Learn Chemistry

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

Resource Overview

Developed by Dr. Claire McDonnell and Dr. Sarah Rawe, Dublin Institute of Technology

This resource was produced as part of the National HE STEM Programme

National HE STEM Programme

RSC | Advancing the Chemical Sciences

www.rsc.org/learn-chemistry

Registered Charity Number 207890

Acknowledgements

The authors would like to thank the people who contributed to this work: Dr. Brigid Lanigan, Mr. Damien Coman, Dr Michael Seery and Dr. Christine O'Connor of the DIT Chemistry Education Research Team for their input and for many useful discussions. We would also like to thank the people who trialled this resource for their very valuable input: Dr. Graham Patrick and Dr. Morag Dagen, University of The West of Scotland, Dr. Trinidad Velasco-Torrijos and Orla Fenelon, National University of Ireland (NUI) Maynooth, and Dr. Julie Dunne, Dublin Institute of Technology. We would also like to thank our external reviewer who provided valuable feedback for the development of the final resource.

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 a 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. The following review on C/PBL can be consulted for further information: T. L. Overton, Context and Problem-Based Learning, *New Directions*, Issue 3, Oct 2007, pages 7-12.

http://www.heacademy.ac.uk/assets/ps/documents/new_directions/new_directions/newdir3_link.pdf

About This Resource

This resource is designed to introduce students 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 the students to adopt the role of a medicinal chemist working for the GHO (Global Health Organisation) in the Tropical Diseases Research Centre. The students 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. The students will work in groups of 3-5 and the overall task will be achieved in a stepwise manner over a number of Workshops.

The resource is designed to map onto the Human Health theme of the RSC Roadmap. The development and use of drugs and therapies to improve human health is a key challenge that the RSC have chosen to promote as part of their Chemistry for Tomorrow's World initiatives. Through this, they aim to demonstrate how harnessing the basic sciences can help transform drug discovery, development and the human healthcare landscape.

An Overview of the Resource

This Tutor Guide accompanies the resource "*Molecules against Malaria: Design of a Structure Activity Relationship Study of Antimalarial 4-Aminoquinolines*", a C/PBL resource developed for the Royal Society of Chemistry in 2012 as part of the HE-STEM programme. It is intended to be part of a pharmaceutical/medicinal chemistry curriculum for students in the last 2 years of an undergraduate chemistry (or related) degree although it could be adapted for more advanced groups (see 'Flexibility within the Resource', below). The resource is composed of:

- A Student Guide.
- This Tutor Guide.
- PowerPoint presentations for each Workshop.
- An optional supporting resource "Hybrid Workshops to Support: *Molecules against Malaria: Design of a Structure Activity Relationship Study of Antimalarial 4-Aminoquinolines*" is also available (see below, 'Navigating the Resource' for more information).

In writing this resource, the authors' intention was to move away from the traditional approach used to deliver their 'Introduction to Medicinal Chemistry' module, which generally required students to rote learn a large volume of material in order to pass an examination, and towards a module that requires students to apply knowledge. It is not envisioned that tutors delivering this module have to be medicinal chemists. Medicinal chemistry can be described as the application of the general principles of organic and physical organic chemistry to the interaction of a small molecule (a drug) with a large biomolecule (drug target e.g. an enzyme). Some specialist terminology is required (e.g. the intermolecular interactions between a drug and its target are referred to as binding interactions). Some knowledge of biomolecules, and the cell and its organelles, would also be useful but is not essential. The authors recommend any one of the two introductory texts listed below (Text Books and Reference Materials) both to students and to tutors delivering this material for the first time.

It should be noted that the biological target of the 4-aminoquinoline antimalarials is unusual in that it is *not* a protein or other macromolecular biomolecule. This has the advantage that no prior knowledge of the structure and function of biomolecules is required prior to undertaking the Antimalarial Workshops described herein, thus allowing students to focus on many of the fundamental principles of drug design and development from a chemist's perspective. However the authors acknowledge that for this reason it may not be suitable as a stand-alone module for those wishing to expose students to a broader pharmacologically based medicinal chemistry syllabus.

Students participating in these Workshops should have some prior knowledge of the fundamental concepts of medicinal chemistry (drugs, drug targets, binding, phases of drug action, stages of drug discovery and development, etc). However, if the student cohort has not had any previous instruction in medicinal chemistry it would be appropriate to provide a further 10 contact hours in which these concepts are introduced. In order to facilitate this learning, the authors of this Guide have developed a number of learning activities that can be adopted as part of a hybrid approach to C/PBL (Hybrid Workshops 1-5). A hybrid approach refers to short periods of traditional lecture activity interspersed frequently with problem solving. The learning outcomes associated with the Hybrid Workshops are given in the Appendices to this Guide and summarise the prior knowledge required for students undertaking the Antimalarial Workshops. Please refer to the accompanying Guide "Hybrid Workshops to Support: *Molecules against Malaria: Design of a Structure Activity Relationship Study of Antimalarial 4-Aminoquinolines*" if appropriate for your student group.

It was assumed when writing this resource that students participating in this module have access to and can use a chemical drawing programme. If not, it may be appropriate to schedule appropriate training in advance. Versions of Accelrys Draw (which has replaced ISIS/Draw) or ChemSketch can be downloaded and used by academic institutions and students for free. In addition, several online tutorials on the use of the software are available.

- http://accelrys.com/products/informatics/cheminformatics/draw/no-fee.php
- http://www.acdlabs.com/resources/freeware/chemsketch/

Navigating the Resource

This Guide describes a classroom-based case study involving seven Workshops (Antimalarial Workshops, Table 1) that require 14 contact hours divided into 7 x 2 hour or 14 x 1 hour sessions. A schedule for the delivery of the Antimalarial Workshops is outlined in Table 1, which also summarises tutor and student activities, what the tutor should do between Workshops, deadlines and learning outcomes. A simplified version of Table 1 can be found in the Student Guide (also Table 1) and tutors should consult the tables for an overview of the resource.

The Appendices to this Guide contain student handouts (Appendix 1) which are organised according to the Workshops with which they are associated. Appendix 2 contains the 'Tutor Notes for Workshops 1-5' (organised according to Workshop) and provides the specialist knowledge concerning the medicinal chemistry of antimalarial 4-AQs – it can also serve as a sample answer when marking the final proposals submitted by the students. A 'Making It Work' section is also provided in the Appendix 10 and gives some tips and advice gained from the authors' and the trial teams' experiences of implementing this and similar resources.

Table 1 and associated Appendices may provide sufficient information for many experienced tutors planning to adopt the resource. However, the Table was obtained by summarising a detailed task-by-task breakdown (for both tutors and students) of the content of every Workshop and so the authors have included detailed descriptions of each Workshop in this Guide (Workshop Content) that can be used for further clarification.

How is the Resource Delivered?

The resource is designed to be delivered to students as a continuously assessed module. Together with the Hybrid Workshops (10 hours of contact time), independent study and writing-up time, it is intended that this resource requires a total of 50 learning hours (a total of 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.

Flexibility within the Resource

The resource can be adapted to suit students at various levels, with varying knowledge and experience of C/PBL. For this reason, the Guides and accompanying materials are provided in a format that can be modified by the tutor. The Student Guide and associated PowerPoint presentations contain stepwise instructions for the students to help them complete the tasks associated with each Workshop. Some tutors will feel that these instructions are too comprehensive / leading for their student group, preferring to let the students find their own way and can edit the Guide as appropriate.

A number of texts, articles and weblinks are listed throughout the Guides and it is up to the tutor to decide which of these are suitable for their students and, again, he /she can amend the Student Guide to suit the student group. For second year undergraduates, it is likely that the recommended text books and a small number of articles and weblinks, along with the student handouts would be sufficient to allow them to engage with the resource at an appropriate level. For final year undergraduates with previous experience of C/PBL and medicinal chemistry, the review articles may be made available as an alternative to much of the information contained within the student handouts (Report: Parts A to C, see Appendices). For very advanced groups (e.g. postgraduates), a more student driven approach may be taken in which the students are required to search the literature in order to find all of the appropriate information for themselves.

The authors have designed the resource as a whole to be delivered as 10 hours of Hybrid Workshops followed by 14 hours of Antimalarial Workshops, but have suggested alternative modes of delivery in the Appendices to this Guide. Tutors with groups who have already completed pharmacology or medicinal chemistry modules should consult this section. It is also envisaged that the Hybrid Workshops could stand-alone as part of an introductory module. Moreover, one or more Workshops could be employed in place of a laboratory in a larger medicinal chemistry module.

In summary, tutors are invited to adapt this resource to suit the needs of their student cohort.

Table 1: Content and Recommended Schedule for Delivery of Antimalarial Workshops 1 to 7

Session Title, Time Allocation	Tutor Aims	Activities	Learning Outcomes On completion of this session, the student should be able to:
Workshop 1: • Introduction to Workshops and the context.	**Module induction** • Assign groups, give an introduction to the context, problem and outline the learning outcomes and assessment of the module. Look over the Student Guide. **Introduction to the Context** Introduce the following topics that will need to be researched further by the student: • 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.	**Hour 1** Tutor presentation of introductory material: Includes a schedule of Workshops, assessment criteria and learning outcomes. Students are provided with a Chemistry World article which reviews aspects of the context (Malaria No More, V.Gill, Chemistry World, April 2008, 50-55). They are given time to read it, to discuss it in their groups and then as a class.	• Gain an awareness of the global impact of malaria. • Identify the malaria parasite as the cause of malaria, to note its lifecycle and importance of this to developing new antimalarial drugs. • Identify chloroquine; explain its mode of action and the need for new therapies to replace chloroquine. • Explain what is meant by the term 'drug resistance' and why this problem is significant.
• Abstract writing. 2 hours or two 1 hour sessions	**Preparing Abstracts** To introduce and discuss the following topics: • What is an abstract? • How is an abstract prepared? • Differences between scientific and lay abstracts. **If you are asking students to peer assess individual contributions to group work as part of this module, you should inform and brief them accordingly.** **In advance of Workshop 2:** **Obtain student emails and invite them to join the group wikis.**	**Hour 2** Using the Chemistry World article students are required to work in groups to: • Select information that they think should be in an abstract of the article. • Feed back and prepare a class abstract (agreed key points and order). • Compare the content of a sample abstract provided to that decided above. • Read newspaper articles concerning malaria. • Compare and contrast the style used in the popular press to that used in Chemistry World and suggest changes to be made to the abstract if it was aimed at a lay audience.	• Construct an abstract and assess the relevance of information provided in articles. • Gain an awareness of the need for scientists to communicate with a lay audience and consider how this can be best achieved.

Session Title and Time Allocation	Tutor Aims	Activities	Learning Outcomes On completion of this session, the student should be able to:
Workshop 2: • Tools to support the project - using a wiki (requires a computer lab if available).	**Using a Wiki (in computer lab if available)** To introduce and discuss the following topics: • What is a wiki? • How to use a wiki. • It's role in group assessment and in production of final report. • Demonstration of how individual contributions to a wiki can be monitored and assessed by the tutor.	Students are shown how to use a wiki and how it can be used to assess their contribution to group work. They will: • Set up the wiki according to the guidelines. • Begin generating group wikis by uploading content researched over the previous week. • Use this content to begin preparing the research proposal including a bibliography and continue it on an ongoing basis.	Use and contribute to a wiki to organise and facilitate collaborative work and understand how this activity contributes to the assessment.
• The relationship between chemical structure and biological activity. 2 hours or two 1 hour sessions	**Identifying the relationship between the chemical structure and antimalarial activity** To guide learners through the following processes, using relevant data (student handout): • Recognising the chemical structure of 4-aminoquinolines (4-AQs). • Using IC_{50} data to determine the relationship between the chemical structure and potency. • Identifying a likely pharmacophore. • Suggesting likely drug target interactions. • Explaining the probable mode of action of 4-AQ antimalarials. **Between Workshops:** **Review student wikis and provide feedback (brief comment). Ensure wikis are set up correctly (correct pages / headings, Appendix 3) to produce the final research proposal.**	From the information provided in the student handout for the Workshop, students will be asked to: • Determine how changes in the structure of compounds affect the activity and therefore identify a likely/probable pharmacophore of 4-AQs. • Describe the mode of action of chloroquine, identifying the drug target and suggest likely drug target interactions. • Determine groups that can be varied in order to investigate the SAR of 4-aminoquinolines with a view to developing more potent analogues. • The tutor will lead a class discussion that aims to critically evaluate the data provided in Report Part A (particularly Table A1).	• Give an overview of the structures and mode of action of clinically useful antimalarial 4-AQs. • Identify a likely pharmacophore. • Explain the mode of action of chloroquine and related antimalarials identifying the drug target and relevant binding interactions. • Explain the outcome of previous SAR studies and recognise the potential to design new antimalarial 4-aminoquinolines. • Critically evaluate biological data obtained from the literature.

Session Title and Time Allocation	Tutor Aims	Activities	Learning Outcomes On completion of this session, the student should be able to:
Workshop 3: **Designing and Planning a SAR Study** **Including:** • Selection of a lead compound. • Design of a structure activity relationship study, including synthetic route(s). • Selection of appropriate bioassay(s). 2 hours or two 1 hour sessions	**Designing and Planning a SAR Study** To guide learners through the following processes, using the information provided in the student handout: • Selection of a lead compound and / or recognition of the desired properties of a lead compound. • Design of a small SAR study (3-5 analogues which are referred to as the target compounds) by proposing molecular modifications of a lead compound and the synthetic route(s) and bioassay(s) to be used. • Use of online chemical catalogues/databases to source commercially available materials for SAR studies. Stepwise nature of experimental design should be emphasised. **Between Workshops:** **Review student wikis and provide feedback in the form of a brief comment.** **Direct students to appropriate section in text book (or other) concerning pharmacokinetics.**	Students will be asked to: Design a SAR study, to suggest the synthetic route(s) to target compounds from commercially available materials and to recommend the appropriate bioassay(s).	• Design a logical SAR study taking into account the pharmacophore and previous SAR studies. • Design the synthetic route(s) to the target compounds. • Use a chemical catalogue to source commercially available materials for the synthesis of target compounds. • Be aware of the criteria for the selection of a biological assay and select the appropriate bioassay(s) for the SAR study.

Session Title and Time Allocation	Tutor Aims	Activities	Learning Outcomes On completion of this session, the student should be able to:
Workshop 4: • Pharmacokinetics. • Timelines. 2 hours or two 1 hour sessions	To guide learners through the following problems, using information provided in the student handout and from their own reading: **Examining the relationship between the chemical structure, drug metabolism and oral availability** • Prediction of the route by which the target compounds could be metabolised. • Analysis of oral availability of the target compounds (designed in Workshop 3). • Evaluation of the importance of the above in early stages of the drug discovery process. **Timelines** • The use of a Gantt chart to plan a small scale SAR study. To ensure learners have an awareness of subsequent steps and the time required for drug development. **Set a deadline for submission of memo and drug-likeness sheets.** **Between Workshops:** • **Review and provide feedback on memo and drug-likeness sheets (see PowerPoint presentation).** • **Review wiki, ensure memo and Gantt chart uploaded.** • **Remind students draft proposal due after Workshop 6.**	Students will be asked to: • Research relevant information about drug metabolism (objectives and the transformations that may take place). • Predict metabolism of the new 4-aminoquinolines and note how this will impact on the design of the SAR study. • Consider how the physiochemical properties of compounds affect oral availability. • Prepare a memo summarising the above and complete drug-likeness sheets for target compounds. • 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.	• Describe the metabolism of antimalarial 4-AQs. • Predict oral availability of drugs. • Explain why it is important to consider pharmacokinetics when designing new drugs. • Be aware of the time that it takes to execute a small scale SAR study. • Use a Gantt chart to show a timeline graphically. • Demonstrate awareness of the stages of the drug discovery process and the time involved in developing a new drug to clinical approval stage from a promising lead.

Session Title and Time Allocation	Tutor Aims	Activities	Learning Outcomes On completion of this session, the student should be able to:
Workshop 5: Parallel synthesis and high throughput screening (HTS). 2 hours or two 1 hour sessions	To guide learners through the following problem, using information provided in the student handout and from their own reading: Evaluation of the impact of parallel synthesis and HTS on the proposed SAR study, both positive and negative. There should be time to help learners review progress to date, and to identify areas of the final proposal that require more work before a draft version is submitted in advance of Workshop 6. **Set deadlines for: Submission of memo, draft proposal and work-in-progress summary.** **Between Workshops:** **Review draft proposals and provide feedback.**	Students will be asked to: • Research relevant information about the tools available to a medicinal chemist. • Critically assess how the use of these tools will impact on their proposed SAR arriving at a recommendation for the use (or not) of these tools. • Prepare a memo summarising the above and incorporate information into the wiki. • Assess progress to date, identifying sections of the proposal that require work. • Consult with tutor if there are any issues / problems that need to be addressed / clarified.	• Explain and critically evaluate the application, advantages and any disadvantages involved in the use of parallel synthesis and HTS in the drug discovery process. • Identify any other appropriate tools for the 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. 2 hours or two 1 hour sessions	• To provide learners with formative feedback on the areas of the proposal requiring more attention and those that have been addressed satisfactorily. • To provide clarification on any student queries, review assessment criteria for module and to promote discussion as appropriate among the learners and encourage peer learning. **If you wish students to peer assess presentations, brief students and circulate forms.**	'Clinic' where each group; • Has submitted a draft 'work in progress' report in advance on which they will receive feedback. • Will discuss any queries or problems that they have encountered.	• Work effectively as a group. • Listen to and act on constructive feedback provided as required. • Identify problems and questions that relate to the assignment and related activities.

Session Title and Time Allocation	Tutor Aims	Activities	Learning Outcomes On completion of this session, the student should be able to:
Workshop 7: Group presentations. 2 hours or two 1 hour sessions.	• To provide feedback to the learners on their presentation skills and the content of their proposal. • To allow students to learn from each other's presentations and to ask each other questions. • To allow students to peer assess presentations (optional). • To arrange /allow students to peer assess individual contributions to group work (optional). • To ask students to complete module evaluation forms (optional). • To review the assessment criteria in detail ahead of the final submission. **Set deadlines for:** **Submission of reflective piece.** **Submission of final research proposal.** **Advise students of format (PDF from wiki or Word® document).**	Students will be asked to: • Give a presentation to peers summarising the proposal followed by questions from the tutor and other students. • Peer-assess presentations (optional). • Peer-assess individual contributions (optional). • Provide feedback to tutor on module (optional). The tutor will: • Give general oral and/or written feedback on each presentation. • Give a deadline for submission of the reflective piece and final proposal.	• Produce a clear and legible PowerPoint (or other) presentation and present findings in a professional manner. • Work effectively as a group, develop oral and written communication skills. • Listen to and act on constructive feedback provided as required. • Reflect on participation in a group project, and the knowledge and skills acquired. • Peer-assess presentations and individual contributions to group work (optional). • Provide constructive feedback about the module (optional).

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 (generated from the wiki).
4. An individual reflective piece.

Assessment components and a guideline for the weighting of the assessment are suggested in Table 2. These are suggestions only and should be adapted to suit the group and tutor. Note that any changes made should also be made to the equivalent tables in the Student Guide and accompanying PowerPoint presentations (Intro to Molecules against Malaria Tutor Presentation, and Molecules against Malaria_Antimalarial Workshops 1-7 Tutor Presentation- slides in Workshops 6 and 7).

Table 2: Assessment components and suggested weightings

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

[#]*You may choose a component of this mark (e.g. 5 %) to be awarded by peer assessment by other class members. More information is given in Workshop 6, below and Presentation Evaluation Forms can be found in the Appendices to this Guide.*

[##]*If incorporating a peer assessment element, Table 2 should be amended (in Guides and PowerPoint Presentations) to include the phrase in parenthesis. In this case, students will be asked to peer-assess contributions of other group members both inside and outside of the classroom, online and face-to-face. Clear guidelines must be provided to the students (see Implementation: Peer Assessment and Evaluation of the Resource, below).*

A Word about Wikis

A wiki is an excellent tool to facilitate group learning and the final research proposal is generated directly from it (by converting it to PDF or printing). It is useful to remind students of this throughout the project. The main benefit to a tutor is that the quality and quantity of contributions made by an individual student can be tracked relatively easily and that the process as well as the product can be assessed.

Advice on monitoring and correcting wikis is provided in the Appendices to this Guide, but briefly, the tutor should log into each group's wiki once per week (assuming 2 hours contact per week), providing feedback on the execution of tasks associated with each Workshop and the extent of individual contributions. Feedback is also provided on the students' draft reports (research proposals), with the remaining correction

time spent on the completed reports (research proposals), presentations and individual reflective pieces. In this manner, students receive feedback as a group and as individuals at various stages throughout the project.

Although it is recommended that a wiki be used as a component of this C/PBL activity, an alternative can be adopted if preferred. Some type of online interaction among a group such as a discussion board or online group is very useful and, if this has been set up by the tutor, there is the advantage that they will be able to monitor progress being made. If this option is not used, the minutes of the weekly group meeting summaries should be submitted regularly and can be used to monitor progress and to check that all members are making a contribution. To provide a facility similar to the wiki for organisation of the work being undertaken, it would be useful for groups to use a ring binder / file with sections that correspond to the main parts of the proposal in which hard copies of useful documents and draft work can be kept. Under these circumstances, it is recommended that this draft work and supporting information is submitted as an appendix to the final proposal.

Implementation: Class Organisation

Whenever possible, the tutor should take a back seat and direct the students to the Student Guide and recommended resources to obtain relevant information. This encourages learners to read and engage fully with the materials provided. The distribution of the workload associated with the tasks should be assigned by the students in their groups.

The resource is designed so that students work together in small groups to complete the tasks associated with each Workshop. The authors recommend groups of 3-5 students, but this will depend on the class size, ability and prior learning. It is recommended that these groups be assigned at (or before) the start of the first class and that the classroom used is a flexible space that allows students to sit near to each other and allow conversation without the need for raised voices. Students should then be asked to sit in their groups for each class. If at all possible, each group should have access to a laptop with internet access so that the wiki can be updated during each Workshop, but this is not a requirement. A computer lab is required for the first part of Workshop 2 and student access to nearby computer facilities is strongly recommended for all Workshops.

Groups must be allocated at the start of Workshop 1. It is a good idea to ask the groups to choose a name and design a logo for their team as, in practice, this has been found to work as a good ice-breaker. Advise the students that 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 to content are required. Each student should adopt each role at least once during the Workshops (an Editor is not required for Workshop 1). Remind the students to nominate these roles at the start of each new Workshop.

Students' email addresses should be collected at the outset of the module and used to set up each group wiki. At the latest, the each student must be invited to join his or her group wiki before the beginning of Workshop 2.

Once the Workshops are underway, it is recommended that you ask the students to stop what they are doing 20 minutes before the end of each 2 hour Workshop or 10 minutes before the end of a 1 hour Workshop. Ask the students to identify all tasks that need completing before the next Workshop, to review the description of the following Workshop and to arrange a date and time to meet outside of the class contact

time. It may be a good idea to ask a spokesperson from each group to very briefly summarise the progress of the group to the class (if there are a large number of groups, each group can take turns to feed back over the course of the module).

Experience in delivering these and similar workshops has demonstrated that a ratio of one tutor to 15 students (5 groups of 3) is most effective. Even so, it is not easy to ensure that equal time is spent with each group due to the nature of the C/PBL approach and tutors must do their best to ensure this is the case. If involved in a particularly interesting discussion with one group that merits more time, it may be a good idea to open up this discussion up to the entire class and in that way include all students. If a group has a problem that requires a significant proportion of your attention (e.g. the group is not functioning as a team, the students do not understand the tasks), it may be wise to meet with that group outside of normal contact time.

Implementation: Tools to Support the Resource

In addition to the group wikis that the students will produce, it is strongly recommended that a Virtual Learning Environment (or a 'central' wiki to which all students are invited) is used to support this module. This will allow the tutor to host the Student Guide, supplementary material (presentations, student handouts, weblinks) and any other information that is deemed appropriate, on a central resource that all the students can access. It also provides a discussion board that may be useful in implementing the resource (providing reminders of tasks to be completed and deadlines, etc).

In addition to the Appendices to this Guide (which contain student handouts, notes for the tutor, tips and advice, etc), PowerPoint presentations are available to help structure each Workshop. The presentations contain an introduction/overview, a description of associated learning outcomes and a checklist of tasks. They can be adapted to meet the individual needs of the tutor and group (slides can be added, removed or amended). It is recommended that the tutor review all supporting information, the slides and the slide notes in advance of each Workshop.

Implementation: Peer Assessment and Evaluation of the Resource

In Table 2 (Assessment components and suggested weightings), the authors have suggested that a component of the marks for some elements can be awarded by peer assessment. If the tutor decides that this is appropriate, the students should be informed at the start of the module. When peer assessing group work, students can be asked to complete a form in which they rate the frequency and quality of contributions of each individual to the group. However, the authors recommend automation of the process by using peer review software such as CATME (Comprehensive Assessment of Team Member Effectiveness) which is available to download for free at https://engineering.purdue.edu/CATME. This software has been developed with support from the National Science Foundation and a range of statements can be selected for use with a given group. In the description of Workshop 6, a note is included about peer-assessment of presentations and Presentation Evaluation Forms are provided in the Appendices to this Guide.

If the tutor wishes to evaluate the implementation of the resource in his / her own institution, a Resource Evaluation Form is included in the Appendices to this Guide and can be distributed and completed by students at the end of Workshop 7. Useful feedback will also be obtained from the students' individual reflective pieces (see Assessment, below, Workshop 7 and Appendix 8).

Learning Outcomes

The learning outcomes associated with each Workshop are presented in Table 1 and are specific to the context described. In general, on completion of the resource 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

Students will be asked to reflect on the development of the following skills at the end of the project:

- 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.