structure, coherence, consistency of style and formatting of the final proposal are important considerations at this stage. If the abstracts were not submitted with the draft proposal, they now need attention.
- Print out and submit the final proposal. Your tutor may require you to produce the final report as a Microsoft Word document to allow page numbering and a word count check (You should just copy and paste the relevant sections from your wiki into the document).
- Produce and submit your individual reflective piece (Guidelines are given in the Appendices to this Guide).
- Peer assessment of the other students in your group based on frequency and quality of contributions to the group (optional).

Desired Learning Outcomes from Workshop 7:

On completion of this session and the related independent learning hours you should be able to:

- Present findings in a professional manner.
- Produce a clear and legible PowerPoint (or other) presentation.
- Reflect on the process involved in preparing the group proposal, the extent to which the stated learning outcomes were met and to which the listed transferable skills were developed.
- Work effectively as a group to:
    - Act on constructive criticism and suggestions.
    - Prioritise the remaining work to be done.
    - Identify problems and questions that relate to the assignment and related activities.

Appendices

Appendix 1: Guidelines for Preparing Abstracts

An abstract is a short version of a longer article or piece of work in which all the major points are summarised without losing the overall meaning. Students are often required to write an abstract for their laboratory practical reports, and you will also notice abstracts at the beginning of scientific journal articles. In scientific abstracts, it is usual to briefly describe the methods used, the results, and the conclusions. The exact length may vary, but they are typically around 100-250 words long.

The recommended approach is as follows:

- Decide how long your abstract should be - typically about 10 % of the length of the full article or whatever word count is specified.
- Identify key points that you think you should include from the full text: Perhaps make a list or use a highlighter pen.
- Do not include tables, detailed examples etc.
- Abbreviations should be defined when first used except if they are very well known (e.g. EU, UK).
- Write a first draft including all of the points that you identified
- Now re-write your first draft so that the final result is a stand-alone 'mini-essay' that can be easily followed by a reader.
- Double check and re-edit if you need to. Check that the word count is within the specification.
- Finally re-read the article and make sure that your abstract is in the same style.

Common difficulties that arise are:

- Deciding on core information.
- Making sure that all important aspects are addressed.
- Linking the information into a coherent piece of writing that stands alone and is clearly written and structured.

Some useful WebPages and textbooks are as follows:

- Information on the "four Cs" of abstract writing, providing some useful examples of good and bad practice: http://undergraduateresearch.ucdavis.edu/urcConf/write.html
- Guidelines and some examples: http://owl.english.purdue.edu/owl/resource/726/07/
- Presentation on writing scientific abstracts: http://owl.english.purdue.edu/owl/resource/706/01/
- Guidelines from the Royal Society of Chemistry to authors of book chapters. The second section (Layout of the Chapter) includes information on writing abstracts: http://www.rsc.org/Publishing/Books/edbookauthor.asp
- Chapter 3 of *Writing for Science and Engineering* by Heather Silyn-Roberts, Butterworth-Heinmenn, Oxford, 2000.

Appendix 2: Using a Wiki

"Wiki: A collaborative website consisting of one or more pages that allow authorized users to contribute to or edit page content." (Source: http://usermanual.pbworks.com/Glossary)

Note that although many wikis are open access, those described for this project are secure and only those invited to join the group / wiki by the tutor administrator will have access.

Why use a wiki?

Wiki software is very easy to use and allows people to work and to write collaboratively to produce a report / presentation / webpage. The wiki is a means of generating a very useful archive of all of the information that is relevant to a project as it proceeds. It provides the added flexibility of being able to work anywhere where a PC or laptop and internet connection are available at any time. Wikis are regularly used in organisations to allow groups to collaborate on projects and documents and to share knowledge and the ability to use one is a valuable transferable skill. For example, a Drug Discovery Today article from 2011 on an in-house wiki used by Hoffman La Roche to share medicinal chemistry knowledge is available; Mayweg, A.; Hofer, U.; Schnider, P.; Agnetti, F.; Galley, G.; Mattei, P.; Lucas, M.; Boehm, H. J., ROCK: the Roche medicinal chemistry knowledge application - design, use and impact. *Drug Discovery Today* **2011,** *16* (15-16), 691-696. For more examples, see the references at the end of this Appendix.

All previous versions of each page can be accessed using the Page History function which means that no work can be permanently overwritten or deleted. Contributions made by each member can be easily tracked to assess their quality, quantity and whether they were made across the entire timeframe of the project. Peer feedback and review is facilitated by the comments and page editing option. The projects and the feedback provided can be accessed easily and stored indefinitely for future reference and are available in a flexible format (pages can usually be saved as PDFs).

What do you need to be able to do?

Instructions on the technical details in relation to using the selected wiki software are given on its website.

The common tasks you will perform using the wiki are:

- Adding and editing wiki pages.
- Adding comments and links to pages.
- Inserting tables and chemical schemes / structures.

Most chemical drawing software allows for structures to be saved as images (the required format is usually specified in the help menu).

If you have a specific technical problem, it is recommended that you check any guidelines that have been provided to you by your tutor and also ask the other members of your group for help. If you are still having a problem, you should then contact your tutor.

Always remember:

- Use folders, link related pages and name files and pages in a logical and structured way so that you can find information on the wiki easily. To help with this, your group are provided with names that should be used for the pages that will make up the main body of your report / presentation (see the 'Structure of your wiki' section, below).

- References should be cited when necessary and all information should be put into your own words
- This information is intended for publication online so **ensure that the information is accurate, will not offend anyone and is not plagiarised.**
- Try to keep the page to a reasonable length. Long pages can cause the reader to lose interest. Try to arrange data in sensible subcategories with pages for each to make it more engaging for the reader.
- The target audience are the reviewers at the Molecules against Malaria programme.
- Note that there is a space limit on each wiki page. If you find that a page is no longer accepting edits, you have probably reached the limit. You will need to add a new page, and link to this page from the end of the existing one to continue that section.

Netiquette and online communication

The concept of "netiquette" is very important because when you are communicating online, there are no visual cues (you can't see the face of the person or people you are in contact with). This means that it is more difficult to communicate clearly and it is more likely that a comment may be misunderstood or misinterpreted. Also, you should remember that all comments made on a wiki remain in the page history even after they are deleted.

It is recommended that you read over a comment carefully before you add it to the wiki to make sure that it is clear and there aren't any spelling mistakes that will make it confusing. You should be respectful and polite to each other, and be conscious of not offending or insulting anyone. Use of capital letters only is the online equivalent of shouting at someone and should be avoided. The same approach applies in any professional environment.

Ground rules for your group

You may want to consider establishing some ground rules about working in your groups such as remaining respectful towards a group member who you feel is not contributing, providing constructive feedback to peers (e.g. posting a comment first before making changes to someone else's work), responding to a query or message within a reasonable timeframe, communicating with the group to let them know if you will be late or absent and consulting with the group in relation to important decisions.

Remember that working in a group can be very productive, but it requires communication, planning and compromise.

Peer feedback and review

In the initial weeks, your group could consider waiting until a group member asks for feedback or editing of their contribution before making changes to their work. It is helpful if contributors are specific about feedback required (e.g. proof-reading for grammar, spelling and formatting or aspects such as relevance, structure, clarity and validity of the conclusions drawn). It is recommended that feedback and changes are constructive. A comment should address what was done well, and also the areas where it is felt changes are required and why.

Structure of your wiki report

The following are the names of the pages that should be used to make up the main body of your report / presentation:

- Table of contents (with links to the other pages) for the grant proposal.

- A page for each section of the research proposal as described in the Call for Funding.
- A page for references.
- A section of the wiki called ‘Group Planning and Communication’ (see below)

If you are unsure, consult your tutor for advice as it is important that your wiki is structured correctly in order for you to make good progress.

There are also a number of pages that your group should consider adding to the wiki that will help with planning and communication. These are:

- Work submitted - Use this page to submit any assignments you are asked to submit via the wiki.
- Project planning and meetings - Use this page for summaries of your group's weekly meetings and any other project planning. Some wikis include templates for reporting on meetings that could be incorporated here.
- Ideas and suggestions - Use this page as a sounding board and suggestion box for general issues.
- Bibliography - Use this page to post links or citations to useful websites, videos, articles or textbooks. Each one must include a short summary of why this information source is useful and refer to a specific page/section in it if necessary.

References on the use of wikis in organisations:

“Corporate Wiki Users: Results of a Survey”, A. Majchrzak, C. Wagner & D. Yates, *WikiSym’06, Proceedings of the 2006 international symposium on Wikis*, D. Riehle, J. Noble, Eds. (ACM Press, 2006), vol. Odense, De, pp. 99-104, accessed 18 October 2011 at https://blog.itu.dk/MVOL-F2010/files/2010/02/corporate-wiki-users-results-of-a-survey.pdf

A wiki to develop policy in the area of green chemistry in California is available here http://cagreenchem.wikidot.com/start and is reported here: http://eponline.com/articles/2009/02/09/calif-launches-wiki-to-develop-green-chemistry-regulations.aspx

Appendix 3: Sample Gantt Chart

Work package	Day X-Y	Day X-Y	Day X-Y	Day X-Y	Day X-Y	Day X-Y
WP1						
WP2						

The work packages must be named and described.

Appendix 4: Checklist for Submission of Final Research Proposal

Have you included the following in your final research proposal?

- A scientific abstract (maximum 200 words).
- A project abstract (aimed at a lay audience, maximum 200 words).
- A short summary that addresses why the problem is significant, the benefit of the proposed work to society in the UK / Ireland and in a country of the applicant's choice in which malaria is endemic (maximum 200 words).
- Have you included your references in the correct format?
- Have you correctly referenced all sources of information and any diagrams, schemes, tables etc that are not your own? See Appendix 7, Plagiarism.
- Is the main body of the proposal less than 1000 words (not including figures, schemes, diagrams and tables)?
- Is your proposal within the word limit of 2000 words?

Be sure all the following are covered in the main body of the proposal:

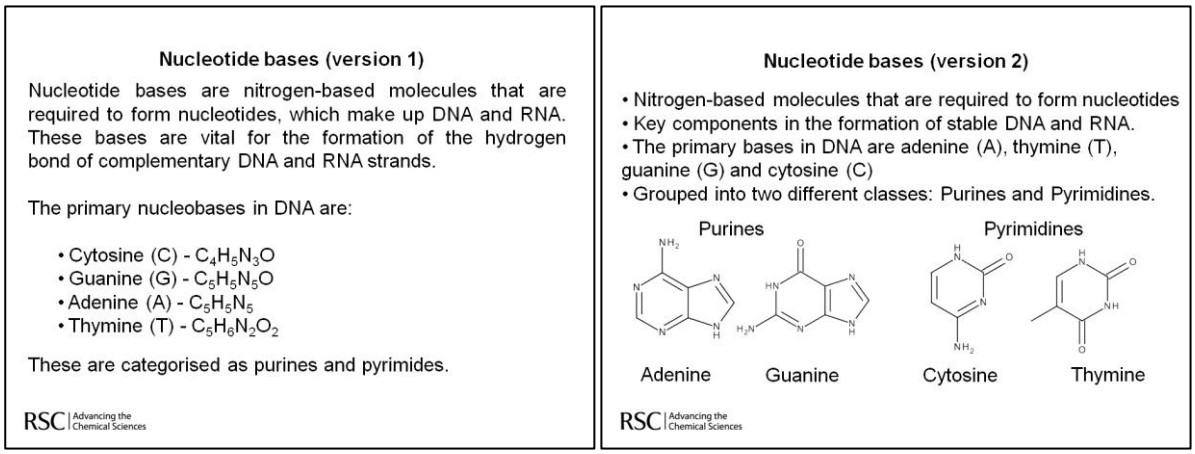
- A section/paragraph outlining the aims and objectives of your SAR study in the main body.
- A section/paragraph providing appropriate background information including the mode of action of quinoline antimalarials (including the drug target and -interactions between the drug and the drug target).
- Have you clearly identified a lead compound and provided a justification for your selection?
- Have you proposed structures for 3-5 new analogues, giving the synthetic route that you intend to use and the method or methods that you will use to assess their antimalarial activity?
- Have you explained why you chose the lead and why you plan to modify the lead compound in the ways suggested?
- Have you explained why you have used the method or methods selected for biological evaluation?
- Have you included a section about the possible route of metabolism of your new analogues, proposing structures of the metabolites and applied Lipinski's rule of 5 and / or other to each of your analogues, explaining the impact of these factors on the overall 'drug-likeness' of the compounds?
- Have you provided definitions for all of the terminology used?
- Have you included a Gantt chart for the proposed work and an estimate of the time for taking any successful compounds from the bench to clinical use?

Appendix 5: Guidelines for Oral Presentations

When preparing a presentation, take care to:

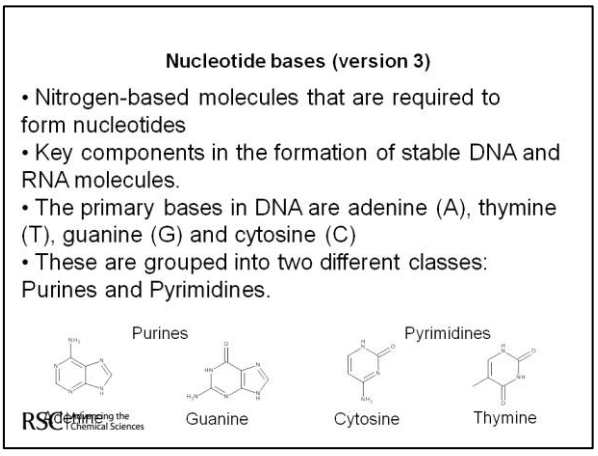
- Tailor the tone and content to the audience.
- Be informative and interesting.
- Keep to appropriate timing.
- Make slides simple and visually engaging.

Slides 1 to 3 show sample presentation slides. Slide 1 shows the common mistake of overloading slides with information. Remember you will be talking about the slides when they are shown so can provide the additional detail then. Slide 2 expresses the same information, but the use of pictures and bullets makes it easier for the audience to take the information on board.



Slide 1 and 2: Dos and don’ts in slide preparation

As Slide 3 image shows, when you have chosen the best content for the slide it is important to present it well. Ensure pictures are big enough and clear so that the audience can read the detail. Make use of the space available to you, and use a reasonable font size (preferably minimum size 20 in Arial).



Slide 3: Poor use of slide space.

Remember:

- Keep slides simple – large font, simple colours.
- Use bullet points - aim for maximum 6 bullet points containing 6 words each.

- Pictures speak a thousand words, but make sure they are clear and big enough.
- Don’t over use animations.
- Credit sources and provide references.

It is important to carefully structure your presentation to ensure it flows well. Content can be split into three categories:

- Beginning - introduce topic on level suitable to audience.
- Core - longest section covering key messages.
- End - summarise results and emphasise main points.

Plan your content carefully. It may not be necessary or possible to include all of the data you collected so be critical when choosing what to include. Too much information may cause you to overrun the time slot, and result in loss of marks or having to stop before you reach the final slide.

When delivering the presentation be sure to:

- Practice several times with your group, preferably with an audience.
- Check you can use the technology.
- Be confident – make eye contact and try to smile.
- Speak slowly and clearly.
- Face your audience when you speak.
- Avoid blocking the screen.
- Stay calm - if you make a mistake or something goes wrong; you may be the only one who notices so take your time, correct the mistake, and move on.
- Take your time answering questions, and if you don’t know an answer, just say so.

Useful resources:

- Key Skills for Scientists – Getting the Message Across, ed. Natalie Mansfield, Royal Society of Chemistry, 2007.
- Effective Communication for Science and Technology, Joan van Emden, 2001, Palgrave, Hampshire (Chapters 6 & 7).
- Chapters 11 and 12 of “Study and Communication Skills for the Chemical Sciences”; Overton, T., Johnson, S., Scott, J.; Oxford University Press (2011).

Appendix 6: Guidelines for the Reflective Piece

In this short document (500 to 800 words approximately), you should:

1. Briefly describe your role in the project and the contribution you made.
2. Discuss how you experienced working in a team (consider both the positive and negative aspects).
3. Discuss any changes that you would make to how you and your group went about the project if you were repeating it.
4. Summarise what you found to be most the interesting aspect of the project as well as the most challenging aspect.
5. Consider whether you think the project was useful to your learning and whether all of the learning outcomes (see page 8) were met.
6. Assess whether you have developed the transferable skills listed on page 8 further as a result of this project. Highlight any that you think are particularly important or that you have now gained confidence in.
7. Consider whether you have found that writing a reflective piece like this helps you to review what you learned over the course of the project.

This reflective piece is assessed based on:

- **Content** (60% - there are no right or wrong opinions but you must make sure that you discuss **all** of the topics listed above).
- **Presentation** (10%).
- **Coherence, accuracy and structure** (30%).

Appendix 7: Plagiarism

Plagiarism is not acknowledging the work of others. Therefore, all work which is not of your own creation must be accompanied by a reference which gives a detailed description of the item from which you have obtained information (e.g. article, website, book).

Important things to remember:

- Make sure that you acknowledge any information that you obtain from a particular source by including a reference.
- You should not reproduce information word for word from a reference even when you have acknowledged the source. The only exception is for a quotation, however direct quotations should be used sparingly. You are expected to communicate the information in your own words.
- Failure to meet these requirements means you have plagiarised work. This is the same as stealing someone else's work.
- If you are found to have plagiarised material, marks will be deducted and you may have to re-submit the work.
- References should be formatted according to the Royal Society of Chemistry Publishing author guidelines format. (See page eleven of the document at this link: http://www.rsc.org/images/Guidelines_tcm18-186308.pdf)

Further reading:
Chapter 10 of "Study and Communication Skills for the Chemical Sciences"; Overton, T., Johnson, S., Scott, J.; Oxford University Press (2011).

Appendix 8: Learning Outcomes of Hybrid Workshops 1-5 (Principles and Concepts)

The following learning outcomes summarise the prior learning that the authors believe is required for students participating in the Antimalarial Workshops. A supporting resource "Hybrid Workshops to Support: *Molecules against Malaria: Design of a Structure Activity Relationship Study of Antimalarial 4-Aminoquinolines*" is available and is designed to take approximately 10 hours of contact time. If you have already had some instruction in medicinal chemistry or pharmacology, these may not be needed and your tutor will inform you accordingly.

- Provide a definition of the term 'drug' suitable for use by a medicinal chemist.
- Provide a definition of the 'therapeutic index', use the therapeutic index to assess drug safety and describe the limitations of the application of the therapeutic index.
- Classify drugs by a number of methods and discuss the reasons for attempting classification and the possible advantages or disadvantages of these methods.
- Describe the drug discovery and development process, be aware of all the stages involved and be able to identify those that require input from a medicinal chemist.
- Describe the stages of drug action and duration, and explain what takes place during each stage and the objectives of the stages.
- Explain what is meant by the term 'pharmacodynamics' and, from the structure of a drug and binding site, identify binding interactions.
- Describe the stages involved in a SAR study.
- Use IC_{50} data to compare the biological activity of drugs.
- Explain what is meant by the term 'pharmacokinetics' and describe the processes that a drug will undergo on entering the body (ADME).
- Describe how the physicochemical properties (i.e. log P, pK_a) of a drug affect drug action and oral availability (i.e. application of Lipinski's Rule of 5, use of PSA and rotatable bonds).
- Explain how pharmacokinetic parameters can be obtained from experimental data and use of these parameters.

In addition to the learning outcomes above, the Hybrid Workshops are also used to introduce students to a PBL approach and allows them to practise other transferable skills that will be developed further in the Antimalarial Workshops.

- Problem solving: Learners work in groups to address the brief presented in the context / scenarios provided.
- Team work: Learners work in teams to complete the problems.
- Independent learning: Learners are required to read about many of the topics in order to solve the problems and must be able to explain their answers in full.
- Communication: Learners will be asked to feed back their answers to the class and to give a short presentation.