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RESEARCH ARTICLE

Identifying the core concepts of pharmacology education: A global initiative

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Background and Purpose: In recent decades, a focus on the most critical and fundamental concepts has proven highly advantageous to students and educators in many science disciplines. Pharmacology, unlike microbiology, biochemistry, or physiology, lacks a consensus list of such *core concepts*.

Experimental Approach: We sought to develop a research-based, globally relevant list of core concepts that all students completing a foundational pharmacology course should master. This two-part project consisted of exploratory and refinement phases. The exploratory phase involved empirical data mining of the introductory sections of five key textbooks, in parallel with an online survey of over 200 pharmacology educators from 17 countries across six continents. The refinement phase involved three Delphi rounds involving 24 experts from 15 countries across six continents.

Key Results: The exploratory phase resulted in a consolidated list of 74 candidate core concepts. In the refinement phase, the expert group produced a consensus list of 25 core concepts of pharmacology.

Conclusion and Implications: This list will allow pharmacology educators everywhere to focus their efforts on the conceptual knowledge perceived to matter most by experts within the discipline. Next steps for this project include defining and

unpacking each core concept and developing resources to help pharmacology educators globally teach and assess these concepts within their educational contexts.

1 | INTRODUCTION

1.1 | What are core concepts?

Core concepts are big, important, fundamental ideas, which experts agree are critical for all students in their discipline to learn, remember, understand, and apply—in other words, to learn deeply. Core concepts in other disciplines include ideas such as *gravity* in physics (Hestenes et al., 1992) and *homeostasis* in physiology (Michael et al., 2017)—these concepts must be learnt and successfully applied by anyone claiming to understand these disciplines. Over the past 30 years, disciplines such as physics (Hestenes et al., 1992), statistics (Allen et al., 2004), information technology (Porter et al., 2019), psychology (Landrum, 1993; Zechmeister & Zechmeister, 2000), physiology (McFarland et al., 2017; Michael et al., 2017), and microbiology (Marbach-Ad et al., 2009; Merkel, 2012) have developed research-based lists of core concepts and related assessments of concept attainment.

In biology, for example, a large, coordinated approach led to the development of a set of core concepts in the early 2000s. The US National Science Foundation and American Association for the Advancement of Science brought together many educators to produce five core concepts of biology within a *Vision and Change Manifesto* (Brewer & Smith, 2011). Subsequent work led to the development of resources for biology educators to incorporate the teaching and assessment of these core concepts into their curricula (Brownell et al., 2014). Subdisciplines within biology, including physiology and microbiology (Hott et al., 2002; Marbach-Ad et al., 2009; Merkel, 2012), have since identified further, more specific core concepts.

1.2 | Why identify core concepts in pharmacology?

Pharmacology, defined as the science of drugs or medicines and their interactions with biological systems, integrates knowledge from a number of disciplines, including, but not limited to, physiology, pathology, chemistry, biochemistry, structural biology, and mathematics. Pharmacology is taught across the breadth of health professional, biomedical and basic science contexts, and draws upon basic science, clinical pharmacology, and therapeutics concepts. It is taught at undergraduate and graduate levels and via a range of instructional modes (Rubaiy, 2021). In these various programs, the enormous volume of pharmacology content is often afforded limited time within curricula. In recent years, the creation of integrated courses and the merging of physiology and pharmacology departments has

What is already known

- Identification of the core concepts of disciplines have helped transform teaching and assessing student understanding.

What does this study add

- This study identifies 25 core concepts that can be applied within all pharmacology education contexts.

What is the clinical significance

- Pharmacology education can now focus on ensuring that graduates develop and apply the critical concepts.

contributed to the decreased time dedicated to teaching pharmacology concepts. No pharmacology program, however well-resourced, has sufficient time to teach students all the knowledge in the discipline. While the sheer volume of the "potential curriculum" increases exponentially each year, available time for teaching continues to decline overall (Lloyd et al., 2013). This is obvious in integrated health professions education, where economic and administrative considerations, medical education reforms shortening the preclinical years, and a focus on competency-based models can all minimise time for teaching foundational sciences, including pharmacology.

Studies of health professional graduates report perceived gaps in pharmacology knowledge (Bullock & Leversha, 2019). Manias and Bullock (2002) conducted six focus groups with clinical nurses in Australia and found that "all nurses experienced difficulties in understanding and demonstrating pharmacological concepts in the clinical practice setting."

The authors of the well-cited investigation into prescriber error for the General Medical Council (London), known as the EQUIP study, argued "More could have been done during undergraduate education to link theory with practice" (Dornan et al., 2009). In order to ensure educational effectiveness and patient safety, we contend that it is essential to first identify the foundational concepts of pharmacology

students require in order to provide them with the ability to link theory to practice.

The COVID-19 pandemic has highlighted the need for a skilled workforce across a range of industries to meet the healthcare requirements of our global communities. From the discovery of new medicines to safe and effective prescribing, our scientists and health professionals require the ability to apply these enduring ideas years after graduation.

In addition to providing consensus on the critical knowledge all students studying pharmacology need, core concepts provide a range of other benefits. Assessments that test their attainment, known as concept inventories, provide students and educators with the tools to measure their progress on the "knowledge that matters." With such tools, educators can compare the effectiveness of innovative paedagogical methods, and administrators can rigorously and reproducibly compare program learning (Sands et al., 2018).

1.3 | How have core concepts been identified in other disciplines?

Over the past 30 years, a range of approaches have been developed to identify core concepts, mostly employing groups of disciplinary experts to identify the critical ideas that all students need to master. Most disciplines have used a Delphi method, involving a group of experts completing cycles of surveying and refinement until consensus is reached (Boneau, 1990; Brownell et al., 2014; Landrum, 1993; Merkel, 2012; Parekh et al., 2017; Wright & Hamilton, 2008). Core concepts have also been extracted from textbooks, either via page-by-page expert analysis (Zechmeister & Zechmeister, 2000) or via data-mining techniques (Foster et al., 2012).

1.4 | Pilot project to identify pharmacology core concepts in Australasia

Beginning in 2019, pharmacology educators based in Australia and New Zealand engaged in research that identified 20 core concepts of pharmacology education (White et al., 2021). This group, including some authors of the present article, initially surveyed 41 Australasian educators, of whom 23 engaged in follow-up workshop activities. Subsequently, an expert group of 12 academics extracted a set of core concepts, which were then refined and confirmed by a survey of an additional 30 academics. The resulting core concepts were then defined and unpacked (Santiago et al., 2021). This project provided proof-of-concept that core concepts could be identified in pharmacology, suggesting that such an approach might work at a broader international level. Building on the experience and findings of this Australasian approach, the authors were confident that a more international approach would have the potential to be impactful on a global scale.

1.5 | Overview of a multi-step, international approach to identify the most important concepts within a discipline

In late 2021, an international group of pharmacology education leaders committed to identifying current core concepts of pharmacology education and to developing resources to help educators around the world teach and assess those concepts. That initiative, described in detail below, set out to answer the following research questions.

- Which ideas do pharmacology educators across many countries believe to be the core concepts of our discipline?
- What are the most common conceptual terms used in pharmacology texts?
- Which of the most common terms from pharmacology texts do educators believe to be core concepts?
- To what extent do lists of potential core concepts derived from surveying educators agree with those produced via text mining?

2 | METHODS

A two-phase approach was used to identify the core concepts of pharmacology education (Figure 1). We used multiple approaches to ensure coverage of the entire field of pharmacology and a variety of sources of information to mitigate personal biases. The first, exploratory phase included an empirical approach, specifically data mining of
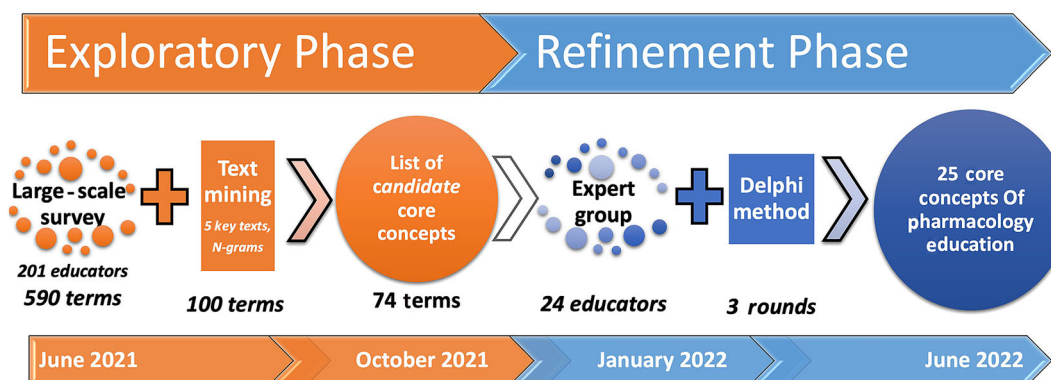
FIGURE 1 Summary of the two-phase approach used to identify the core concepts of pharmacology education. An n-gram is a contiguous sequence of n items from a given sample of text or speech.

five key textbook introductory sections. In parallel, an online survey of pharmacology educators was used to complement the text mining, and the terms identified using these two methods were merged to develop a list of 74 candidate terms.

The second, refinement phase involved the expert group of 24 in three rounds of a Delphi Method through which they analysed the candidate terms and produced a consensus list of 25 core concepts of pharmacology education.

2.1 | Survey of pharmacology educators from 17 countries

2.1.1 | Ethics

The survey was conducted under approved protocol #22727 of the Monash University Ethics in Human Research Committee. The data and statistical analysis comply with the recommendations of the *British Journal of Pharmacology* on experimental design and analysis in pharmacology.

2.1.2 | Survey development

The research team developed an online survey to gather potential core concepts from a wide range of international pharmacology educators. The survey was based on that used for the pilot study (White et al., 2021; see survey in Data S1). The survey consisted of three parts: (i) theoretical information about core concepts; (ii) a series of demographic questions; and (iii) the key prompt and question to elicit potential core concepts, shown below.

> Imagine your current/recent pharmacology students 3 to 5 years after their graduation: What few essential core concepts would you expect them to remember, understand deeply, and apply effectively in their professional work? Please list a few—ideally between 3 and 7—core concepts that are foundational for pharmacology students in the text box below. Feel free to write as much or as little as you wish about your core concepts. Your draft concepts should be big ideas that are useful to solve problems and enduring, and they should not be topics or facts.

2.1.3 | Demographics

The survey was distributed online via national pharmacology societies and networks of pharmacology educators. A total of 201 pharmacology educators voluntarily responded to the survey, resulting in 163 complete responses (81% response rate). Respondents were from a total of 17 countries across six continents (Table 1). Almost two-thirds of the respondents identified as female (66%) and 32% identified as male, with 1% preferring not to identify. The majority (73%) of respondents had been teaching pharmacology for more than 10 years, while 18% had 3–10 years' experience and 9% had less than 3 years' experience. Eighty-two percent recorded a PhD as their highest academic qualification, with 11% reporting a Masters qualification and 6% a combined MD/PhD or PharmD. The respondents taught a range of health professional and science students, and the disciplines taught similarly encompassed the range of basic and clinical sciences (Table 1). Most respondents taught students from more than one disciplinary or professional cohort.

2.1.4 | Text mining of key pharmacology textbooks

The introductory sections of each of five key textbooks, selected by the research team as the most commonly used texts in their local context, were mined to extract the pharmacology terms that were most commonly used. The relevant texts and sections were:

1. Rang & Dale's Pharmacology, 8th Edition Section I: General Principles ISBN 978-0702053627

TABLE 1　Demographic and educator context for the survey respondents

Educator location (number of respondents in the location)	Student cohorts (number of respondents who teach the cohort)	Disciplines taught (number of respondents who teach the discipline)
Japan (67)	Medical (83)	Basic pharmacology (100)
United Kingdom (27)	Pharmacy (67)	Systems pharmacology (28)
Canada (20)	Nursing (39)	Clinical Pharmacology (20)
United States (18)	Dentistry (27)	Pharmacotherapy/clinical management (18)
New Zealand (5)	Physiotherapy (9)	ADME/pharmacokinetics (8)
Ireland (4)	Osteopathy (3)	Physiology (8)
Nigeria, Australia (3)	Science (27)	Microbiology, medicinal chemistry and epidemiology (1)
Brazil, Sweden, Colombia, Haiti, Hong Kong, Indonesia, Qatar, South Africa, Zambia (1)	Biomedical Science (58)	
	Post-graduate research (49)	

2. Goodman and Gilman's Manual of Pharmacology and Therapeutics, 13th Edition Section I: General Principles ISBN 978-0071624428
3. Katzung's Basic and Clinical Pharmacology, 14th Edition Section I: Basic Principles ISBN 978-1259641152
4. Golan's Principles of Pharmacology, 4th Edition Section I: Fundamental Principles ISBN 978-1451191004
5. Bryant and Knights' Pharmacology for Health Professionals, 4th Edition Unit II: Principles of Pharmacology ISBN 978-0729541701

Contents of the introductory chapters were converted to a raw text file using PyPDF2 as the source texts were in PDF format. Pre-processing was conducted using the Natural Language Tool Kit (NLTK). To begin, stop words (e.g., "the" and "an"), punctuations, numbers, tags, and special characters were removed, and uppercase letters were converted to lowercase. Words shorter than two characters were also removed. Next, additional user-defined keywords such as "chapter" and "section" were excluded from the corpora. Artefacts arising from encoding (e.g., "\u02da" and "\n") and ligatures (e.g., "ff" appearing as "©") were also addressed. Subsequently, since the majority of the keywords were nouns, words with noun tags were extracted using parts-of-speech tagging. Finally, all of the extracted words were normalised using stemming, which removes suffixes and prefixes from word roots, such that keywords "drugs" and "drug" would all be considered equal under the word root "drug." Key terms were extracted using scikit-learn's Term Frequency-Inverse Document Frequency (TF-IDF) Vectorizer with an N-gram range between 2 and 3. The top 100 terms sorted by TF-IDF score were then selected for further analysis.

2.1.5 | Delphi method

The expert group used a criterion-based Delphi method to identify core concepts of pharmacology education. The following six best-practice elements of the Delphi method (see Bhandari & Hallowell, 2021) were incorporated into our study. First, an expert group technique was used to answer the question "What are the core concepts of pharmacology education?" Indirect interaction between participants was maintained for Rounds 1 and 2. A predefined threshold was set at 80% agreement for any candidate term to be adopted as a core concept. The anonymity of voting was maintained for the expert group throughout the process. Controlled feedback was provided in the form of a summary of voting after Round 2 and 3. Three iterative rounds of analysis were conducted.

2.1.6 | Research team and expert group composition

The research team (PW, TA, CG, JK, and LG) was formed at the beginning of the process, and oversaw the Delphi process. The research team aimed to recruit a minimum of 20 expert group members based on best practice guidelines for "15 to 30 participants from the same discipline" in health sciences education research

(De Villiers et al., 2005). In order to remove any conflict of interest, members of the research team led discussions regarding potential core concepts but were not voting members of the expert group. To select the expert group, the roles and experience needed were first identified. Each member of the research team was asked to invite experienced pharmacology educators to participate. All expert group members selected met at least two of the inclusion criteria shown in Table S1.

Consequently, 24 pharmacology educators were recruited by direct invitation from the research team to be members of the expert group, comprising 14 women and 10 men, from a total of 15 countries across six continents: Australia, Brazil, Canada, China, Colombia, India, Ireland, Japan, Lebanon, Malta, Nigeria, Qatar, Sweden, the United States, and the United Kingdom. Twenty of the expert group members reported their highest qualification as PhD, two MBBS/MD, and one PharmD. The group included a number of practising health professionals and scientists from industry and academia. Fourteen members reported a teaching qualification at Graduate Certificate or higher level. Expert group members' pharmacology teaching experience ranged from 2 to 60 years, with a median of 15 years.

The expert group used the Delphi method to identify core concepts of pharmacology education, conducted under the approved protocol #31379 of the Monash University Ethics in Human Research Committee. A multi-faceted approach was used, in which the expert group were provided with a range of resources to achieve the aim of ensuring coverage of the entire field; deriving terms from a variety of sources to mitigate personal biases and including empirical data (text mining) and expert opinion (educator survey).

2.1.7 | Training of the expert group

Expert group members attended an initial online workshop in which they received information about the project, core concepts, and the Delphi method. Five criteria were presented to the group as a means by which to evaluate candidate core concepts for inclusion: fundamental, useful, enduring, complex and challenging. These criteria were refined from those used in the Australasian study (White et al., 2021).

2.2 | Three rounds of Delphi method

In Round 1, expert group members were given the consolidated list of 74 candidate terms, which was produced by merging the outcomes of text mining of five key textbooks with the survey responses from 163 pharmacology educators. Individually and without consultation, expert group members analysed each term using the five core concepts criteria and then voted as to whether they perceived each term in the list to be a core concept of pharmacology education or not. Members were also asked to identify any potential core concepts of pharmacology absent from the list of 74 terms. The terms that achieved a minimum threshold of 80% agreement by the expert group members were accepted as core concepts and not discussed further.

Terms that were agreed to be core concepts by less than 50% of expert group members in Round 1 were rejected and not discussed further. In Round 2, the terms deemed missing from the candidate list within Round 1 were analysed and voted on using the same criteria.

Additional online workshops were held between Rounds 2 and 3. The intention of these workshops was to refine the list of core concepts, by clarifying areas of duplication, overlap, and hierarchical disconnect. Expert group members attended one of two online sessions into which they self-selected, depending on their area of expertise: (i) pharmacokinetic (PK, led by CG and ST) core concepts or (ii) pharmacodynamic (PD, led by JK and LG) core concepts. In the workshops, the co-leads facilitated a discussion on the small groups of related terms, which we called clusters (for example, *margin of safety* and *therapeutic index*) that had emerged during Rounds 1 and 2. The research team recommended a single term from each cluster to be included in Round 3 voting, and these recommendations were voted on by the experts prior to the workshop. Discussions within the workshop focused on recommendations for which there was less than 80% agreement.

In Round 3, expert group members analysed the terms that received between 50% and 79% agreement in Rounds 1 and 2. The co-leads for the two subgroups (pharmacokinetics [PK]; CG and ST,

and pharmacodynamics [PK]; JK and LG) separated the terms into PK and PD groupings (Table 2).

3 | RESULTS

The exploratory phase of the project was designed to provide the expert group with a comprehensive list of proposed core concepts, comprised of both the terms most frequently found in the five key textbook chapters and those identified through the survey of 163 international educators.

3.1 | Survey free-text responses: Development and refinement of a list of terms

Five hundred and ninety individual terms were submitted as core concepts of pharmacology education by 163 respondents who addressed this survey question. A term was defined as one or more words that capture a single idea. Duplicates were removed by two raters (YS and PW), and clusters of words judged to have equivalent or similar meanings were grouped under the term that best reflected the central

TABLE 2 Purpose, response format, and the number of responses for each of the three rounds of the Delphi method

Round	Purpose of survey	Response format	# of responses
1	Analyse list of terms from exploratory phase using criteria	Likert scale (ranging from 0 to 5)	21
	Vote on inclusion of each of 74 terms from Exploratory phase as core concepts	Vote term to be core concept or *other*. *Other* included *broad topic, simple concept, fact, term not specific to pharmacology*	
	Propose any terms that were missing from exploratory phase list	Free text	
2	Analyse list of terms proposed by expert group during Round 1	Likert scale	23
	Vote on inclusion of each term proposed during Round 1 as core concept	Vote term to be core concept or *other*. *Other* included *fact, simple concept, broad topic, no specific meaning in pharmacology*	
3	Vote on inclusion of each term that reached 70%–79% agreement during Round 1 or Round 2 as core concept	Vote term to be core concept of pharmacology education or not	20

Note: The number of responses was based on the availability of the 24 expert group members at that stage and that all 24 experts voted at least twice.

TABLE 3 Resolution of repeated terms and synonyms

Terms proposed by respondents	Related terms proposed by respondents	Representative term used in Delphi method
drug target (8); drug targets, targets, drug target and off-target; target identification; drug target interaction; drug targeting; molecular drug targets; targets for drug action	drug-target interaction; the difference between a classical receptor and other types of drug targets; target identification; drug/target interactions (especially G-coupled receptors); approaches in terms of targeting a physiological system; drug-receptor interaction	Drug target Drug–receptor interaction

Note: The example of terms related to "drug target" illustrates the process used by the research team to choose a single term to represent closely related synonyms. Respondents proposed 16 terms as core concepts that were identical or close synonyms of "drug target" and a further six terms related to this term. The research team consolidated these 24 terms to two terms for inclusion in the Delphi process: "drug target" itself and "drug–receptor interaction."

meaning (see Table 3 for an example). The final list of 48 individual terms is shown in Table 4.

3.2 | Text mining: Generation of a list of terms

The 100 most frequent terms specific to the discipline were mined from the corpus produced by combining the five texts. Research team members (CG, JK, LG, ST, and PW) performed the same consolidation process as that used in the previous exploratory phase to yield a list of 38 terms from the text mining (Table 4).

3.3 | Consolidation of survey and text mining terms into a single list of terms

The 48 terms produced by refinement of the survey responses and the 38 terms produced by refinement of the text mining terms were further refined by the research team, resulting in a final list of 74 proposed core concepts.

3.4 | Refinement phase

3.4.1 | Delphi Rounds 1 and 2

Of the 74 terms considered by the expert group members in Round 1, seven were automatically adopted as core concepts, having reached the voting threshold (80% agreement), 35 terms were flagged for further discussion (50–79%), and 32 terms were automatically rejected (<50%). Note that two of the seven terms accepted during Round 1 were later merged—*concentration-response relationships* and *dose-response curve*—to form *Dose/concentration response relationships*. During Round 1, expert group members collectively proposed an additional 97 terms that they felt were missing from the Round 1 list of terms. In Round 2, 23 terms were flagged for further discussion, and the remaining 74 terms were rejected. As the total number of responses for the Delphi rounds varied from 20 to 23, the 80% threshold for acceptance varied from 16 to 18 respondents.

3.4.2 | Consolidation of "clusters" of related terms prior to Round 3

Prior to Round 3, the research team worked with the expert group to consolidate a subset of some closely related terms that had reached the threshold for further discussion during Rounds 1 and 2. For example, *structure–activity relationship* and *structure–function relationship* had both reached the threshold for discussion, and a single term to represent them was required to avoid the inclusion of close synonyms in the final round of the Delphi method.

Thirteen such "clusters" were identified, and the research team came to agreement on a single term that met the criteria to be a core concept and best represented each cluster. Seven of the 13 recommendations were endorsed by 80% of the expert group. In the two workshops held between Rounds 2 and 3, single terms were identified to represent each of the remaining six clusters in the final round.

3.4.3 | Delphi Round 3

In Round 3, expert group members voted online on each of the 25 terms that had reached the threshold for further consideration in Rounds 1 and 2, and that had been chosen for inclusion during the consolidation of clusters. Eighteen terms were accepted as core concepts: 14 outright from Round 3 voting; and the remaining four by consensus of the research team on the basis that they reached 70%–79% agreement in Round 3 and filled an essential gap. A total of 25 terms were therefore accepted as international core concepts of pharmacology education (Table 5).

3.5 | Comparison of final list of core concepts with initial survey and text mining results

Given that this is the first time that a combination of text mining and survey have been used to elicit candidate core concepts, it was of interest to analyse the source of the final list of 25 terms. Nineteen of the 25 core concepts (76%) were exact matches to terms in either the text mining refined list or the survey refined list, and eight were present in both. A further eight core concepts were present in the survey list but not the text mining list and three core concepts were present in the text mining list but not the survey list (Data S1). Six terms had no exact match in either text mining or survey list and were derived from the merging of synonyms during the workshops between Rounds 2 and 3.

4 | DISCUSSION

Our project has significance for the international pharmacology community, in that a consensus list of concepts central to the teaching and learning of our discipline was produced. This is the first time to our knowledge that a truly international initiative has produced a consensus list of f-focused core concepts. Over 200 pharmacology educators from 22 countries across six continents contributed to the effort: 201 responded anonymously to the survey; and there were 24 expert group members and 6 research team members. Given the range and complexity of content and context, we employed a phased approach to the identification of core concepts, building on the lessons from other disciplines (Hott et al., 2002; Merkel, 2012; Michael et al., 2017; Parekh et al., 2017; Tweedie et al., 2020; Zechmeister & Zechmeister, 2000) and our own pilot studies in Australia and

TABLE 4 Synthesis of text mining and survey terms

Text mining (refined list of 38)	Survey (refined list of 48)	Merged list (74 terms)	
Agonist	ADME	ADME	Drug receptor
Amount of drug	Agonists/antagonists	Agonist	Drug response
Concentration of drug	Allosteric drugs	Agonists/antagonists	Drug safety
Dose response	Bioavailability	Allosteric drugs	Drug selectivity/specificity
Dose–response curve	Biologics	Amount of drug	Drug target
Drug absorption	Common systemic pharmacology	Bioavailability	Drug therapy
Drug action	Compartment models	Biologics	Drug tolerance
Drug administration	Competitive/non-competitive inhibition	Compartment models	Drug–receptor interaction
Drug binding	Concentration–response relationship	Competitive/non-competitive inhibition	Drugs
Drug bioavailability	Dose regimens	Concentration of drug	Duration of action
Drug clearance	Drug absorption	Concentration–response relationship	ED_{50}
Drug compartment	Drug action	Dose regimens	First-order kinetics
Drug concentration	Drug affinity	Dose–response curve	First pass effect
Drug distribution	Drug design	Drug absorption	Individual variation
Drug dose	Drug development	Drug action	Integrative pharmacology
Drug effect	Drug discovery	Drug administration	Ion channel
Drug effect	Drug distribution	Drug affinity	LD_{50}
Drug elimination	Drug efficacy	Drug binding	Lead optimization
Drug interaction	Drug elimination	Drug bioavailability	Mechanism of drug action
Drug mechanism of action	Drug excretion	Drug clearance	Molecular pharmacology
Drug metabolism	Drug half life	Drug compartment	Pharmacodynamics
Drug molecule	Drug interactions	Drug concentration	Pharmacogenomics
Drug plasma concentration	Drug metabolism	Drug design	Pharmacokinetic calculations
Drug receptor	Drug potency	Drug development	Pharmacokinetics
Drug response	Drug safety	Drug discovery	PKPD
Drug–receptor interaction	Drug selectivity/specificity	Drug distribution	Plasma protein binding
Duration of action	Drug target	Drug dose	Rate of drug elimination
First-order kinetics	Drug therapy	Drug effect	Receptor antagonist
First pass effect	Drug tolerance	Drug efficacy	Receptor type
Ion channel	Drugs	Drug elimination	Routes of administration
Mechanism of drug action	ED_{50}	Drug excretion	Signal transduction
Plasma protein binding	Individual variation	Drug half life	Side effect
Rate of drug elimination	Integrative pharmacology	Drug interaction	Structure–function relationship
Rate of drug elimination	LD_{50}	Drug mechanism of action	Systems pharmacology
Receptor antagonist	Lead optimization	Drug metabolism	Therapeutic window
Receptor type	Mechanism of drug action	Drug molecule	Volume of distribution
Side effect	Molecular pharmacology	Drug plasma concentration	
Volume of distribution	Pharmacodynamics	Drug potency	
	Pharmacogenomics		
	Pharmacokinetic calculations		
	Pharmacokinetics		
	PKPD		Accepted Round 1
	Receptors		For Discussion Round 1
	Routes of administration		Rejected Round 1
	Signal transduction		

TABLE 4 (Continued)

Text mining (refined list of 38)	Survey (refined list of 48)	Merged list (74 terms)
	Side effects	
	Structure–function relationship	
	Therapeutic window	

Note: A single combined list of terms produced by consolidation of the text mining and educator survey terms. Shading on the merged list shows the outcome of Delphi Round 1 for each of the terms: green shading indicates Core Concepts with 80+% agreement, yellow shading indicates 50%–79% agreement and brown shading indicates less than 50% agreement.

Abbreviations: ADME, absorption, distribution, metabolism, and excretion; ED50, effective dose in 50% of animals or participants; LD50, lethal dose required to kill 50% of animals in the study; PKPD, pharmacokinetic/pharmacodynamic modelling.

TABLE 5 The terms accepted as core concepts of pharmacology education

Core concept	Round agreement threshold reached	% agreement
Drug elimination	1	90
Dose/concentration–response relationship	1	86
Drug bioavailability	1	81
Drug distribution	1	81
Drug tolerance	1	81
Drug metabolism	1	81
Drug half-life	3	100
Drug absorption	3	95
Drug potency	3	95
Drug efficacy	3	95
Volume of distribution	3	90
Steady state concentration	3	90
Mechanism of drug action	3	90
Agonists and antagonists	3	90
Adverse drug reaction	3	90
Therapeutic index	3	90
Drug affinity	3	85
Drug selectivity	3	85
Drug clearance	3	80
Drug target	3	80
Drug interaction	3	80
Zero- and first-order kinetics	3[a]	75
Drug–receptor interaction	3[a]	75
Individual variation in drug response	3[a]	75
Structure–activity relationship	3[a]	70

[a]Between 70% and 80% agreement within the final Delphi round and deemed by the research team to fill an essential gap in the overall list of concepts.

New Zealand (Santiago et al., 2021; White et al., 2021). The exploratory phase ensured that we covered the full scope of concepts in pharmacology, by identifying 100 terms used frequently in

pharmacology texts and 590 terms from large-scale survey. The research team then analysed and refined these large lists to create a manageable 74 potential core concepts for the expert group to resolve. To ensure genuine accord within the Delphi method, we set a high (80%) acceptance threshold, providing confidence in the final list of 25 core concepts. For comparison, a median acceptance threshold of 75% was reported in a review of nursing Delphi studies (Foth et al., 2016).

4.1 | The Delphi method ensured early contributions were made without the influence of other group members

The three rounds of Delphi method were critical to the development of the final list. In particular, the comments from the experts in Round 2 and associated workshops were invaluable in dealing with the challenge of choosing a single core concept from a cluster of related terms. For example, numerous expert comments were received regarding the related terms *margin of safety*, *therapeutic window*, and *therapeutic index*. These comments informed the final decision to propose *therapeutic index* in Round 3 and subsequent 90% endorsement of this concept. This is consistent with earlier findings supporting the use of three rounds of expert analysis (Hallowell & Gambatese, 2010). An innovative part of our Delphi method was the use of workshops between Rounds 2 and 3, with workshop discussions useful in shaping the clustering of terms around a central concept. The workshops also permitted discussion and input from a wider team outside of the core research team. That said, the workshops may have affected the independent nature of the expert ratings on the final Delphi round, so that only the expert group ratings in the first two rounds were truly independent.

4.2 | Comparison to the ASCEPT list

As the current study builds upon the foundation initiated by the Australasian pilot (White et al., 2021), it is of interest to compare and contrast the two lists of core concepts. The pilot study was conducted by a group of educators from Australian and New Zealand, only one

of whom participated in the expert group in the current study. The present final list includes 15 of the 19 core concepts from the pilot study, namely, *drug absorption*, *concentration response relationships*, *drug distribution*, *drug target*, *drug metabolism*, *mechanism of drug action*, *drug efficacy*, *drug selectivity*, *drug affinity*, *drug tolerance*, *bioavailability*, *drug potency*, *therapeutic window*, *drug elimination*, and *individual variation*.

Our current list does not include the pilot study core concepts *drugs and homeostasis*, *drug excretion*, *drug safety*, and *drugs and complex systems*. Our current list does however include 10 core concepts that were not included in the pilot study: *drug half-life*; *volume of distribution*; *steady state concentration*; *agonists and antagonists*; *drug clearance*; *drug interactions*; *zero and first order kinetics*; *drug–receptor interaction*; *structure–activity relationship*; *adverse drug reaction*. The observed differences in the lists may be linked to the different methodological approaches taken, or the differences between Australasian and international expert views. Interestingly, the terms *volume of distribution* and *drug–receptor interactions* were both derived in our study from the text mining process, and reached the consensus threshold in our study. The Australasian study did not involve text mining.

4.3 | Comparison to other international resources

Many disciplines have identified core concepts and developed concept inventories over the past 30 years, with physics and biology notable for the scope and depth of work. Hestenes and colleagues' seminal work to develop the force concept inventory (Halloun & Hestenes, 1985; Hestenes et al., 1992) heralded a transformation of learning across the discipline, with the rigour and reproducibility of the inventory enabling the identification of effective, evidence-based teaching practices (Deslauriers & Wieman, 2011; Hake, 1998). In the United States, in biology, "Vision and Change" was a National Science Association funded endeavour to develop core concepts and related tools for educators (Brewer & Smith, 2011; Brownell et al., 2014). The current project aimed to follow in the footsteps of these seminal initiatives, with the goal of providing educators with truly global pharmacology core concepts, concept inventories, and related resources.

Of note, there are already a number of valuable resources for pharmacology educators. The Pharmacology Education Project (Faccenda et al., 2019), an initiative of the International Union of Basic and Clinical Pharmacology, is a web-based resource with a wide range of information, teaching, learning, and assessment tools. The "Knowledge Objectives in Medical Pharmacology" initiative sponsored by the Association of Medical School Pharmacology Chairs (AMSPC) has provided medical educators with extensive guidance on their pharmacology curricula since 1985. The British Pharmacological Society has several very extensive and paedagogically advanced core curricula and has published work on clinical pharmacology for medical students (Ross & Maxwell, 2012) and undergraduate pharmacology (Wallace et al., 2021). These invaluable resources complement our work in that they provide a breadth of material, allowing educators to ensure adequate coverage in their programs and courses, whereas our

core concepts work aims to provide focus for educators and program directors/chairs to assure both students and stakeholders that graduates have acquired the fundamental knowledge necessary to be successful in their careers.

4.4 | Limitations

The total number of pharmacology educators around the world has not been rigorously determined, but is likely to be many thousands. Our study involved educators from every continent, but we would need a far larger, more representative sample size to claim international consensus on our list of core concepts. Additionally, volunteer bias could have contributed to the outcomes of this study. These concerns are offset by the high degree of similarity between the list of core concepts identified by rigorous, multi-stage methodology in this study with that of the pilot work in Australia and New Zealand. Perceptions held by individuals regarding the core concepts for any discipline are likely to be heavily influenced by their expertise, background, beliefs and experiences. While we did this work from the perspective of pharmacology education, our various health professional, industry and basic science research backgrounds and current roles influenced our thinking. Future work specifically focusing on the core concepts of pharmacology utilised in industry, research and clinical practice will assist educators to contextualise their concept-based teaching approach.

Finally, the poor response rate to the survey from some countries and the overrepresentation of others has the potential to bias the results towards the views of educators in those over-represented countries. Nevertheless, the use of the text mining approach and the high degree of similarity between the pilot study and the present work both provide confidence that the list of core concepts we have developed are broadly representative of the views of experts in the discipline.

Finally, we note that the list of core concepts generated in our work are *foundational concepts*. The majority of the concepts are relevant to drugs of all categories, including small molecule drugs, biologics, nucleic acid medicines and emerging modalities. For example, *selectivity* applies not only to drugs that target receptors and enzymes, but also to antibodies and other more recent additions to our therapeutic arsenal. Some concepts are specific to sub-categories of drugs, for example the efficacy that agonists display when bound to receptors.

We are currently working to unpack each core concept to identify underpinning sub-concepts. These sub-concepts will shed further light on the concepts that apply to all drugs, regardless of target, and those that are specific to sub-categories of drug classes or targets.

4.5 | Future work

The list of core concepts that we have produced in this study is a new, evidence-based resource that will be of interest and use to pharmacology educators globally. Realising the full potential of this initiative will require resources to help educators around the world

develop concept-based curricula, including definitions of each core concept, identification of underpinning sub-concepts, development of teaching methods and learning resources to embed attainment of these concepts into courses. Our global initiative will produce and disseminate these resources, and more broadly initiate a conversation about concept-driven pharmacology education. Finally, we will conduct research to identify misconceptions held by students on each core concept. The outcomes of this work will underpin development of a concept inventory, a validated assessment of learner attainment of each concept.

AUTHOR CONTRIBUTIONS

Paul White: Conceptualization; data curation; formal analysis; methodology; project administration; visualization; writing-original draft; writing-review and editing. **Clare Guilding:** Conceptualization; formal analysis; methodology; writing-review and editing. **Tom Angelo:** Conceptualization; formal analysis; investigation; methodology; visualization; writing-review and editing. **John P. Kelly:** Formal analysis; investigation; methodology; writing-review and editing. **Laurel Gorman:** Formal analysis; investigation; methodology; writing-review and editing. **Steven J. Tucker:** Formal analysis; investigation; methodology; writing-review and editing. **Ashleigh Fun:** Investigation; methodology. **Jae Han:** Investigation; methodology; writing-review and editing. **Guanliang Chen:** Investigation; methodology. **Yassmin Samak:** Formal analysis; investigation; methodology. **Anna-Marie Babey:** Investigation; methodology; writing-review and editing. **Fabiana A Caetano:** Investigation; methodology; writing-review and editing. **Sudhir Chandra Sarangi:** Investigation; methodology; writing-review and editing. **Jennifer Keonig:** Investigation; methodology; writing-review and editing. **Haiping Hao:** Investigation; methodology; writing-review and editing. **Joseph Goldfarb:** Investigation; methodology; writing-review and editing. **Kelly Karpa:** Investigation; methodology; writing-review and editing. **Luciene Vieira:** Investigation; methodology; writing-review and editing. **Carolina Restini:** Investigation; methodology; writing-review and editing. **Margaret Cunningham:** Investigation; methodology; writing-review and editing. **Patrik Aronsson:** Investigation; methodology; writing-review and editing. **Roisin Kelly-Laubscher:** Investigation; methodology; writing-review and editing. **Mark Hernandez:** Investigation; methodology; writing-review and editing. **Patangi K. Rangachari:** Investigation; methodology; writing-review and editing. **Janet Mifsud:** Investigation; methodology; writing-review and editing. **Fatima Mraiche:** Investigation; methodology; writing-review and editing. **Ramzi Sabra:** Investigation; methodology; writing-review and editing. **Octavio Piñeros:** Investigation; methodology; writing-review and editing. **Xuechu Zhen:** Investigation; methodology; writing-review and editing. **Helen Kwanashie:** Investigation; methodology; writing-review and editing. **Betty Exintaris:** Investigation; methodology; writing-review and editing. **Nilushi Karunaratne:** Investigation; methodology; writing-review and editing. **Kuniaki Ishii:** Formal analysis; investigation; methodology. **Yannee Liu:** Data curation; formal analysis.

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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.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request. Some data may not be made available because of privacy or ethical restrictions.

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