RESEARCH ARTICLE

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Defining and unpacking the core concepts of pharmacology: A global initiative

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[Correction added on 29 September 2023, after first online publication: Janet Mifsud's surname has been corrected in this version.]

Abstract

Background and Purpose: Development of core concepts in disciplines such as biochemistry, microbiology and physiology have transformed teaching. They provide the foundation for the development of teaching resources for global educators, as well as valid and reliable approaches to assessment. An international research consensus recently identified 25 core concepts of pharmacology. The current study aimed to define and unpack these concepts.

Experimental Approach: A two-phase, iterative approach, involving 60 international pharmacology education experts, was used. The first phase involved drafting definitions for core concepts and identifying key sub-concepts via a series of online meetings and asynchronous work. These were refined in the second phase, through a 2-day hybrid workshop followed by a further series of online meetings and asynchronous work.

Key Results: The project produced consensus definitions for a final list of 24 core concepts and 103 sub-concepts of pharmacology. The iterative, discursive methodology resulted in modification of concepts from the original study, including change of 'drug–receptor interaction' to 'drug–target interaction' and the change of the core concept 'agonists and antagonists' to sub-concepts of drug–target interaction.

Conclusions and Implications: Definitions and sub-concepts of 24 core concepts provide an evidence-based foundation for pharmacology curricula development and evaluation. The next steps for this project include the development of a concept inventory to assess acquisition of concepts, as well as the development of case studies and educational resources to support teaching by the global pharmacology

community, and student learning of the most critical and fundamental concepts of the discipline.

KEYWORDS

core concept, curriculum development, Delphi method, health science education, pharmacology education, science education, sub-concept

1 | INTRODUCTION

In an era of increasingly interdisciplinary research and teaching, and with an ever advancing and expanding knowledge of the biosciences, there have been moves to identify the important overarching ideas and concepts in individual disciplines. These big ideas or core concepts have been reached by discussion and consensus-building at a broad level, for biology (Brewer & Smith, 2011; Brownell et al., 2014), chemistry (Mulford & Robinson, 2002) physics (Hestenes et al., 1992) and at a discipline level for physiology (Michael, Cliff, McFarland, Modell, & Wright, 2017), biochemistry and molecular biology (Tansey et al., 2013), and genetics (Hott et al., 2002). The core concepts identified in this way define the discipline's knowledge pillars and reflect the current direction of research; therefore, it should be reflected in the curriculum, guide its development and define the way it is assessed.

Pharmacology is taught across a range of health professional and scientific courses, in which it may provide the primary focus or take a more secondary role. Historically, the discipline of pharmacology has focussed on receptors. Indeed, Rang (2006) proposed that the receptor concept is 'pharmacology's big idea ... the receptor concept is as important to pharmacology as homeostasis is to physiology and as metabolism is to biochemistry'. As a wider diversity of drug targets has become known (e.g., **enzymes**, antibodies and nucleic acids), the knowledge base and foundational principles of pharmacology have expanded.

Concurrent with an increasing knowledge base, medical and healthcare schools in many countries are implementing systems- and competency-based education (Frank et al., 2010), reducing the number of pharmacology courses led by pharmacologists and reducing curricula time for teaching the core knowledge that underpins practice (Wallace et al., 2021). It is thus critical to define and teach pharmacology's core concepts at an initial stage, which then can be reinforced in case studies or integrated later into more advanced clinical or discipline-specific educational activities (Quesnelle et al., 2021).

In 2020, pharmacology education experts in Australia and New Zealand developed a rigorous, peer-reviewed process for identifying the core concepts of pharmacology (White et al., 2021). They subsequently defined and unpacked 20 core concepts (Santiago et al., 2021). This initial work set the foundation on which the international pharmacology community could build. In late 2021, the International Union of Basic and Clinical Pharmacology Education Section (IUPHAR-Ed) Core Concepts in Pharmacology project was formed (Project, 2022).

What is already known

- Development of core concepts in science, engineering, technology and maths can transform learning and teaching.
- An initial international consensus list of core concepts in pharmacology education is available.

What does this study add

- This study provides consensus definitions for the core concepts of pharmacology and underpinning sub-concepts.
- This study represents an evidence-based foundation for pharmacology curricula development.

What is the clinical significance

- Study results can support pharmacology education in various clinical and scientific contexts.
- These core and sub-concepts of pharmacology support safe and effective development, and use, of medicines.

This international project aims to facilitate a transformation in pharmacology education for both students and educators, with a strong focus on foundational knowledge. To date, over 250 pharmacology educators from 21 countries across 6 continents have contributed. The first task undertaken by this group was to identify an international consensus list of core concepts of pharmacology (White et al., 2023). The next and subsequent steps in the process (see Figure S1) are to draw upon the expertise and experience of this group to

1. develop a consensus definition of each core concept;
2. unpack sub-concepts for each core concept;
3. develop concept maps that explicitly show relationships between concepts;
4. develop and validate a concept inventory; and
5. develop teaching, learning and assessment resources for educators.

This paper describes the multistep collaborative process addressing Steps 1–3 above. It is recognised that the depth to which sub-concepts are unpacked will vary according to the target audience (e.g., first year vs. final year students) and the type of degree programme (e.g., undergraduate vs. postgraduate, and science vs. healthcare) (Michael, Cliff, McFarland, Modell, Wright, Michael, et al., 2017). This project aims to clarify the core conceptual understanding required for a higher education student beginning their study of pharmacology, which would ensure a sound knowledge of the fundamentals of the subject. The development of consensus definitions for each core concept together with underpinning sub-concepts has led to a foundational proposal for the essential knowledge for pharmacology curricula in higher education.

2 | METHODS

2.1 | Ethics approval

The Monash University Human Research Ethics Committee (MUHREC) project ID 31379 'Core concepts of Pharmacology' was approved as low risk by the MUHREC.

2.2 | Overall study design

2.2.1 | Research and expert group composition

Our previous study (White et al., 2023) identified 25 core concepts of pharmacology, namely, those that all students who have completed a module or course should understand and be able to apply. In this study, an expert group was established to develop definitions and identify sub-concepts for each of the core concepts. A total of 60 pharmacology education experts contributed to this current project. These consisted of 23 experts who had participated in the previous study and the remainder who responded either to emails sent out by IUPHAR member societies or after direct contact by the research team. Experts represented 17 countries across 6 continents from 54 different institutions (Figure 1). Our experts work across many fields of pharmacology including as research scientists, clinicians, pharmacists and veterinarians and in education-focussed roles. They teach, develop and lead undergraduate and postgraduate programmes in basic and clinical pharmacology, biomedical sciences, medicine, veterinary medicine and other allied healthcare programmes.

The research team began by dividing the 25 core concepts into 8 clusters, with each cluster consisting of 2–4 related concepts. The clusters were designated as being broadly pharmacokinetic (PK) or pharmacodynamic (PD) in nature. Expert group members were allocated to sub-groups, each of which was facilitated by a member of the research team (Table S1).

2.3 | Modified Delphi method—Defining and unpacking the core concepts

A two-phase, iterative approach was used to identify the core concept definitions and sub-concepts (Figure 2). The first phase involved the development of draft concept definitions and sub-concepts via a series of online meetings and asynchronous work. These were refined in the second phase, through a 2-day hybrid workshop in the Monash University Prato Centre in Italy, followed by a further series of online meetings and asynchronous work.
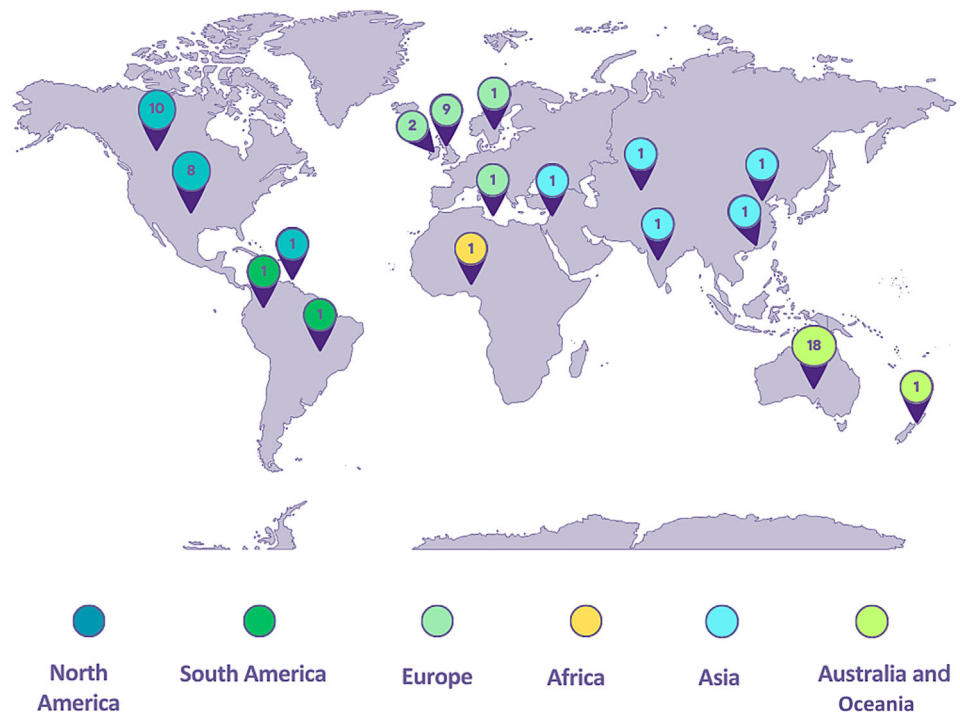

FIGURE 1 World map showing the geographic spread by country and number of pharmacology education experts involved in this project.

North America   South America   Europe   Africa   Asia   Australia and Oceania
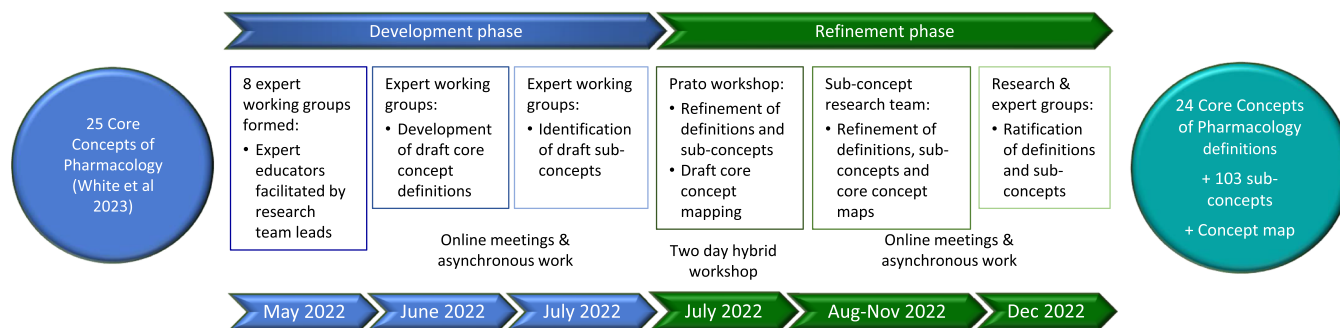
FIGURE 2 Summary of the approach used to develop the core concept definitions and sub-concepts. The process was iterative, and each stage involved re-working, drafting, discussing and revising the core concepts, definitions and sub-concepts.

1. Development of sub-group draft definitions

Expert sub-groups produced a one-sentence definition for each of core concept allocated to their group. The process was, as follows: sub-group facilitators contacted the members of the group by email to outline the task; next, all expert sub-group members provided an independent draft definition of each concept, submitted anonymously via Google Forms; facilitators undertook content analysis of the draft definitions to create a single, synthesised version for discussion within their respective groups (Figure 3) (Bassett et al., 2018). Definitions were refined further in the sub-groups and then checked against other resources as appropriate, for example, the IUPHAR Pharmacology Education Project website (Faccenda et al., 2019) and the core concepts from the Australasian project (Santiago et al., 2021; White et al., 2021), before consensus draft definitions were produced.

2. Identification of sub-concepts for each core concept

Following the completion of draft definitions, the sub-groups were asked to produce a consensus list of around three to five sub-concepts that underpin the core concept in question, each expressed as a sentence that included the name of the core concept. The following guidance on the nature of sub-concepts was used, based on an earlier project in Australia and New Zealand, and informed by the seminal work unpacking core concepts in physiology (Michael, Cliff, McFarland, Modell, & Wright, 2017; Santiago et al., 2021).

Sub-concepts are key underpinning ideas that are critical in order to fully understand the core concept. Sub-concepts are general statements, not specific to any pharmacological context (specific teaching points will be addressed in the next phase of this project). For example, in physiology, a sub-concept of the core concept homeostasis was, as follows; Homeostatic sensor: Homeostatic processes require a sensor inside the body. Sub-concepts are likely to have the same characteristics as core concepts themselves—i.e., fundamental, useful, enduring, and in some cases challenging and complex.

All expert sub-group members initially provided sub-concepts independently. Facilitators identified common elements using a content analysis approach like that depicted in Figure 3. Teams then worked together to develop draft sub-concept statements.

3. Refinement of core concept definitions and sub-concept statements at the Prato workshop

The draft definitions and sub-concept statements for each core concept were then refined further at a Core Concepts of Pharmacology workshop in Prato, Italy, in July 2022 (IUPHAR, 2022). The meeting was attended in person by 15 educators (4 research team members and 11 expert group members) and attended online by an additional 31 educators (4 research team members and 27 expert group members). On the first day of the workshop, sub-group facilitators presented the definitions of each concept and, following discussion and debate, participants voted either to accept or reject each definition via the anonymous audience response system Poll Everywhere. A predefined threshold was set at 80% agreement for any concept definition to be accepted (Santiago et al., 2021; White et al., 2023). Participants were asked to provide feedback on definitions with which they did not agree via a shared Google document. Concept definitions were then amended, based on the feedback received, and these revised concept definitions were discussed and debated, and then voted on again on Day 2. Twenty-one participants voted on the definitions presented on Day 1, and 27 participants voted on the revised definitions on Day 2.

4. Ratification of concepts, definitions and sub-concepts

Following the Prato workshop, 19 educators including the research team worked via a series of asynchronous activities and 20 online meetings to develop, finalise and order the sub-concepts. To facilitate this process, the following criteria for the form and style of items were established:

i. Sub-concepts would not refer to each other.
ii. Equations would not be used in definitions.
iii. Schematics would not be used in the sub-concepts.

Suggestion: Drug half-life (t ½) is the time taken for the concentration of drug in the plasma to fall by half

- Amount of time needed for the drug's concentration to reduce to exactly half the original.

- The amount of time necessary for plasma levels of drug to fall by 50%; this concept is only applicable to drugs eliminated via first-order elimination kinetics

- Drug half-life is the time taken for the concentration of drug in the plasma to decrease to half of its original value

- The period of time it takes to eliminate half the amount of a drug from the body

- Half-life can be used to describe various rates of drug movement – elimination half-life is the time it takes for half the drug to be removed from the tissue (so plasma half-life is when plasma concentration reduces by half; muscle tissue half-life is when concentration of drug in edible muscle tissue is reduced by half); absorption half-life is the time it takes for 50% of drug absorption to occur.

Suggestion: agonists and antagonists are molecules that interact with a drug target to elicit a biological response (agonist) or limit the opportunities for agonists to elicit a response (antagonists).

- An agonist is a molecule that elicits an action that is identical or similar to a specific drug on the same locus. An antagonist is a molecule that prevents a drug from eliciting the intended effect.
- Agonists and antagonists are drugs that bind to a receptor and produce an effect either in the case of the agonist or in the case of the antagonist do not produce an effect and limit the opportunities for other ligands to bind.
- An AGONIST is a drug that interacts with a receptor to produce a biological response. An ANTAGONIST is a drug that interacts with a receptor to prevent or dampen a biological response.
- A molecule that binds to a receptor and alters the receptor state, resulting in a biological response (agonist). A molecule that interacts with a receptor to block a biological response.
- A molecular entity that binds to a receptor, activating it to cause a biological effect; a molecular entity that binds to a receptor without activating it but blocking the effects of an agonist at that receptor
- Agonist is a chemical substance that can selectively bind and activate a receptor to induce a biological reaction.
- Antagonist is a chemical substance that can selectively bind and blocks the receptor activation by agonist.

FIGURE 3 Examples of the facilitator analysis of individual definitions and creation of single draft definition for discussion. The colour coding represents the content analysis conducted by the facilitator. The suggested consensus definition derived is shown at the top, and the individual expert group member definitions are summarised in the bullet points below.

iv. Descriptions of how a concept is taught would not be included.

Through an iterative and detailed analysis of all concepts and sub-concepts collectively, researchers identified changes needed to enhance the accuracy, clarity and coherence of the core concepts themselves, concept definitions and sub-concepts. These were shared with the wider expert group who had the opportunity to comment and suggest revisions. A final synchronous online workshop was then hosted to discuss the rationale for the changes and receive verbal feedback. Subsequently, the research team considered the written and verbal feedback to create the final concepts, definitions and sub-concepts.

5. Concept mapping of the core concepts

It is clear from similar work undertaken in other disciplines that a thorough, applied understanding of core concepts involves a knowledge of the relationships between concepts and an understanding of

the individual concepts themselves. Concept mapping was undertaken through the following exercises:

a. Prato concept mapping exercise

As part of the Prato workshop, participants worked in teams to produce concept maps that showed the relationships between the original 25 core concepts of pharmacology. The 15 workshop attendees were divided into four groups of three to five members. Two of the groups were asked initially to focus on the PK concepts, while the other two groups focussed on the PD concepts. Attendees were given an introduction to concept mapping, as framed by the work of Joseph Novak (1990). Each group was asked to produce a concept map 'of the explicit relationships amongst the core concepts of pharmacology'. They were advised that concepts should be shown as nodes, and that directional links between concepts using arrows must be labelled. Participants were advised to group related concepts together in clusters first before refining into specific relationships.

b. Post-Prato development of consensus concept map of core concepts

Five of the participants of the Prato concept mapping exercise then worked together to consolidate the elements of the four concept maps into a single consensus map. This process was not intended to produce a 'correct' or ideal map; rather, it was intended to combine the best elements of the maps produced by the Prato groups into a single exemplar of how the core concepts might logically be represented on a single diagram, from the perspectives of educators in the field.

2.4 | Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in https://www.guidetopharmacology.org and are permanently archived in the Concise Guide to PHARMACOLOGY 2021/22 (Alexander et al., 2021).

3 | RESULTS

3.1 | Defining the core concepts

The process of developing the core concept definitions involved multiple iterations. Even when these definitions reached 80% consensus, the subsequent development of sub-concepts at times revealed instances in which further clarity of the main concepts was required. Our iterative approach led to the re-writing of some definitions or, on occasion, modification of the core concept itself.

Seven core concept definitions were not accepted on Day 1 of the Prato workshop, which included individual variation in drug response, drug clearance, zero- and first-order kinetics, agonists and antagonists,

therapeutic index, dose/concentration–response relationship and drug potency (highlighted in Table 2). These were resolved through modification of the definitions, the addition of sub-concepts, and group debate and discussion. For example, the expert group raised the point that 'Drug clearance' could be defined as 'the volume of plasma cleared per unit time', as opposed to the proposed 'refers to the efficiency of drug elimination, defined as the ratio of the rate of drug elimination (e.g., $mg \cdot h^{-1}$) to the concentration of drug in plasma (e.g., $mg \cdot L^{-1}$)'. Ultimately, the former suggestion was included as a sub-concept (see Table 1). The other definitions that did not reach 80% agreement on Day 1 of Prato are discussed in more detail in Section 3.3.

In voting on Day 2 of the Prato workshop, all core concept definitions reached 80% or above consensus, except for 'Drug half-life' (see Table 1). The original definition was 'Drug half-life (t ½) is the time taken for the concentration of drug in the plasma to fall by half'. Debate focussed on the need for clarity regarding the half-life to which it referred: absorption, distribution and/or elimination. Following discussion, the core concept was modified to 'Drug elimination half-life (t ½)', and the definition expanded to include the fact that it is calculated during the elimination phase, because there was the potential for misconception without this clarification.

3.2 | Unpacking sub-concepts

Sub-concepts were drafted prior to the Prato workshop in July 2022. Refinement began in Prato and progressed through a series of online meetings with the sub-concepts team from August to November 2022. Following a final review by the expert group, the sub-concepts were agreed in December 2022 (see Table 2).

3.3 | Reaching consensus: Barriers and resolutions

Gaining consensus from such a broad range of international educators with differing expertise and diverse backgrounds was particularly challenging for some concept definitions and sub-concepts. Common areas of disagreement related to who the target audience were basic science students versus healthcare students, and first year students versus final year students. The educators' own areas of expertise influenced what they thought should be included. Clinical educators argued for outcomes to encompass concepts thought to be relevant for clinical practice, for example, one and two compartment models. Receptor theory specialists argued that concepts and sub-concepts were too basic and lacked critical quantitative pharmacological principles. One area of contention was the inadequate coverage and inclusion of the rates of drug–receptor interactions even though they are central to the original paper on quantitative pharmacology by AV Hill in 1909. Educators with strong mathematical backgrounds argued for greater inclusion of mathematical models and equations (Colquhoun, 2006). Through the consensus formation process, there was a clear need to establish the boundaries between core and threshold concepts (Stopford, 2021), with a focus on the criteria set in

TABLE 1 Voting on the definitions of each core concept. The table shows the results of the two votes that were taken at the Core Concepts workshop in Prato in July 2022. The results show the number and percentage of participants that endorsed the draft definition of each concept on Day 1 and the revised definition on Day 2. Definitions not accepted by >80% of participants are highlighted in yellow.

Core concept	Day 1		Day 2	
	Number of endorsing definition	% of endorsing definition	Number of endorsing definition	% of endorsing definition
Mechanism of drug action	21	100	27	100
Drug absorption	21	100	27	100
Drug bioavailability	21	100	26	96
Drug distribution	21	100	24	89
Drug metabolism	21	100	27	100
Structure–activity relationship	21	100	26	96
Steady-state concentration	21	100	25	93
Drug target	20	95	27	100
Drug affinity	20	95	26	96
Drug efficacy	19	90	25	93
Drug tolerance	19	90	27	100
Drug selectivity	19	90	27	100
Drug elimination	19	90	27	100
Adverse drug reaction	18	86	27	100
Drug interaction	18	86	26	96
Volume of distribution	18	86	26	96
Drug half-life	18	86	20	74
Drug–receptor interaction	17	81	24	89
Individual variation in drug response	16	76	25	93
Drug clearance	16	76	25	93
Zero- and first-order kinetics	16	76	23	85
Agonists and antagonists	16	76	22	81
Therapeutic index	14	67	25	93
Dose/concentration–response relationships	13	62	24	89
Drug potency	13	62	23	85

Section 2 (Part 4) that the sub-concepts would be applicable to students doing foundational courses in pharmacology. Because of the foundational level of the unpacking, consensus was reached that concepts should be framed as text, not as equations. It was agreed that the current level of unpacking should reject the inclusion of pictures/schematics and sub-concepts that were thought to be too complex at this stage and/or relate to how a concept would be taught. For example, it was agreed to reject a suggestion to define the additive and synergistic effects of antagonists because it was considered too complex for this level of unpacking and something that could be taught while covering the sub-concept '23.3. Drug interactions can have additive, synergistic or antagonistic effects'.

This paper represents the first level of unpacking of the core concepts. Many of the suggestions that were debated and rejected will form the basis of subsequent and more detailed unpacking, which will aim to develop learning outcomes and teaching resources associated with each outcome. In addition to the common areas of debate outlined above, the following section illustrates some other notable areas of discussion and the subsequent modifications to the concept that resulted.

3.4 | Drug–target interaction, agonists and antagonists

In the first stage of the process in 2022, '*agonists and antagonists*' were identified as a core concept of pharmacology (White et al., 2023). However, at the Prato meeting, it was decided to separate agonists and antagonists for ease of definition. When these concept definitions were voted on Day 1 in Prato, they only obtained 76% consensus, below the cut-off point of 80% for acceptance. The definition at this point for agonist was 'Agonists are molecules that interact with a drug target to elicit a biological response', and that for antagonist was 'Antagonists are molecules

TABLE 2 The consensus definitions core concepts (CC1-24) and sub-concepts (CC1.1 *etc.*) of pharmacology education. They can be broadly classified as related to pharmacodynamics (what the drug does to the body) or pharmacokinetics (what the body does to the drug).

A drug is a substance that, when introduced to the body, produces a biological effect for an intended purpose.

CC1. **Drug targets** are molecules (often proteins), the function of which can be modulated by a drug to produce a biological effect.

    1.1. Drug targets can refer to a range of molecules such as receptors, ion channels, enzymes, transporters, nucleic acids and signalling proteins.

    1.2. Drug targets can be located extracellularly, on the cell membrane, or intracellularly.

    1.3. Interaction of a drug with a target is described in different ways depending on the target (e.g., agonist, antagonist, substrate and inhibitor).

CC2. **Drug–target interaction** describes the different ways a drug interacts with a target to produce a biological effect.

    2.1. A drug's ability to interact with a drug target is determined by the intermolecular forces and steric match between drug and binding site.

    2.2. Drugs can bind to their targets reversibly or irreversibly depending on the type of bonds formed.

    2.3. Competitive interactions occur at the active/orthosteric site while allosteric interactions occur elsewhere on the drug target.

    2.4. Agonists are endogenous or exogenous molecules that have affinity for and efficacy at a receptor to elicit a biological response.

    2.5. Antagonists are molecules that have affinity for a receptor to limit the effect of agonists but lack intrinsic efficacy.

    2.6. Enzyme inhibitors are molecules with affinity for an enzyme to limit their enzymatic activity.

    2.7. Transporter inhibitors are molecules that have affinity for transporter proteins to limit the transport of ions, electrolytes or molecules across membranes.

    2.8. Biological therapeutics (biologics) are compounds derived from living organisms that target specific mediators of biological responses (e.g., inflammatory and immunological).

CC3. **Structure–activity relationship** describes the relationship between the structural characteristics of a drug and its binding site, and the resultant biological effect.

    3.1. Structure–activity relationships form the basis of rational drug design.

    3.2. Structure–activity relationships aim to predict potential targets from the molecular structure of the drug.

    3.3. Structure–activity relationships can be manipulated during drug development processes to alter therapeutic and adverse effects.

CC4. **Mechanism of drug action** refers to the process by which a drug produces a biological effect.

    4.1. Multiple mechanisms of action may be necessary to explain the consequences resulting from administration of a drug.

    4.2. The mechanism of drug action can be observed at multiple levels, including molecular, cellular and organ/system events that produce the observed outcomes.

    4.3. The mechanism of drug action may involve activating, enhancing, blocking or limiting a physiological process.

CC5. **Dose/concentration–response relationship** is the relationship between the dose/concentration of a drug and the magnitude of the response produced.

    5.1. Dose/concentration–response relationship can be graphically depicted as a curve with the dose/concentration on the x-axis and the response on the y-axis.

    5.2. For ease of visualisation, the x-axis of the dose/concentration–response is converted to a logarithmic scale that results in a sigmoid (s) shape known as the log dose/concentration–response curve.

    5.3. Dose refers to the amount of drug administered in vivo to an organism (e.g., mg or $mg \cdot kg^{-1}$) while concentration refers to in vitro/ex vivo the amount of drug per unit volume (e.g., $ng \cdot ml^{-1}$ or μM).

    5.4. From a graded dose/concentration–response curve, the potency (measured as the ED_{50} or EC_{50} for an agonist, or IC_{50}, K_b or pA_2 for an antagonist) and the maximal response (E_{max}) of a drug can be determined.

    5.5. Dose/concentration–response curves enable the pharmacodynamic responses of drugs to be compared and contrasted, and to determine whether drugs are full agonists, partial agonists, inverse agonists or antagonists.

    5.6. A quantal dose–response curve reflects the frequency of a defined response in a population at different doses of the drug rather than the fraction of maximal response, as reflected on a graded response curve.

CC6. **Drug affinity** is the binding strength of a drug to a target.

    6.1. Binding of drugs to receptors obeys the law of mass action.

    6.2. Affinity is commonly quantified through the determination of the equilibrium dissociation constant (Kd) and is formally defined as the ratio of the dissociation rate constant to the association rate constant.

    6.3. The lower the value of Kd, the lower the concentration of drug required to occupy a proportion of target, and the higher the affinity [Correction added on 26 January 2024, after first online publication: The preceding sentence has been corrected in this version.]

    6.4. The structure of a drug molecule and the conformation of the target determines affinity.

    6.5. The affinity of a drug can change as a consequence of the binding of an allosteric modulator.

CC7. **Drug efficacy** is the ability of a drug to elicit a response once bound to a drug target.

    7.1. Efficacy depends on the drug's ability to favour stabilisation of active conformational states of the agonist-bound receptor.

TABLE 2 (Continued)

7.2. Different agonists will produce varying levels of response: Full agonist (maximal response), partial agonists (sub-maximal response) and inverse agonists (suppress basal constitutive response).

7.3. A drug's maximum response can change as a consequence of the binding of an allosteric modulator.

CC8. **Drug potency** refers to the amount of a drug, expressed as the concentration or dose, needed to produce a defined effect.

8.1. Potency depends on both target (affinity and efficacy) and tissue (receptor number and drug availability) parameters.

8.2. Agonist potency is most commonly measured as the effective concentration/dose required to produce 50% of the maximum response (EC_{50} or ED_{50}).

8.3. Antagonist potency can be measured as the concentration that reduces the response to an agonist (pA_2).

8.4. Drugs are often compared by their potency.

CC9. **Drug selectivity** is a drug's ability to discriminate between drug targets.

9.1. Drug selectivity is dependent on the structure of the drug and the structure of the target.

9.2. Drug selectivity depends on the preferential affinity for one molecular target compared to a second.

9.3. At higher concentrations, the apparent drug selectivity may be reduced.

CC10. **Drug absorption** is the process by which a drug moves from its site of administration to the systemic circulation.

10.1. Drug absorption involves the movement of drugs across membranes and may include passive diffusion, carrier-mediated transport and active transport.

10.2. The rate and extent of drug absorption depends in part on the drug's physicochemical properties such as molecular size, hydrophobicity, or hydrophilicity and ionisation, as well as the formulation in which it is administered.

10.3. Different routes of drug administration (e.g., oral, buccal, subcutaneous and intramuscular) produce different rates and extents of absorption, based on the drug's physicochemical properties and the biological factors affecting absorption such as blood flow, local pH, gastrointestinal motility and diet.

CC11. **Drug bioavailability** is the fraction of administered dose of the parent drug that reaches the systemic circulation.

11.1. The bioavailability of an intravenous dose is defined as 1 (or 100%).

11.2. Absolute bioavailability, F, can be obtained by comparing the area under the curve (AUC) of a concentration–time relationship of one route of administration with that of the same drug given intravenously.

11.3. Relative bioavailability compares the proportion of parent drug reaching the systemic circulation from one non-intravenous route of administration to another non-intravenous route.

11.4. A formulation is the form in which the drug is administered (e.g., dermal patch, capsule and injectable) and can alter the rate and extent of release of soluble drug and, therefore, the bioavailability.

11.5. First-pass metabolism of drug in the liver or gut before it reaches the systemic circulation may decrease parent drug bioavailability as can other factors that decrease drug absorption.

CC12. **Drug distribution** is the reversible passage of drug between tissues, organs and compartments.

12.1. Drug distribution occurs initially in the central compartment (plasma and highly perfused tissues) before distribution into peripheral compartments (poorly perfused tissues).

12.2. Drug distribution occurs primarily through passive diffusion and is influenced by the physicochemical characteristics of the drug (e.g., molecular size, partition coefficient and ionisation).

12.3. Drug distribution is influenced by anatomical and physiological factors (e.g., local pH, blood flow and transport mechanisms) and by disease processes such as inflammation.

12.4. Drug distribution is influenced by the degree of reversible binding to proteins in the plasma; only unbound (free) drug can distribute into tissues.

CC13. **Volume of distribution** is an indication of the extent to which a drug is distributed to the tissues of the body and is defined as the theoretical volume needed to dilute the total amount of drug in the body at a given time to achieve the measured plasma concentration.

13.1. Drugs with large volumes of distribution are extensively distributed throughout the tissues of the body, while drugs with a small volume of distribution are more restricted to the plasma.

13.2. The volume of distribution can be affected by physicochemical factors of the drug (e.g., lipophilicity and protein binding), patient factors (e.g., body fat content and plasma protein levels) and tissue-specific factors (e.g., tissue blood flow and permeability).

13.3. The volume of distribution is related to elimination half-life: Given similar clearances, drugs with a small volume of distribution tend to have a relatively short half-life; large volumes of distribution tend to indicate prolonged half-life due to the reservoir effect of tissue distribution.

CC14. **Drug metabolism** is the chemical transformation of a drug into one or more products within the body.

14.1. Drug metabolism generates products (metabolites) that have their own chemical properties and may be biologically active or inert.

14.2. Drug metabolism does not occur for all drugs.

14.3. Drug metabolism can be mediated by enzymes and involves reactions such as oxidation, reduction, hydrolysis and/or conjugation.

(Continues)

TABLE 2 (Continued)

14.4. Drug metabolism can be modified by endogenous and exogenous factors such as genetics, disease states and xenobiotics.

14.5. Drug metabolism can alter the biological activity of a drug, terminate its action and facilitate its excretion.

CC15. **First- and zero-order kinetics** refers to changes in the amount of drug in the body as a function of time: Zero order refers to change by a constant amount per unit time, whereas first order refers to change by a constant fraction per unit time.

15.1. Most drugs follow first-order kinetics, which is observed when the rate of change of plasma concentration is proportional to the plasma concentration.

15.2. When the drug is eliminated by first-order kinetics, clearance and half-life are constant.

15.3. Zero-order kinetics is observed when a process is saturated. Saturation occurs when a process is operating at a maximum rate due to all the active sites on an enzyme or transporter protein being occupied.

15.4. Kinetics can change from first order to zero order as the drug concentration increases and elimination mechanisms become saturated.

15.5. First- and zero-order kinetics are mathematical models that can be distinguished graphically: A plot of drug plasma concentration versus time shows simple exponential decay for first-order kinetics and linear decline for zero-order kinetics. A plot of the log concentration versus time shows linear decline for first-order kinetics.

CC16. **Drug elimination** is the removal of drug from the body through metabolic and/or excretory processes.

16.1. Drug excretion refers solely to the physical processes that lead to the irreversible removal of a drug and its metabolites from the body, while metabolism refers to the chemical modification of drugs within the body.

16.2. Drugs and metabolites are excreted primarily via the kidneys into the urine. Other physiological excretion mechanisms include biliary, lactation, exhalation, sweating and salivation.

16.3. Rates of elimination can be constant (zero-order kinetics) or can be proportional to the plasma concentration (first-order kinetics).

16.4. The elimination rate constant describes the fraction of drug eliminated per unit time (e.g., /h).

16.5. The elimination rate is the mass of drug eliminated per unit time (e.g., $mg \cdot h^{-1}$).

CC17. **Drug elimination half-life (t ½)** is the time taken for the drug plasma concentration to decrease by 50% and is calculated during the elimination phase.

17.1. Drug elimination half-life is constant when drug elimination follows first-order kinetics.

17.2. Drug elimination half-life is proportional to volume of distribution when clearance is constant.

17.3. Drug elimination half-life is inversely proportional to clearance when volume of distribution is constant.

17.4. Drug elimination half-life can vary between patients, as patient, drug and environmental factors (e.g., disease state and age-related physiological changes) can alter drug clearance or volume of distribution.

17.5. Drug elimination half-life is used to estimate the time at which steady state is achieved following repeated administration of a drug that follows first-order kinetics.

CC18. **Drug clearance** refers to the efficiency of drug elimination, defined as the ratio of the elimination rate (e.g., $mg \cdot h^{-1}$) to the concentration of drug in plasma (e.g., $mg \cdot L^{-1}$).

18.1. Drug clearance can be represented as the volume of plasma that would be completely cleared of drug per unit time (e.g., $L \cdot h^{-1}$).

18.2. Drug clearance is constant when drug elimination follows first-order kinetics.

18.3. Drug clearance can vary due to patient, drug and environmental factors (e.g., disease state and age-related physiological changes).

18.4. Overall drug clearance is the sum of hepatic clearance, renal clearance and clearance by other routes.

CC19. **Steady-state concentration** is the concentration of drug in the plasma reached when the rate of drug absorption is equal to the rate of drug elimination following repeated or continuous dosing.

19.1. The time taken to reach steady-state concentration depends on the elimination half-life.

19.2. The plasma concentration achieved at steady state is influenced by the dose and dosing interval: Higher doses and/or more frequent dosing will result in higher steady-state concentrations.

19.3. The steady-state concentration is influenced by drug clearance and the dosing regimen may need to be adjusted for patients with altered clearance (e.g., patients with renal or hepatic disease).

19.4. The steady-state concentration can be reached more rapidly by administration of a loading dose at the start of therapy.

CC20. **Drug tolerance** is the diminished response to a drug following repeated or prolonged exposure.

20.1. Drug tolerance may occur through pharmacodynamic and/or pharmacokinetic mechanisms.

20.2. Drug tolerance can occur at a molecular or a systemic level.

20.3. When drug tolerance occurs, increasing concentrations of the drug will be required to evoke the same biological or clinical effect.

CC21. **Adverse drug reaction** and **adverse drug event** are terms that refer to harmful or undesirable response to a drug.

21.1. An adverse drug event is harm caused by appropriate or inappropriate use of a drug whereas adverse drug reactions are a subset of these events, wherein harm is directly caused by a drug under appropriate use (i.e., at normal doses).

TABLE 2   (Continued)

21.2. Adverse drug reactions are traditionally classified as predictable/dose-dependent (Type A) or unpredictable/idiosyncratic (Type B).

21.3. Type A adverse drug reactions are often inherently linked to the pharmacological effects of a drug and show a dose–response relationship and, thus, can be predicted.

21.4. Type B adverse drug reactions are idiosyncratic and have no link with the pharmacological mechanism of action and are thus unpredictable.

21.5. Adverse reactions can be impacted by changes in plasma concentration due to drug–drug interactions, drug–food interactions, changes in metabolism and additional disease states.

21.6. Adverse drug reactions may require the dose of the drug to be reduced or substituted with a different drug.

CC22. **Therapeutic index**, a measure of drug safety, is the ratio between the dose/concentration of a drug producing toxicity and the dose/concentration that produces a therapeutic effect.

22.1. In order to calculate the therapeutic index of a drug, the median effective dose (ED_{50}) and the median toxic dose (TD_{50}) or median lethal dose (LD_{50}) are derived from quantal log dose–response curves.

22.2. The therapeutic index is calculated by dividing the TD_{50} (or LD_{50}) by the ED_{50}.

22.3. The larger the therapeutic index, the more favourable the drug's margin of safety.

22.4. When administering a drug with a low therapeutic index, greater care needs to be taken to minimise drug toxicity, including monitoring its plasma concentration.

CC23. **Drug interaction** is the process by which a substance alters the action and/or kinetics of a drug.

23.1. Drug interactions can be direct, indirect and bidirectional.

23.2. Drug interactions may result in effects that are beneficial, deleterious and/or unexpected.

23.3. Drug interactions can have additive, synergistic or antagonistic effects.

23.4. Drug interactions between drugs and food constituents primarily change the bioavailability of a drug.

CC24. **Individual variation** in drug response refers to differences in response between individuals to the same dose of a drug.

24.1. Individual variation can arise from intrinsic factors such as genetics, age, sex, disease status or physiological conditions such as pregnancy.

24.2. Individual variation can arise from extrinsic factors such as concomitant medications, diet and exposure to chemicals and other environmental causes.

24.3. Individual variation in drug response can be due to changes in the biological consequence of drug–target interactions.

24.4. Differences in concentrations of a drug reaching its target site can be a major source of individual variation in drug response.

24.5. Individual variation in drug response may lead to treatment failures and/or toxicity that could require dose adjustment or substitution with another drug.

that have affinity for a drug target to limit the effect of agonists but lack efficacy'.

Members of the expert group who did not agree with a specific definition were invited to comment and provide their opinion in the shared definitions document. Some examples of the concerns raised included the following:

> I did not agree with this because I am not sure agonist would classify as a core concept (big idea).

> Receptor vs. target? We are broadly considering any interaction resulting in a biological response to be an agonist—substrates at enzymes, ions at **ion channels**, all agonists?

It became clear from these comments and subsequent discussions that many of the core concepts had a focussed bias on receptors as targets, in particular **G-protein coupled receptors** (GPCRs). It was suggested that this may have arisen for historical reasons, wherein receptors were the major drug target and that many textbooks still focus on such receptors as the main target for drugs. As a result of this discussion, it was suggested that by changing the wording of the core

concept of '*Drug-receptor interaction*' to '*Drug-target interaction*'; agonists, antagonists, inhibitors and modulators could be included as sub-concepts, which all represent ways in which drugs can interact with drug targets. In line with this, agonists and antagonists were incorporated as a sub-concept within the renamed concept of '*Drug-target interaction*', and the term 'drug target' in the definition of an agonist was changed to 'receptor'. Consensus was reached on Day 2 following these changes.

3.5 | Drug affinity, efficacy and potency

In the initial stages of the identification of the core concepts, drug affinity, efficacy and potency were all recognised as being important terms. Consensus agreement on definitions for drug affinity and efficacy was reached relatively early in the workshop (see Table 2); however, it was not reached for the original definition of '*Drug potency*' on Day 1. Written comments and feedback within discussions were used by the research team to modify the definition from 'Drug potency is the concentration of a drug needed to produce a defined effect' to 'Drug potency refers to the **amount** of a drug, **expressed as the concentration or dose**, needed to produce a defined effect',

before the second round of voting on Day 2, when a threshold of 85% was reached. The key issues arising, as evidenced through comments in Table S2, revolved around the definition being too simplistic, needing to be used as a comparator or point of reference (i.e., potency of one drug is relative to another drug), inclusion or exclusion of how it is quantified in the sub-concepts and the need to consider dose in addition to concentration in the definition and unpacking of this core concept.

Despite reaching a high level of agreement, aspects of the core concept of '*Drug efficacy*' were also debated at the sub-concept stage. Discussions focussed on differentiation between intrinsic versus therapeutic efficacy, which relied upon further contextualisation on application or background; for example, clinical pharmacologists often referred to therapeutic efficacy, while molecular pharmacologists thought of intrinsic efficacy. Ultimately, it was decided that '*Drug efficacy*' has a specific meaning within receptor pharmacology, thus the definition agreed for the concept was 'Drug efficacy is the ability of a drug to elicit a response once bound to a drug target'.

3.6 | Dose/concentration–response relationships and therapeutic index

Both core concepts represented a balancing act between providing the essence of their mathematical underpinnings, while being meaningful as stand-alone concepts. Prior to the Prato workshop, the main areas of discussion revolved around whether dose and/or concentration ought to be employed in describing these concepts, concerns that have been highlighted with other core concepts such as potency and efficacy. The differences in viewpoint often reflected the backgrounds of the expert group. For example, dose–response is applied in clinical settings, while in experimental studies using in vitro preparations, a concentration–response would be the preferred term. Similarly, there was a divergence amongst the group as to whether a therapeutic index is solely derived from the dose (as opposed to the concentration) of a drug. On Day 1 of the Prato workshop, the dose/concentration–response concept had been revised to state that it refers to 'the relationship between the dose/concentration of a drug and the response produced'. This wording received 62% agreement, and the main concern was the lack of the magnitude of the response elicited being mentioned. Thus, the wording was changed to incorporate this important element, and at the subsequent round of voting, the revised concept received 93% agreement.

On Day 1 of the Prato workshop, the definition for '*Therapeutic index*' was confined to using the phrase 'dose of a drug', as a means of constructing a ratio from which the therapeutic index is derived. This wording received 67% agreement from the expert group. During the subsequent discussion, the main reason for not agreeing with the wording was that concentration also should be included, because often in clinical scenarios (such as evaluating the safety of digoxin and gentamicin), the plasma concentration, as opposed to the dose, is used. Ultimately, in the revised core concept, it was agreed to include

dose/concentration to acknowledge that both terms are valid. In addition, 'a measure of safety' was incorporated into the concept to emphasise that this was a characteristic with which the relative harm of a drug could be determined. With these modifications, the '*Therapeutic index*' core concept achieved 93% consensus on the second round of voting.

3.7 | First- and zero-order kinetics

The original definition of '*Zero- and first-order kinetics*' only received 76% agreement in Day 1 of Prato: 'Zero- and first-order kinetics refers to changes in the amount of drug as a function of time: Zero order refers to change by a constant amount per unit time, whereas first order refers to change by a constant fraction per unit time.' Questions arose around the ordering of the kinetics (most drugs undergo first order—should this come before zero order in the concept title), or whether both models should become sub-concepts of a new core concept 'drug kinetics'. The use of equations in the definition was mooted, generating comments such as

> the definition for first order is traditionally a process where the rate of change of a substance, A, is proportional to the amount of that substance, i.e., $dA/dt = kA$. This applies to radioactive decay which is where students are most likely to have seen it in school-level science (in the UK). Zero order is where the rate of change is a constant ($dA/dt = k$).

Following discussions, and reinforcement of the agreement that equations would not be used in definitions, the only change made was to rename the concept '*First- and zero-order kinetics*', and a consensus level of 82% was reached in the second round of voting.

3.8 | Individual variation in drug response

The original definition pre-Prato was 'Individual variation in drug response refers to the differences in pharmacodynamic and/or pharmacokinetic responses to a drug due to the contribution of genetic and other factors'. On Day 1 of Prato, the wording of the definition was discussed, revised and simplified to remove reference to PD and/or PK wording, resulting in a new definition: 'Individual variation in drug response refers to the differences between individual responses to a drug.' Only 76% consensus was reached with the revisions implemented. This definition was further refined over the course of the workshop discussions. On Day 2, the concept definition was re-developed to include '**same dose of a drug**' with the sub-concepts exploring the 'other factors' that need to be considered in relation to individual variation. This led to the revised definition 'Individual variation in drug response refers to differences in response between individuals to the same dose of a drug', which received 93% consensus.

3.9 | Order of core concepts

The order of the core concepts generated extensive debate. Each student and educator orders information in a manner they believe is logical, but this 'logical' order is not necessarily shared; indeed, when working on this project, some educators were surprised at the order in which others taught pharmacology. One order may focus on the fact that the drug must access the body, move around until it finds its target(s), exert whatever effect it mediates and then is removed (i.e., starting with absorption). Alternatively, the focus may start with what a drug does, moving onto its access and removal from the system as secondary considerations (i.e., starting with drug binding to targets). The core concepts are presented linearly for this publication, starting with the concept of a 'drug target' (Table 2). While ordering the concepts, both linearly (see Table 2) and as a concept map (see Figure 4), it was realised that there was a need to define what constituted a 'drug' in the most basic sense and, further, that the notion of 'drug' has expanded to include biological agents such as **monoclonal antibodies** and small interfering RNA. Consequently, a definition of 'drug' was added as an overarching definition rather than a core concept (Table 2).

3.10 | Concept mapping

Four draft concept maps were produced by the teams at Prato, and an analysis was conducted after the meeting. The two PK maps and the two PD maps showed several common elements but also some key differences. The PK maps both included the sequence of drug absorption, distribution, metabolism and elimination as a central 'spine' in the diagram. One PK map added biodistribution, volume of distribution and drug clearance as measurements of drug absorption, distribution and elimination, respectively. The concept of 'drug' or 'drug dosing' was central to the two PK maps. In the second PK map, the group had incorporated both PK and PD core concepts together and had linked the PK and PD concepts using an intersection of '*drug distribution to a drug target*'. In the second PK map, there was also a group of other core concepts at the intersection of the PK and PD concept clusters that were broadly related to patient outcomes of these PK and PD concepts, and this idea was retained for the consensus concept map. The two PD concept maps represented drug target, drug–receptor interaction, drug affinity and drug selectivity as all linked but, overall, had fewer common elements than the PK maps.
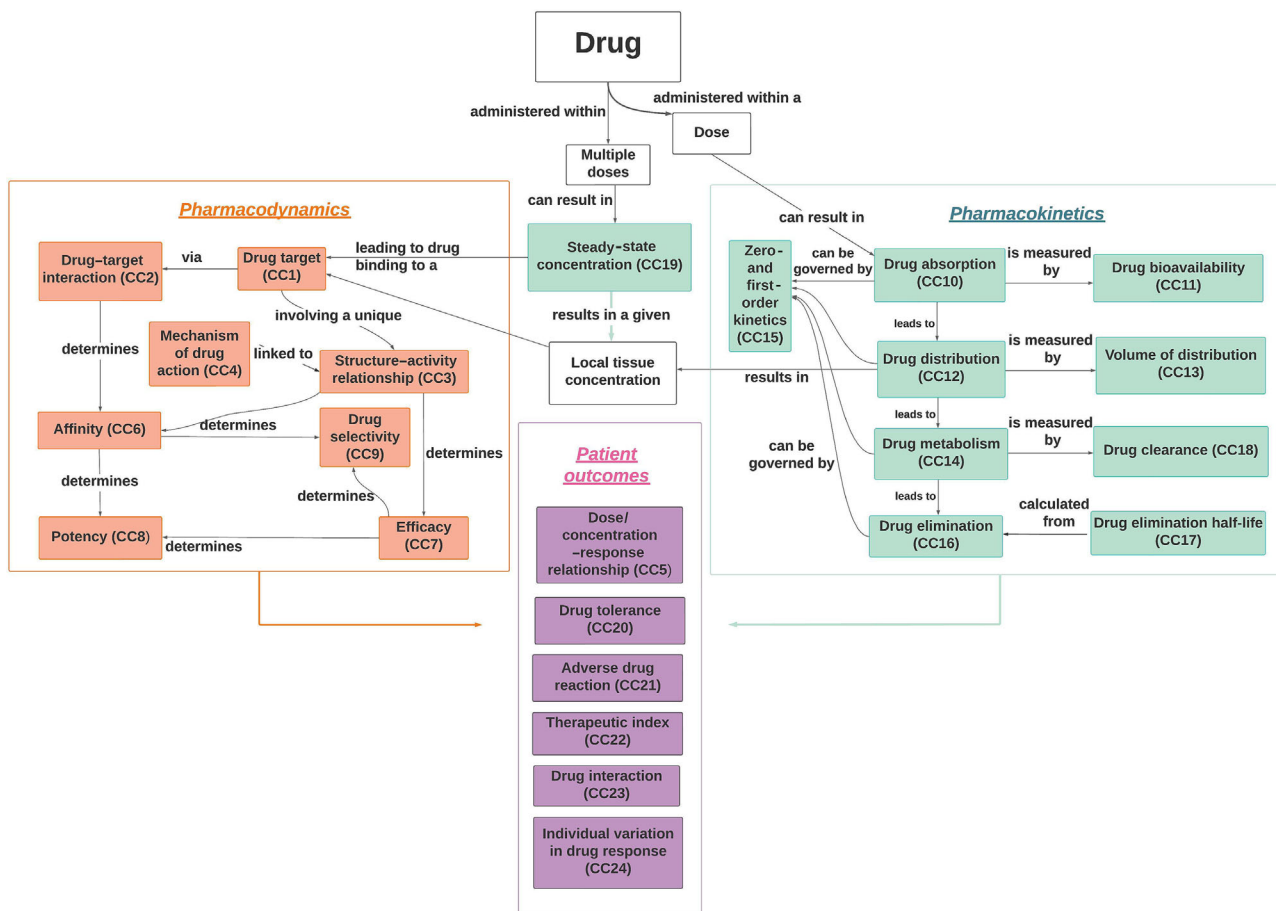

FIGURE 4   Overall consensus concept map: developed from the four original concept maps in Prato, showing the relationships between the various core concepts of pharmacology, ranging from the fate and action of drugs in the body to the resulting patient outcomes.

Following this analysis, one team member produced a first draft of an overall consensus map, which was distributed to the four other team members via the application Lucidspark. Two major iterations followed, based on feedback from the group, to produce the consensus concept map shown in Figure 4.

4 | DISCUSSION

In the first stage of this international project (White et al., 2023), the IUPHAR-Ed Core Concepts of Pharmacology expert group identified 25 core concepts of pharmacology that higher education students studying foundational courses in pharmacology should know, understand and be able to apply after graduation. This paper describes the next stages of the project. Through a robust methodology informed by previous core concept research in science, technology, engineering and maths (STEM) subjects including pharmacology (Michael, Cliff, McFarland, Modell, Wright, Michael, et al., 2017; Michael, Martinkova, McFarland, Wright, Cliff, Modell, & Wenderoth, 2017; Santiago et al., 2021), a collaborative and iterative research model was implemented, which refined the initial 25 core concepts to 24, unpacked 103 sub-concepts and developed a concept map of the relationships between the concepts.

For several of the core concepts, experts struggled to agree on a definition. Such disagreement is not unique to pharmacology, and also has been seen in the broader sciences, wherein scientists asked about the same crosscutting topic activated different knowledge depending on the context within which they work. More specifically, Slominski et al. (2020) found that scientists from physics and biology framed problems on fluid dynamics differently and, therefore, drew on different conceptual and epistemological resources to answer problems. While that study included scientists from different disciplines, a similar pattern emerged in our field, such that pharmacologists from different backgrounds (e.g., clinical vs. laboratory vs. computational backgrounds and research foci) also tended to frame problems differently and, thus, drew on slightly different resources and emphasised distinct facets of the information.

The current study builds on the foundations of the Australasian pilot (Santiago et al., 2021), which defined and unpacked 20 core concepts of pharmacology education. As in the Australasian study, this study limited the unpacking of sub-concepts to one hierarchical level, in contrast to the work of Michael and colleagues who unpacked their core concepts to four levels (Michael, Cliff, McFarland, Modell, & Wright, 2017; Michael, Cliff, McFarland, Modell, Wright, Michael, et al., 2017). Further unpacking of the core concepts of pharmacology may be important to assist educators to help students attain these concepts. A core concept included in our international, but not the Australasian, study was '*Drug–receptor interaction*' (White et al., 2021, 2023). The change of this core concept to '*Drug–**target** interaction*' in the current study is a significant one. It reflects the broad array of targets that modern drugs interact with (beyond the traditional pharmacology focus on receptors), from enzymes to **transporters** to nucleic acids (Santos et al., 2017).

Furthermore, it is possible that new drug targets will be discovered, and so by using the broader term 'target', this core concept can be future proofed.

Another difference between the concepts defined in this international project compared with those of the Australasian pilot (White et al., 2021) is the inclusion of numerous terms related to pharmacokinetics, which, it was debated, could be defined either conceptually or mathematically (e.g., drug elimination half-life, drug clearance, first- and zero-order kinetics and volume of distribution). This group is not the first to grapple with the question of the place for equations and graphs. As an example, a debate arose amongst biological scientists that examined whether the use of equations hampers communication between experts in biology (Chitnis & Smith, 2012; Fawcett & Higginson, 2012; Fernandes, 2012; Gibbons, 2012; Kane, 2012). Furthermore, concern was repeatedly expressed about the foundational pre-requisite knowledge, without which students would struggle with pharmacokinetics. This concern is supported by a growing body of literature that demonstrates that success in mathematics at the secondary level predicts performance in tertiary first-year science subjects and that students often come into science degrees unprepared for the quantitative nature of many fields (Koenig & Pike, 2013; McMillan & Edwards, 2019; Rylands & Coady, 2009). Additionally, 6% of the population experiences dyscalculia; 20% of individuals have dyslexia, 60% of whom have difficulty with maths; and 25% of the overall population struggle ((BDA), 2023; Shaywitz et al., 2021), which is reflected in approaches to teaching maths that remove the use of equations (Chazan et al., 2012). Ultimately, in this study, the research team decided that rather than being used as the definition of a core concept, equations and graphs should be introduced into teaching activities to expand upon these basic tenets and facilitate the development of students' critical thinking skills. It is noteworthy that, in the concept map, the core concepts that referred to the parameters for which there were discussions about the use of equations (e.g., half-life, drug bioavailability and volume of distribution) were grouped with and placed alongside the processes to which they related (e.g., elimination, absorption and distribution).

Reflecting the extensive breadth and depth of the educational experience of the expert group, the decision to omit equations and graphs in the definitions of pharmacokinetic sub-concepts was not without its opponents. Robust discussion and healthy conflict, which encourage diverse points of view, created a focus on how students new to the field would perceive the material. There was a recognition that what might seem logical or obvious to educators generally requires the lens of experience, which is inaccessible to the novice. Where possible, consensus was reached, but when differences of opinion persisted, the team agreed that acceptance was needed to move the project forward. Acceptance of a decision is not necessarily consensus; however, as Beatty (2006) pointed out,

> Consensus is critical in the case of joint acceptance, but it is consensus at a different level: not agreement concerning [an idea] per se … but rather agreement to let [it] stand as the position of the group.

It is a fundamental strength of this project that it brought together a global group of experts, with diverse backgrounds and educational experience, and often markedly different perspectives. Such disagreements, which are often informed by experiences with the misconceptions of varied cohorts of students, provide an excellent opportunity to address the uncertainty in the current body of knowledge. Students, particularly in science and medicine, often want clear unalterable facts and definitive answers (Patel et al., 2022; Scott et al., 2020), and therefore, an essential frameshift in their evolution from students to scientists is the ability to come to terms with this uncertainty (Bradley et al., 2021; Rosenberg et al., 2022; Witt et al., 2022). Our exposure to such diverse opinions in our own discussions will facilitate the development of learning activities that support students in their own transition.

In the current study, pharmacology educators often struggled to communicate complex mental models and thought processes across the different PD and PK expert groups during online discussions. It was through the process of concept mapping in person in Prato that the diversity in individual experts' conceptualisation of the pharmacology concepts, how they interrelate and how they explained them to their students became apparent. The theoretical foundations of concept mapping arose from cognitive psychologist David Ausubel's assimilation theory of meaningful learning (Ausubel, 1963) and were later developed and coined by Joseph Novak (Novak & Gowin, 1984). Since then, concept mapping has been increasingly used for teaching and assessment within health professions such as medicine, nursing and pharmacy (Cernusca & Strand, n.d.; Machado & Carvalho, 2020), in addition to supporting the processes of design and evaluation of curriculum in higher education (Noble et al., 2011). The creative interactions arising from the in-person concept mapping workshop in Prato provided a valuable learning opportunity for the visual depiction of the learning process and translating expert knowledge in a playful way. Although traditionally used to support teacher–student dialogue in the learning environment (Kinchin, 2003), the mapping exercise aided dialogue between experts. Unsurprisingly, although maps were developed cooperatively across PD and PK group members, many experts in the field differed in their approach to the mapping exercise, each integrating and bringing together their own theoretical knowledge aligned to their own teaching practices and experiences.

With the diverse student audiences that this project is aiming to capture, it was imperative to determine the foundational and essential concepts of pharmacology, rather than concepts that are more advanced and specific to particular student populations. While healthcare accrediting bodies and professional society recommendations throughout the world provide typical benchmarks for the foundational requirements for learner competencies, literature is still lacking on basic core teaching concepts in some science disciplines (QAA, 2023; Quesnelle et al., 2021; Santiago et al., 2021; Werners & Fajt, 2021). In the United Kingdom, the British Pharmacological Society has developed a set of core curricula for medicine (Ross & Maxwell, 2012) and another for pharmacology science degrees, which they have recently unpacked into broad learning outcomes and resources (Tucker et al., 2022; Wallace et al., 2021). Recent trends in US and international medical and healthcare education transformation have reduced the time allocated to foundational sciences like pharmacology, making it even more critical for educators to unite behind a shared vision of what must be included for students to achieve a basic conceptual understanding (Wallace et al., 2021). Research by the American Association of Pharmacology and Experimental Therapeutics (ASPET) Division for Pharmacology Education supports the need for consistent consensus-driven data to support a framework for effective pharmacology education across institutions and programmes (AMSPC, 2022). The current study builds on these aspirations, having drawn together an international team of pharmacologists to lay the groundwork for what could potentially be a global educational transformation. The overarching aim of this work is to inspire pharmacology educators across the breadth of the discipline to contribute to the creation of tools that will engage and inspire generations of students.

5 | CONCLUSIONS AND IMPLICATIONS

Twenty-four core pharmacology concepts have been defined and their underlying sub-concepts identified. An international consensus was developed by engaging faculty who teach in a wide variety of countries across a multitude of programmes. The project methodology, using iterative rounds of online meetings, asynchronous work and a hybrid meeting, led to rich debates that challenged expert educators to consider their foundational understanding and beliefs. While presentation of the concepts in tabular and mapped form is only one approach for ordering and presenting this body of knowledge, this work sets a framework that will guide understanding of the core concepts and inform curriculum design and assessment in pharmacology. The focus will now be on the identification of misconceptions associated with these concepts and sub-concepts and the development of teaching resources, including learning outcomes and concept inventories to support the acquisition and application of core knowledge. This will entail further coordinated research efforts to ensure that both concept inventories and teaching resources are evidence based and engage the global pharmacology community.

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Data are available on request. The data underlying this article will be shared on reasonable request to the corresponding author.

DECLARATION OF TRANSPARENCY AND SCIENTIFIC RIGOUR

This Declaration acknowledges that this paper adheres to the principles for transparent reporting and scientific rigour of preclinical research as stated in the *BJP* guidelines for Design and Analysis, and as recommended by funding agencies, publishers and other organisations engaged with supporting research.

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REFERENCES

(BDA)., B. D. A. (2023). About dyscalculia. Retrieved from https://www.bdadyslexia.org.uk/dyscalculia/how-can-i-identify-dyscalculia

Alexander, S. P. H., Christopoulos, A., Davenport, A. P., Kelly, E., Mathie, A., Peters, J. A., Veale, E. L., Armstrong, J. F., Faccenda, E., Harding, S. D., Pawson, A. J., Southan, C., Davies, J. A., Abbracchio, M. P., Alexander, W., Al-Hosaini, K., Bäck, M., Barnes, N. M., Bathgate, R., … Ye, R. D. (2021). The Concise Guide to PHARMACOLOGY 2021/22: G protein-coupled receptors. *British Journal of Pharmacology, 178*, S27–S156. https://doi.org/10.1111/bph.15538

AMSPC, A. (2022). Pharmacology knowledge objectives. Retrieved from https://amspc.org/resources/Documents/KOs%20Final-2022%20-edition-01092023.pdf

Ausubel, D. P. (1963). *The psychology of meaningful verbal learning*. Grune & Stratton.

Bassett, A. M., Brosnan, C., Southgate, E., & Lempp, H. (2018). Transitional journeys into, and through medical education for first-in-family (FiF) students: A qualitative interview study. *BMC Medical Education*, 18(1), 102. https://doi.org/10.1186/s12909-018-1217-z

Beatty, J. (2006). Masking disagreement among experts. *Episteme*, 3(1-2), 52–67.

Bradley, C. L., Schwartz, S. E., & Cooper, J. B. (2021). Communicating definitive uncertainty: Teaching pharmacy students to say "I don't know". *Currents in Pharmacy Teaching and Learning*, 13(8), 1032–1039. https://doi.org/10.1016/j.cptl.2021.06.020

Brewer, C. A., & Smith, D. (2011). *Vision and change in undergraduate biology education: A call to action* (p. 81). American Association for the Advancement of Science.

Brownell, S. E., Freeman, S., Wenderoth, M. P., & Crowe, A. J. (2014). Bio-Core guide: A tool for interpreting the core concepts of vision and change for biology majors. *CBE—Life Sciences Education*, 13(2), 200–211. https://doi.org/10.1187/cbe.13-12-0233

Cernusca, D., & Strand, M. (n.d.). Exploratory steps to stimulate a deep learning micro-culture. Introducing concept mapping strategies into a pharmacy curriculum. *rdannual*, 69. https://members.aect.org/pdf/Proceedings/proceedings20/2020/20_07.pdf

Chazan, D., Sela, H., & Herbst, P. (2012). Is the role of equations in the doing of word problems in school algebra changing? Initial indications from teacher study groups. *Cognition and Instruction*, 30(1), 1–38. https://doi.org/10.1080/07370008.2011.636593

Chitnis, N., & Smith, T. A. (2012). Mathematical illiteracy impedes progress in biology. *Proceedings of the National Academy of Sciences*, 109(45), E3055. https://doi.org/10.1073/pnas.1213115109

Colquhoun, D. (2006). The quantitative analysis of drug-receptor interactions: A short history. *Trends in Pharmacological Sciences*, 27(3), 149–157. https://doi.org/10.1016/j.tips.2006.01.008

Faccenda, E., Maxwell, S., & Szarek, J. L. (2019). The IUPHAR Pharmacology Education Project. *Clinical Pharmacology & Therapeutics*, 105(1), 45–48. https://doi.org/10.1002/cpt.1278

Fawcett, T. W., & Higginson, A. D. (2012). Heavy use of equations impedes communication among biologists. *Proceedings of the National Academy of Sciences*, 109(29), 11735–11739. https://doi.org/10.1073/pnas.1205259109

Fernandes, A. D. (2012). No evidence that equations cause impeded communication among biologists. *Proceedings of the National Academy of Sciences*, 109(45), E3057. https://doi.org/10.1073/pnas.1211892109

Frank, J. R., Snell, L. S., Cate, O. T., Holmboe, E. S., Carraccio, C., Swing, S. R., Harris, K. A., Glasgow, N. J., Campbell, C., Dath, D., Harden, R. M., Iobst, W., Long, D. M., Mungroo, R., Richardson, D. L., Sherbino, J., Silver, I., Taber, S., Talbot, M., & Harris, K. A. (2010). Competency-based medical education: Theory to practice. *Medical Teacher*, 32(8), 638–645. https://doi.org/10.3109/0142159X.2010.501190

Gibbons, J. (2012). Do not throw equations out with the theory bathwater. *Proceedings of the National Academy of Sciences*, 109(45), E3054. https://doi.org/10.1073/pnas.1212498109

Hestenes, D., Wells, M., & Swackhamer, G. (1992). Force concept inventory. *The Physics Teacher*, 30(3), 141–158. https://doi.org/10.1119/1.2343497

Hill, A. V. (1909). The mode of action of nicotine and curari, determined by the form of the contraction curve and the method of temperature coefficients. *The Journal of Physiology*, 39(5), 361–373. https://doi.org/10.1113/jphysiol.1909.sp001344

Hott, A. M., Huether, C. A., Mcinerney, J. D., Christianson, C., Fowler, R., Bender, H., Jenkins, J., Wysocki, A., Markle, G., & Karp, R. (2002). Genetics content in introductory biology courses for non-science majors: Theory and practice. *Bioscience*, 52(11), 1024–1035. https://doi.org/10.1641/0006-3568(2002)052[1024:GCIIBC]2.0.CO;2

IUPHAR, C. C. o. o. P. (2022). Concept-based pharmacology education workshop—18–20 July 2022. Retrieved from https://coreconcepts-pharmacology.org/2022/04/08/concept-based-pharmacology-education-workshop-18-20-july-2022/

Kane, A. (2012). A suggestion on improving mathematically heavy papers. *Proceedings of the National Academy of Sciences*, 109(45), E3056. https://doi.org/10.1073/pnas.1212310109

Kinchin, I. M. (2003). Effective teacher ↔ student dialogue: A model from biological education. *Journal of Biological Education*, 37(3), 110–113. https://doi.org/10.1080/00219266.2003.9655864

Koenig, J., & Pike, N. (2013). Perspectives from the UK and the US on integrating mathematics into the teaching and learning of the biological sciences in higher education. Retrieved from https://www.advance-he.ac.uk/knowledge-hub/perspectives-uk-and-us-integrating-mathematics-teaching-and-learning-biological

Machado, C. T., & Carvalho, A. A. (2020). Concept mapping: Benefits and challenges in higher education. *The Journal of Continuing Higher Education*, 68(1), 38–53. https://doi.org/10.1080/07377363.2020.1712579

McMillan, J., & Edwards, D. (2019). Performance in first year mathematics and science subjects in Australian universities: Does senior secondary mathematics background matter? Final Report.

Michael, J., Cliff, W., McFarland, J., Modell, H., & Wright, A. (2017). What are the core concepts of physiology? In *The core concepts of physiology* (pp. 27–36). Springer. https://doi.org/10.1007/978-1-4939-6909-8_3

Michael, J., Cliff, W., McFarland, J., Modell, H., Wright, A., Michael, J., Cliff, W., McFarland, J., Modell, H., & Wright, A. (2017). What does it mean to "unpack" a core concept? *The core concepts of physiology* (pp. 37–44). https://doi.org/10.1007/978-1-4939-6909-8_4

Michael, J., Martinkova, P., McFarland, J., Wright, A., Cliff, W., Modell, H., & Wenderoth, M. P. (2017). Validating a conceptual framework for the core concept of "cell-cell communication". *Advances in Physiology Education*, 41(2), 260–265. https://doi.org/10.1152/advan.00100.2016

Mulford, D. R., & Robinson, W. R. (2002). An inventory for alternate conceptions among first-semester general chemistry students. *Journal of Chemical Education*, 79(6), 739. https://doi.org/10.1021/ed079p739

Noble, C., O'Brien, M., Coombes, I., Shaw, P. N., & Nissen, L. (2011). Concept mapping to evaluate an undergraduate pharmacy curriculum. *American Journal of Pharmaceutical Education*, 75(3), 55. https://doi.org/10.5688/ajpe75355

Novak, J. D. (1990). Concept mapping: A useful tool for science education. *Journal of Research in Science Teaching*, 27(10), 937–949. https://doi.org/10.1002/tea.3660271003

Novak, J. D., & Gowin, D. B. (1984). *Learning how to learn*. Cambridge University Press. https://doi.org/10.1017/CBO9781139173469

Patel, P., Hancock, J., Rogers, M., & Pollard, S. R. (2022). Improving uncertainty tolerance in medical students: A scoping review. *Medical Education*, 56(12), 1163–1173. https://doi.org/10.1111/medu.14873

Project, I. C. C. o. P. E. (2022). The International Core Concepts of Pharmacology Education Project. Retrieved from https://coreconceptspharmacology.org/

QAA. (2023). Biomedical science and biomedical sciences subject benchmark statements. Retrieved from https://www.qaa.ac.uk/the-quality-code/subject-benchmark-statements/subject-benchmark-statement-biomedical-science-and-biomedical-sciences

Quesnelle, K. M., Zaveri, N. T., Schneid, S. D., Blumer, J. B., Szarek, J. L., Kruidering, M., & Lee, M. W. (2021). Design of a foundational sciences curriculum: Applying the ICAP framework to pharmacology education in integrated medical curricula. *Pharmacology Research & Perspectives*, 9(3), e00762. https://doi.org/10.1002/prp2.762

Rang, H. P. (2006). The receptor concept: Pharmacology's big idea. *British Journal of Pharmacology*, 147, S9–S16. https://doi.org/10.1038/sj.bjp.0706457

Rosenberg, J. M., Kubsch, M., Wagenmakers, E.-J., & Dogucu, M. (2022). Making sense of uncertainty in the science classroom. *Science & Education*, 31(5), 1239–1262. https://doi.org/10.1007/s11191-022-00341-3

Ross, S., & Maxwell, S. (2012). Prescribing and the core curriculum for tomorrow's doctors: BPS curriculum in clinical pharmacology and prescribing for medical students. *British Journal of Clinical Pharmacology*, 74(4), 644–661. https://doi.org/10.1111/j.1365-2125.2012.04186.x

Rylands, L. J., & Coady, C. (2009). Performance of students with weak mathematics in first-year mathematics and science. *International Journal of Mathematical Education in Science and Technology*, 40(6), 741–753. https://doi.org/10.1080/00207390902914130

Santiago, M., Davis, E. A., Hinton, T., Angelo, T. A., Shield, A., Babey, A.-M., Kemp-Harper, B., Maynard, G., al-Sallami, H. S., Musgrave, I. F., Fernandes, L. B., Ngo, S. N. T., Christopoulos, A., & White, P. J. (2021). Defining and unpacking the core concepts of pharmacology education. *Pharmacology Research & Perspectives*, 9(6), e00894. https://doi.org/10.1002/prp2.894

Santos, R., Ursu, O., Gaulton, A., Bento, A. P., Donadi, R. S., Bologa, C. G., Karlsson, A., al-Lazikani, B., Hersey, A., Oprea, T. I., & Overington, J. P. (2017). A comprehensive map of molecular drug targets. *Nature Reviews. Drug Discovery*, 16(1), 19–34. https://doi.org/10.1038/nrd.2016.230

Scott, A., Sudlow, M., Shaw, E., & Fisher, J. (2020). Medical education, simulation and uncertainty. *The Clinical Teacher*, 17(5), 497–502. https://doi.org/10.1111/tct.13119

Shaywitz, S. E., Shaywitz, J. E., & Shaywitz, B. A. (2021). Dyslexia in the 21st century. *Current Opinion in Psychiatry*, 34(2), 80–86. https://doi.org/10.1097/YCO.0000000000000670

Slominski, T., Fugleberg, A., Christensen, W. M., Buncher, J. B., & Momsen, J. L. (2020). Using framing as a lens to understand context effects on expert reasoning. *CBE−Life Sciences Education*, 19(3), ar48. https://doi.org/10.1187/cbe.19-11-0230

Stopford, R. (2021). Threshold concepts and certainty: A critical analysis of 'troublesomeness'. *Higher Education*, 82(1), 163–179. https://doi.org/10.1007/s10734-020-00628-w

Tansey, J. T., Baird, T. Jr., Cox, M. M., Fox, K. M., Knight, J., Sears, D., & Bell, E. (2013). Foundational concepts and underlying theories for majors in "biochemistry and molecular biology". *Biochemistry and Molecular Biology Education*, 41(5), 289–296. https://doi.org/10.1002/bmb.20727

Tucker, S., Zecharia, A., Guilding, C., Engel, K., & Page, L. (2022). Recognising and redressing inequity and bias through pharmacology education: A modern, practical and inclusive curriculum. *Pharmacology Matters*. Retrieved from https://www.bps.ac.uk/publishing/pharmacology-matters/august-2022/recognising-and-redressing-inequity-and-bias-throu

Wallace, M. J., Zecharia, A., Guilding, C., Tucker, S., & McFadzean, I. (2021). Developing a new undergraduate pharmacology core curriculum: The British Pharmacological Society Delphi Method. *Pharmacology Research & Perspectives*, 9(4), e00832. https://doi.org/10.1002/prp2.832

Werners, A., & Fajt, V. (2021). What a veterinary graduate should know about basic and clinical pharmacology: A Delphi study to finalize day-1 competencies. *Journal of Veterinary Pharmacology and Therapeutics*, 44(4), 568–574. https://doi.org/10.1111/jvp.12920

White, P. J., Davis, E. A., Santiago, M., Angelo, T., Shield, A., Babey, A.-M., Kemp-Harper, B., Maynard, G., al-Sallami, H. S., Musgrave, I. F., Fernandes, L. B., Ngo, S. N. T., & Hinton, T. (2021). Identifying the core concepts of pharmacology education. *Pharmacology Research & Perspectives*, 9(4), e00836. https://doi.org/10.1002/prp2.836

White, P. J., Guilding, C., Angelo, T., Kelly, J., Gorman, L., Tucker, S., Fun, A., Han, J., Chen, G., Samak, Y., Babey, A. M., Caetano, F. A., Sarangi, S. C., Koenig, J., Hao, H., Goldfarb, J., Karpa, K., Vieira, L., Restini, C., … Liu, Y. (2023). Identifying the core concepts of pharmacology education: A global initiative. *British Journal of Pharmacology*, 180(9), 1197–1209. https://doi.org/10.1111/bph.16000

Witt, E. E., Onorato, S. E., & Schwartzstein, R. M. (2022). Medical students and the drive for a single right answer: Teaching complexity and uncertainty. *ATS Scholar*, 3(1), 27–37. https://doi.org/10.34197/ats-scholar.2021-0083PS

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