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REVIEWED BY
Zhe Li,
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Nilushi Karunaratne,
Monash University, Australia

*CORRESPONDENCE Faraz Khurshid ☑ F.Khurshid@westernsydney.edu.au; ☑ docfarz@gmail.com

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Pedagogical interventions and their influences on university-level students learning pharmacology-a realist review

Faraz Khurshid 1*, Elizabeth O'Connor¹, Rachel Thompson¹,² and Iman Hegazi¹

¹School of Medicine, Medical Education Unit, Western Sydney University, Campbelltown, NSW, Australia, ²Institute for Interactive Media and Learning, University of Technology Sydney, Sydney, NSW, Australia

Introduction: The knowledge complexity and varied delivery formats in pharmacology education can leave students unprepared in essential pharmacotherapy skills. This significantly influences their ways of thinking and working in clinical environments, resulting in a challenging clinical transition. This need demands pedagogical innovations to strengthen pharmacology education and improve learners' skills and competencies in pharmacotherapy. This evidence-based realist review aimed to examine the contextual factors and program theories or causal mechanisms crucial for effective pedagogical interventions in pharmacology, seeking to answer the question of 'what works for whom, under what circumstances, how, and why'.

Method: The realist synthesis was initiated after retrieving data from Medline (OVID), Cochrane, EBSCO hosted ERIC, SCOPUS, and Embase (OVID) including other sources for additional records. The preliminary analysis enabled the establishment of context, mechanism, and outcome configurations (CMOC) and formulation and refinement of the initial program theory regarding the pedagogical interventions in pharmacology. Data synthesis iteration helped to identify the relevant context and unravel its relationships with underlying causal mechanisms through which said interventions generate outcomes of interest.

Results: A realist review analyzed 1,217 records and identified 75 articles examining a range of educational interventions from individual efforts to faculty-wide curriculum changes in pharmacology education. The key contexts for pharmacology education were troublesome content, traditional delivery methods, inadequate and limited opportunities for knowledge integration, and application. Active participation in interactive learning, along with enjoyment and motivation, was proposed as a causal mechanism for optimizing cognitive load and achieving positive outcomes. The outcomes of the review include subjective perceptions of improved confidence and satisfaction, objective measurements of high post-test scores.

Discussion: Pedagogical scaffolding in constructivist learning environments helps students overcome challenges in learning troublesome pharmacology knowledge. Considering the human cognitive system's processing capacity, these interventions improve learning by effectively using cognitive resources. Innovations that focus on enhancing cognitive load through task construction can also promote positive emotional experiences in students, such as engagement and enjoyment, as explained by flow theory. A constructive learning environment, where the cognitive load is optimized and high flow is achieved, can maximize the impact of pedagogical interventions in pharmacology.

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KEYWORDS

realist review/synthesis, program theory, pedagogical interventions, pharmacology, social constructivism, cognitive load theory, flow theory, core concepts

Introduction

Pharmacology is encompassed by a set of discrete, but interacting, concepts that are often categorized as a complex web of ideas. A comprehensive understanding of core/key pharmacological concepts is critical for effective pharmacotherapy and drug prescription (Engels, 2018). Core pharmacological concepts are defined by their significance, endurance, challenge, applicability across contexts, and contribution to problem-solving (White et al., 2021a,b). In the undergraduate pharmacology program constructing knowledge around these core concepts and their application in clinical scenarios is imperative (Zuna and Holt, 2017). For instance, the fundamental knowledge of underlying pharmacodynamics and pharmacokinetic principles in professional practice informs health professionals' decisions on rational dose and drug selection to produce intended clinical outcomes, in addition to the monitoring of therapeutic and adverse effects (Maxwell, 2016). Thus, a proactive and applicationoriented approach to pharmacology can influence effective ways of thinking and practicing within the discipline.

Pharmacology has been widely recognized as an inherently troublesome subject to learn (Khurshid et al., 2020). Health professional students, whether in medicine, pharmacy or nursing, often face substantial difficulty applying their pharmacology knowledge in different contexts (Zuna and Holt, 2017). Many students fail to appreciate how the application of pharmacokinetics or pharmacodynamics concepts earlier in their learning journey relates to their future clinical practice. A proper understanding of fundamental principles of clinical pharmacology is required to maximize therapeutic benefit and to minimize the therapeutic errors (Zuna and Holt, 2017).

Equally important, is the counterintuitive nature of pharmacology concepts that poses problems for both experienced clinicians and novice students. Among the many complex concepts identified in pharmacology, it is not fully understood why some learners find them difficult to understand, and despite efforts to facilitate their learning, these concepts remain challenging for many students. In addition, students often struggle when it comes to holistic understanding of this basic sciences course, as it requires them to integrate biochemical, physiological and mathematical knowledge (Aronsson et al., 2015). Many students find basic science content less interesting because it does not seem clinically relevant. Even though basic science content is essential to understanding clinical practice, students may not be interested in those courses (Kolluru and Varughese, 2017). Nevertheless, these foundational sciences form a significant part of primary medical education and hold a crucial developmental function in promoting effective learning for clinical practice (Malau-Aduli et al., 2019). Furthermore, poor multidisciplinary approach often fails to establish connections across subject matter thus making the acquired knowledge inert (Harr et al., 2015).

The traditional teacher-centered learning of pharmacology neither actively engages students in higher order thinking nor stimulates the critical thinking and clinical reasoning integral to effective patient care (Kaylor, 2014; Baumann-Birkbeck et al., 2017; van Wyngaarden et al., 2019). A lack of clinically oriented teaching offers minimal opportunity for students to hone their pharmacotherapeutic skills while transitioning from the theoretical to the experiential, manifesting as an ill-preparedness for prescribing (Maxwell, 2012; Karpa et al., 2015). The didactic approach to teaching pharmacology not only lacks clinical relevance, but can also result in information overload (Nicolaou et al., 2019). The high cognitive load in pharmacology hampers learning by exhausting the working memory thus making it difficult to retain core pharmacological concepts (Mauldin, 2021). Similarly, acquisition of pharmacological skills and competencies relies on long term retention of knowledge that is also challenged by the overwhelming load of facts and concepts.

Achieving optimal learning outcomes in pharmacology courses, which are highly complex and multidisciplinary, requires significant commitment from both educators and students. It is therefore critical to create an environment that facilitates student engagement, success, and achievement in order to enhance the learning environment (Rubaiy, 2021). Numerous interventions have been undertaken so far, including blended learning, flipped classrooms, team-based learning, case-based learning, and integrated teaching modules. These have assisted students in the development of understanding that has improved their performance in exams (Persky and Dupuis, 2014; Wong et al., 2014; Gorman et al., 2015; McLaughlin et al., 2015; Yadav et al., 2016; Ambwani et al., 2017; Kurup et al., 2017). However, it is unclear whether this improved understanding is reflected in improved ways of thinking and practice of the discipline. Our interest also lies in identifying the mechanisms through which the interventions work under different contexts.

This realist review explores the emerging body of literature in pharmacology education that reports on the adoption of numerous, wide-ranging pedagogical interventions, to facilitate student understanding of the subject. It aims to identify the specific challenges that underpin the rationale for educational interventions and the mechanisms by which these pedagogical efforts make a difference in the students learning of pharmacology. Furthermore, we explore the "how" and "under which circumstances" these interventions improve/influence university-level medical students' understanding of pharmacology, with the aim of improving ways of thinking and practicing.

Methodology

Review question

The first step undertaken in our systematic review was to formulate the review/research question. The review question, based on the PICO (population, intervention, comparative intervention or context and outcomes) framework (Wright et al., 2007) was collaboratively developed through constructive discussions among the review team and collaborators as presented in Table 1.

Eligibility criteria

All members of our research team (FK, ¹ EO, ² RT, ³ IH⁴) were engaged in medical education and actively participated in teaching and learning of basic sciences courses at the undergraduate level. We developed the eligibility criteria as a review team in response to our research question, which defined the scope of the literature search, with a primary focus on pedagogical interventions in pharmacology for undergraduate medical and allied health science students. Table 2 shows the inclusion and exclusion criteria for the systematic review in terms of the PICO question.

Realist synthesis

We opted for a theory-driven approach of realist inquiry or synthesis, philosophically embedded in realism; it takes into account the interplay of context, mechanism and outcome (Pawson, 2006). The key concept of context either encourages or discourages the intervention. Having relational and dynamic characteristics, it shapes the causal mechanism by which the intervention works (Richmond et al., 2020). The mechanisms are emotional or cognitive responses to the interventions; they are not integral to the interventions (Wong et al., 2012). The outcome of interest is established by the context in the setting of the relevant underlying mechanisms (Wong et al., 2013). The framework that helps to understand the dynamics between "context-mechanism-outcome (CMO)" is known as CMO configuration (CMOC).

Literature mining and data searching

After registering our protocol with PROSPERO (CRD42020160441), we followed the systematic process outlined by Pawson et al. (2005) and Wong et al. (2013). The first 40 articles from an initial exploratory background search not only helped refine our

1 Faraz Khurshid.

TABLE 1 Review question (PICO) question for the systematic review.

Why, how and under which circumstances does pedagogical support for pharmacology teaching and learning improve/influence university-level health professional students' understanding and reasoning of the discipline?		
Population	University level student, Undergraduate student	
Intervention	Teaching, learning, education, pedagogical interventions	
Comparative intervention/Context	Pharmacology curriculum	
Outcome	Influences on student understanding and reasoning of the discipline	

TABLE 2 Eligibility criteria for systematic search.

PICO	Inclusion criteria	Exclusion criteria
Population	University level/ undergraduate health professionals' students	Postgraduate students/ Master's students
Intervention	Pedagogical interventions to enhance teaching, learning and educational experiences of students studying pharmacology	Education of patient Education of caregivers Health promotion/ awareness education
Comparative intervention/Context	Pharmacology and therapeutics Pharmacology curriculum	Pharmaceutical education
Outcomes	Student competencies and educational experience	NONE

review question and eligibility criteria but also informed the initial program theory (IPT).

We conducted data and evidence searches across multiple databases, including Medline (OVID), Cochrane, ERIC, SCOPUS, and Embase (OVID), covering articles published from 2013 to September 2019. The search strategy employed MeSH Terms and free text with Boolean operators, as outlined in Table 3. This search, conducted between July 30 and September 10, also encompassed additional records and grey literature from sources such as WorldCAT, Google, Open MD, EThOS British Library, OUT e-prints, and Semantic Scholars. We included unpublished studies like theses and dissertations using the same search strategy.

After identification of the literature through selected databases and additional sources, we started the screening process based on the formulated review question and set of eligibility criteria discussed above. The structural outline of the systematic step by step process of screening is shown in PRISMA (preferred reporting items for systematic reviews and meta-analyses) 2020 Flow diagram (Figure 1).

² Elizabeth O Connor.

³ Rachel Thompson.

⁴ Iman Hegazi.

Data extraction and synthesis

After completing the preliminary literature searches on educational interventions in pharmacology learning, FK randomly divided the 75 papers including additional records into three distinct pools, assigning 25 articles to each team member (IH, RT, EO) for review. To facilitate data collection, we used an Excel table based on the Context, Mechanism, Outcome Configuration (CMOC). Once data synthesis was completed by the respective team members, FK reviewed the entire pool of papers using the CMOC table, comparing

TABLE 3 Example of the search strategy used for EBSCO hosted ERIC.

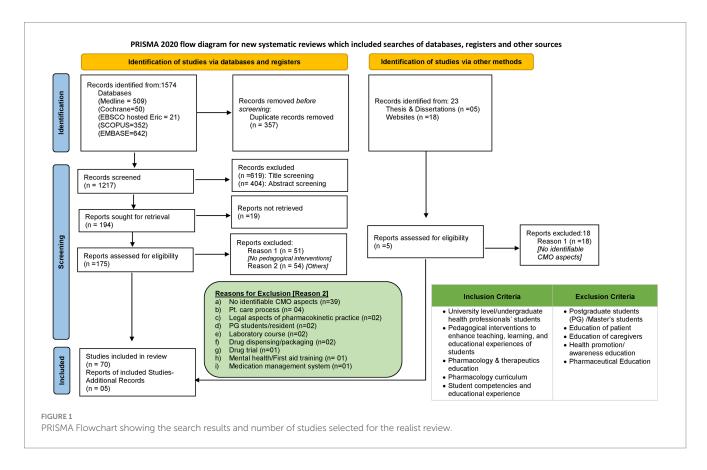
EBSCO hosted ERIC			
Population	Students: (DE "Students") OR (DE "College Students")		
	TI (Student* AND (College OR University)) OR AB		
	(Student* AND (College OR University))		
Intervention	Teaching	DE "Instruction"	
	Learning	DE "Learning"	
	Education	(DE "Education")	
	Pedagogy	Use Instruction	
	Curriculum	DE "Curriculum"	
	TI (Instruction OR learning OR Education OR curriculum) OR AB (Instruction OR learning OR Education OR curriculum)		
Context	Pharmacology: (DE "Pharmacology") TI Pharmacy* OR AB pharmacy*		

it with the Excel sheets of the other team members. To ensure consistency and rigor, FK served as the common denominator across all pools, conducting cross-checks on data gathering and analysis approaches with other team members, reinforcing the process. FK also facilitated consensus building among the team regarding educational interventions to enhance the understanding and reasoning abilities of university-level medical students.

Initial CMOC drafts were created based on exploratory searches and team feedback, leading to the development of an IPT. Iterative data synthesis refined the program theory, helping us identify relevant contexts and their interaction with mechanisms to generate desired outcomes for each theory. The IPT, integrating theories like cognitive and social constructivism, cognitive load theory, and flow theory, guided the exploration of causal mechanisms in pedagogical interventions. By integrating the principles of social constructivism and cognitive load theory into pedagogical interventions, it may be possible to promote interactive knowledge construction in dynamic environments and optimize learners' cognitive processing abilities for effectively applying acquired knowledge and skills in new situations (Sweller, 1994; Kalina and Powell, 2009). Furthermore, the flow theory posits that effective pedagogical interventions should aim to facilitate students' flow experiences, characterized by deep engagement, enjoyment, and satisfaction in their learning activities (Schmidt, 2010).

Risk of bias (quality) assessment

In our realist review, the selection of studies and quality assessment was a continual, iterative process conducted in parallel with the data synthesis and extraction phase. Quality assessment



involved multiple methods, including the appraisal of sections related to theory and evidence, to enhance the program theory. This process was critical for determining the credibility of inferences drawn by authors and promoting transparency, validity, and reliability of findings (Pawson et al., 2005; Greenhalgh et al., 2008; Kastner et al., 2011).

During the course of literature review, we employed two well-established tools, the BEME criteria and the Kirkpatrick model, to appraise the final set of articles (Harden et al., 1999; Smidt et al., 2009). The BEME criteria encouraged critical thinking, evidence-based decision-making, and teacher improvement (Harden et al., 1999). The Kirkpatrick model helped assess improvements in the acquisition and application of relevant knowledge (Smidt et al., 2009). After this assessment, FK cross-checked the results and sought input from the rest of the team members.

Results

Realist review data attributes

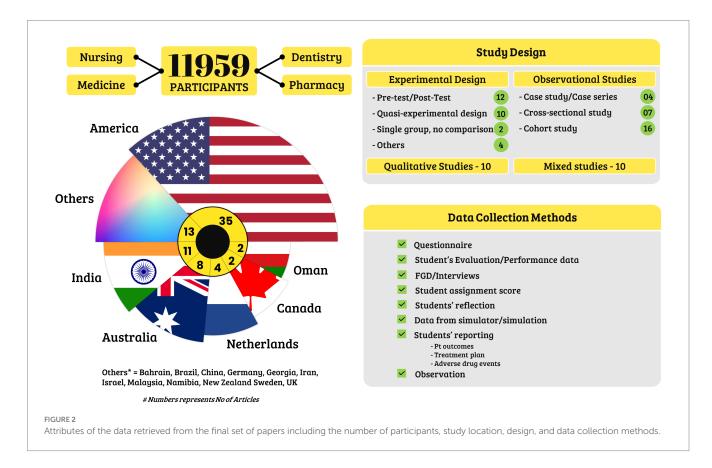
A total of 1,217 records were screened, with 175 full articles assessed for eligibility after title/abstract exclusion criteria were applied. Seventy articles from major bibliographic databases along with 5 additional records retrieved from different websites met the final inclusion/exclusion criteria for the realist review. The list of the 75 papers is enclosed as Appendix 1.0 in Supplementary material. Figure 2 outlines the data characteristics including the number of participants, study location/design and data collection methods.

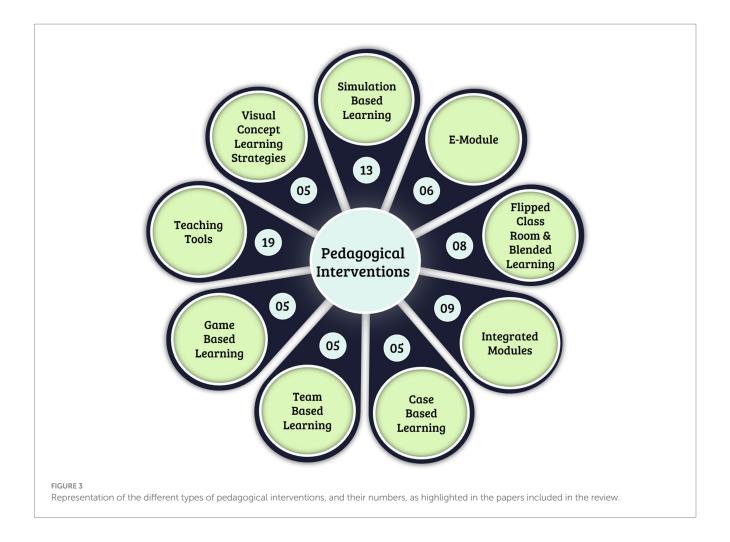
The variety of educational interventions ranged from individual teacher-driven endeavors to faculty-wide curriculum changes (Figure 3). These interventions were intended to assist students' comprehension and articulation of difficult concepts of pharmacology such as understanding the fundamental principles of pharmacokinetics and pharmacodynamics. In addition, these interventions also focused on improving students' long-term pharmacotherapeutic skills, including patient-centered communication, prescription writing and reporting adverse drug reactions (ADRs).

Initial program theory

The preliminary analysis of the literature facilitated the inception of the initial layout of the CMO configurations, which helped to devise the initial program theory (also known as logic model). To illustrate a CMO configuration and program theory: In a low-income district health clinic (CONTEXT), community outreach and education (MECHANISM) develop trust and enhance health literacy, promoting informed healthcare decisions (OUTCOME). This program theory suggests that implementing these programs in this context will lead to improved healthcare utilization.

Our initial program theory took into account the key contexts of students struggle with the troublesome discipline of pharmacology, didactic formats of content delivery and inadequate opportunities for knowledge application. The mechanism was based on pedagogical innovations/tools that enabled students to manage the cognitive load associated with troublesome content, while also maintaining their interest and comprehension of subject knowledge. This eventually led to outcomes such as student satisfaction and improved ways of





thinking and practicing in the discipline. The initial program theory states that:

"Students' difficulty understanding pharmacology, chalk-and-talk instruction, and limited opportunities to apply their knowledge is addressed by the scaffolding provided by pedagogical innovations. Scaffolding facilitates students' ability to cope with cognitive overload associated with overwhelming content, while retaining their interest and understanding, thus increasing student satisfaction and enhancing their ability to think and practice within the discipline."

Relevant educational theories

We discovered that many pedagogical interventions, while not explicitly referencing specific educational theories, appeared to be guided by the principles and values inherent in three key theories:

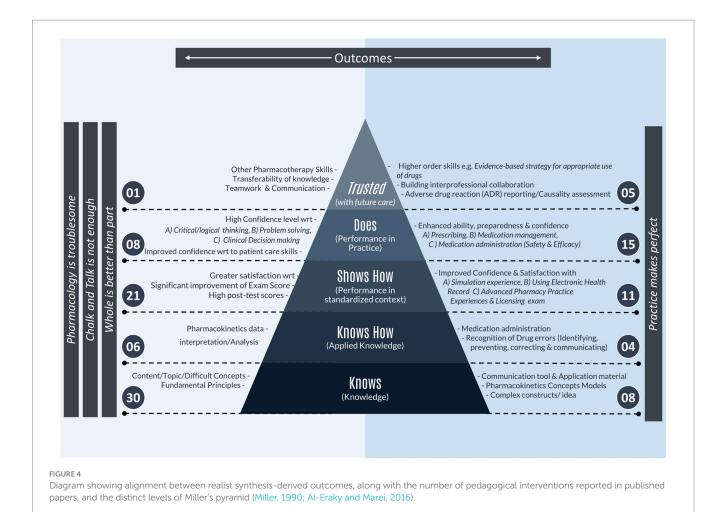
 Cognitive and Social Constructivism: This theory, rooted in the work of Jean Piaget and Lev Vygotsky, recognizes knowledge construction as an individualized process in cognitive constructivism, while in social constructivism, it emphasizes knowledge construction through dynamic interactions in a social learning environment (Kalina and Powell, 2009).

- i) Cognitive load theory: This theory focuses on developing instructional techniques that optimize the use of learners' cognitive processing capacity, particularly in handling complex cognitive tasks (Sweller, 1994; Paas et al., 2003; Kalyuga and Plass, 2009).
- Flow theory: Flow theory focuses on understanding the determinants that enhance student engagement in learning, emphasizing the concept of the "flow experience" characterized by complete engagement, focus, and enjoyment (Csikszentmihalyi and Csikzentmihaly, 1990; Csikszentmihalyi, 1997; Schmidt, 2010).

These theories underpinned the pedagogical interventions, which not only acted as scaffolding aids for student learning but also facilitated effective cognitive load management and promoted flow experiences for optimal learning.

Realist synthesis outcomes in light of Miller's pyramid

The outcomes of educational interventions can be anticipated (mastery of a skill), unanticipated (collateral effects on the participants or their workplace), positive (knowledge expansion) or negative (e.g., psychological impact of badly guided debrief session) (Graham and McAleer, 2018). The outcomes that materialized through this realist review included a mix of subjective perceptions (improved student

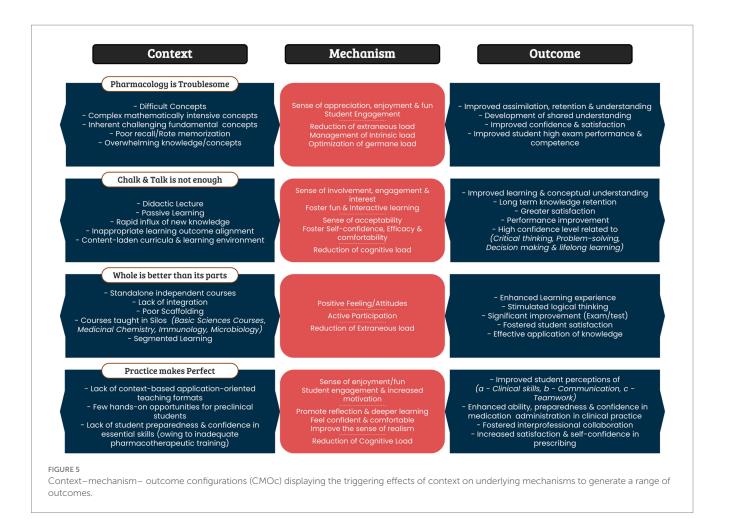


confidence and satisfaction) and objective measurements (significantly high score in post-test, transferability of skills to authentic patient care). The outcomes generated by most of the pedagogical innovations were linked to students' improved performance in examination or high post-test score mostly close to the intervention, suggesting short-term cognitive gain (Gaikwad and Tankhiwale, 2014; Persky and Dupuis, 2014; Thomas et al., 2014; Choudhury et al., 2015; Jones et al., 2015; Karpa et al., 2015; McLaughlin et al., 2015; Tankel, 2015; Nguyen et al., 2016; Sukhlecha et al., 2016; Tichelaar et al., 2016; Yadav et al., 2016; Dagenais et al., 2017; Islam et al., 2017; Kurup et al., 2017; MacDougall, 2017; Persky et al., 2017; Sirota, 2017; Ying et al., 2017; Al-Sallami and Loke, 2018; Bernaitis et al., 2018; Bryant et al., 2018; Chan et al., 2018; Dubovi et al., 2018; Patel et al., 2018; Hanson et al., 2019).

We observed a significant alignment between the outcomes from our realist synthesis and Miller's pyramid of assessment in medical education (Miller, 1990). Miller's pyramid categorizes assessment into four hierarchical processes, emphasizing different assessment types for various educational outcomes as shown in Figure 4. For instance, mastery of knowledge and skills, termed adaptive expertise, can be assessed through a range of methods. In parallel, our analysis of pedagogical interventions revealed diverse outcomes, notably enhancing comprehension of complex concepts such as pharmacokinetics concepts models which aligns with the 'Knows' level of Miller's pyramid (Dagenais et al., 2017).

Moreover, in congruence with level 2 (Knows How), improved understanding of these core pharmacological concepts bolstered students' confidence in interpreting pharmacokinetic data, and deepened their grasp of drug administration, side effects, errors, and knowledge gain (Zuna and Holt, 2017; Dubovi et al., 2018). This comprehensive understanding also translated into improved exam performance, simulation experiences (Cropp et al., 2018), using electronic health records (EHR) (Vana and Silva, 2014; Coons et al., 2018) and advanced pharmacy practice experiences (APPES) and licensing exams (Hirsch and Parihar, 2014; Sanko and McKay, 2017).

At level 4 (Does), students demonstrated high confidence in critical thinking, problem-solving, clinical decision-making for patient care, and the assessment of the efficacy and safety of drugs, particularly for rational prescribing, especially in clinical settings conducive to experiential learning (Karpa et al., 2015; Tichelaar et al., 2015; Howard and Gaviola, 2018). The new proposed level 5 of entrustment (trusted) of Miller's pyramid involves more than the observation of "doing"; it reflects educators' trust in students' ability to respond effectively in unforeseen healthcare situations (Ten Cate et al., 2021). While most of the pedagogical implementations lacked defined outcomes that can be ascribed to level 5, the long-term implications of changes in pedagogy suggested by authors are included Teamwork/communication skill versus less "testable" evidence-based approach to medication management.



CMO configurations and statements

The iterative process helped to establish connections across the data in the form of a Context-Mechanism-Outcome (CMO) table (Figure 5), producing the final program theories. Our analysis involves the exploration of patterns and relationships among contexts, mechanisms, and outcomes. For instance, we frequently encounter the context of pharmacology as a challenging subject across many articles, where a range of pedagogical interventions has been employed. Nevertheless, the outcomes tend to vary, contingent upon the researchers' objectives. By examining the context and outcomes, we are able to deduce or support the underlying mechanisms that underpin educational theories. This analytical approach enables us to construct Context-Mechanism-Outcome (CMO) configurations, shedding light on how specific contexts influence mechanisms to yield distinct outcomes. Throughout this journey, we consistently refine and validate these configurations, a process we bolster with a thorough literature review and insights from experts in the field.

The supporting evidence leads us to four important CMO configuration narratives/statements about each context:

- Students struggle with troublesome knowledge of pharmacology.
- 2) Students do not engage with didactic instructional formats.
- 3) Students find it difficult to understand and apply knowledge due to non-integration of basic sciences subjects.

 Students lack opportunities to gain knowledge application from the classroom to clinical settings.

Proper scaffolding can assist in facilitating an easier grasp of troublesome knowledge [pharmacology is troublesome]

Students find it difficult to understand and internalize certain concepts in pharmacology integral to the development of discipline-related competencies. To address this issue, teachers/educators adopt pedagogical approaches as scaffolding aids to facilitate the understanding of these core concepts. Students' active engagement with these pedagogical innovations can result in a range of emotive and cognitive responses that may influence the understanding of those troublesome concepts along with retention.

Students often face challenges in pharmacology, especially in comprehending the complex, mathematically intensive concepts and principles of pharmacokinetics and pharmacodynamics (Jones et al., 2015; Dagenais et al., 2017; Hall et al., 2017; Hermanns et al., 2017; Khurshid and Noushad, 2017; MacDougall, 2017; Zuna and Holt, 2017; Al-Sallami and Loke, 2018; Bryant et al., 2018; Chan et al., 2018; Khurshid et al., 2018; Patrick et al., 2018; Hanson et al., 2019). For

instance, understanding the relationship between the dose and response in patients with warfarin is challenging for clinicians and students as it is "not intuitively predictable" (Al-Sallami and Loke, 2018).

To address these challenges, various pedagogical interventions, such as evidence-based strategies, gamification, molecular modeling, computer simulations, and visual aids, have been implemented (Fidalgo-Neto et al., 2014; Vana and Silva, 2014; Jones et al., 2015; Hall et al., 2017; Meyer et al., 2017; Sanko and McKay, 2017; Aggar et al., 2018; Aynsley et al., 2018; Bryant et al., 2018; Chan et al., 2018; Khurshid et al., 2018; Patrick et al., 2018; Hanson et al., 2019). The cognitive scaffolding provided by these innovations, as well as the element of fun learning that they offer, contributed to students' improved understanding and engagement with troublesome content. Thus, enhancing their confidence and satisfaction in analyzing the complex models of pharmacokinetics and pharmacodynamics (Al-Sallami and Loke, 2018). It eventually resulted in higher post-test scores and better long-term performance in assessments.

Paradigm shift to learner-centered approach stimulates life-long learning ["chalk and talk" is not enough]

The passive "didactic lectures" with minimal emphasis on clinical application often makes students disengaged and deprives them of developing clinical skills and competencies. Lack of scaffolding and inappropriate alignment of learning outcomes imposes a high cognitive load on learners. A "paradigm shift" to a learner-centered approach facilitating contextual understanding and optimizing the cognitive load fosters student interest and enjoyment in the discipline. This may improve student satisfaction and learning experiences and prepare them as independent life-long learners.

This context reflects curricular challenges that students come across learning a subject that is troublesome at heart (Gaikwad and Tankhiwale, 2014; Kaylor, 2014; Trujillo et al., 2014; Wong et al., 2014; Ahsan and Mallick, 2016; Eachempati et al., 2016; Galvez-Peralta et al., 2018; Patel et al., 2018). The challenges primarily stem from didactic lectures coupled with inappropriate alignment of the learning outcomes (Gupta et al., 2014; Persky and Dupuis, 2014; Choudhury et al., 2015; Kibuule et al., 2015; Arora and Hashilkar, 2016; Nguyen et al., 2016; Islam et al., 2017; Patrick et al., 2018; Saba et al., 2019). Many European Union (EU) medical schools follow a traditional approach in teaching and assessing Clinical Pharmacology and Therapeutics (CPT), with inadequate alignment of learning outcomes and curriculum content. About 50% of teaching methods consist of formal lectures, self-directed learning through textbooks, oral and written exams, and essays (Brinkman et al., 2017). Didactic lecturebased learning, apart from lacking clinical relevance, often fosters passive learning and cognitive overload.

Amid the array of active learning strategies, curricular innovation emphasizes a shift toward learner-centered approaches that promote lifelong learning and independent problem-solving. These strategies encompass flipped teaching, blended learning, team-based learning, elective e-modules, and elective courses.

These interventions not only enhance knowledge, skills, and learning satisfaction but also boost student engagement in active learning (Persky and Dupuis, 2014; Saba et al., 2019). It has also been demonstrated that active interaction among students fosters peer learning, while active communication in turn improves students' academic performance and learning experiences (McLaughlin et al., 2015; Eachempati et al., 2016; Islam et al., 2017). Empirical data highlights team-based learning (TBL) as a more effective method for teaching pharmacy students, fostering qualitative learning, teamwork, collaboration, and lifelong learning skills, surpassing traditional lectures (Remington et al., 2017).

The integrative, multidisciplinary learning reinforces conceptual understanding for effective application [whole is better than its parts]

The standalone approach to teaching and learning pharmacology and other basic sciences subjects puts additional responsibility on students to connect disparate knowledge parts for a holistic understanding of integrated principles. The collaborative design and multidisciplinary integrative approach of basic and clinical science with proper scaffolding facilitates clinically integrated learning of pharmacology with greater satisfaction and focused attention. This may help to develop the relevant conceptual understanding of other disciplines with pharmacology cohesively in students' minds.

This context highlighted how a lack of disciplinary integration hinders the holistic approach to knowledge comprehension and the transition from basic sciences to therapeutic application (Fidalgo-Neto et al., 2014; Beleh et al., 2015; Gorman et al., 2015; Islam and Schweiger, 2015; Yadav et al., 2016; Ambwani et al., 2017; Kolluru and Varughese, 2017; Kurup et al., 2017; Howard and Gaviola, 2018; Steinel et al., 2019). The realist approach demonstrated that effective integration of multidisciplinary basic science courses likely contributed to students' improved understanding, retention and performance (Beleh et al., 2015; Gorman et al., 2015; Kurup et al., 2017).

This realist review demonstrated that multidisciplinary basic science courses, including integrated teaching modules, longitudinal multicourse progressive disclosure courses (PDC) (Howard and Gaviola, 2018), and utilization of education-centered platforms (e.g., Piazza) (Kolluru and Varughese, 2017), contribute to improved student understanding, retention, and performance. In addition to enriching students' learning experiences, these diverse pedagogies enhanced their cognitive capabilities, logical thinking (Fidalgo-Neto et al., 2014), and their ability to effectively apply integrated knowledge in clinical scenarios for optimal patient care (Islam and Schweiger, 2015). Case-based learning in integrated courses, such as pathophysiology, medicinal chemistry, pharmacology, and therapeutics, underscores the positive impact of progressive disclosure courses on pharmacy students' confidence in patient care skills, including information gathering, assessment, pharmacotherapy planning, and monitoring (Howard and Gaviola, 2018).

Real/simulated clinical contexts offer avenues to safe experiential learning [practice makes perfect]

The effective translation of pharmacology concepts into skills, demands the context-based application of knowledge in a real or simulated clinical environment. The gap between theoretical knowledge and practical experience of pharmacotherapeutic skills drastically affects students therapeutic decision-making aptitude, prescribing practice and adverse drug reactions reporting. Interventions aiming for interprofessional collaboration in relatively realistic settings, such as patient simulation, can familiarize students with standardized clinical scenarios and make them motivated and engaged. This theory emphasizes the pivotal role of prescribing and medication administration in patient safety, fostering the development of skills, confidence, and satisfaction essential for safe medical practice among future doctors.

The papers that encompassed this context are mainly based on safe experiential learning theory (Hirsch and Parihar, 2014; Thomas et al., 2014; Tittle et al., 2014; Vana and Silva, 2014; Brinkman et al., 2015; Karpa et al., 2015; Keijsers et al., 2015; Tichelaar et al., 2015; Hanson, 2016; James et al., 2016; Tichelaar et al., 2016; Dang, 2017; Funk et al., 2017; Javadi et al., 2017; King and Khan, 2017; Patel et al., 2017; Persky et al., 2017; Sanko and McKay, 2017; Tinnon and Newton, 2017; Aggar et al., 2018; Coons et al., 2018; Cropp et al., 2018; Dubovi et al., 2018; Patel et al., 2018; Hasamnis et al., 2019; Kirsch et al., 2019). The transformation of students' understanding of pharmacology relies not only on acquiring theoretical knowledge but also on applying that knowledge in a clinical context. The absence of a structured model for contextualizing clinical application often hinders students in acquiring skills like prescribing, ADR reporting, or treatment planning (Tichelaar et al., 2016; Funk et al., 2017; King and Khan, 2017; Patel et al., 2017; Hasamnis et al., 2019). Additionally, the lack of sufficient opportunities for experiential learning hinders the development of a collaborative practice environment, crucial for optimizing learning outcomes through shared understanding and multidisciplinary knowledge application (Wilson et al., 2016; Meyer et al., 2017). Pedagogical interventions in this context underscore the importance of hands-on learning in a controlled, simulated environment to help students safely apply theoretical knowledge in a clinical setting.

To address challenges in this context, various pedagogical approaches were employed, including case-based learning and simulation of complex clinical scenarios (Hirsch and Parihar, 2014; Hasamnis et al., 2019), flipped classrooms (Hanson, 2016), medication optimization curriculum (Karpa et al., 2015), acronym-based teaching tool (King and Khan, 2017), high fidelity patient simulations (Meyer et al., 2017; Sanko and McKay, 2017; Tinnon and Newton, 2017), simulated electronic health record (EHR) case studies (Vana and Silva, 2014; Coons et al., 2018), and numerous other interventions (Tittle et al., 2014; Javadi et al., 2017; Patel et al., 2017; Cropp et al., 2018). In an interprofessional collaboration using medium-fidelity manikins for pharmacokinetics simulation, pharmacy and nursing students demonstrated effective learning, increased appreciation for pharmacology knowledge, and improved teamwork skills. They emphasized the importance of interprofessional communication and

collaborative practice in enhancing patient outcomes (Cropp et al., 2018). Additionally, medical students reported positive effects when using the validated World Health Organization's 6-step rational prescribing method for basic and clinical knowledge of pharmacotherapy education (De Vries et al., 1994). This program improved their pharmacotherapy skills, increased satisfaction with the educational process, and enhanced self-confidence in prescribing (Keijsers et al., 2015).

Discussion

In our realist review, we explore the intricate realm of pharmacology knowledge, often termed as basic, fundamental, key, or core concepts—interchangeable labels. Aronsson et al. (2015) spotlight vital core concepts in pharmacology, including pharmacodynamics, pharmacokinetics, and drug interactions. While students possess a reasonably acceptable level of knowledge about these core concepts, integrating them effectively into pharmacological interpretations remains a challenge (Aronsson et al., 2015).

Pedagogical interventions aim to enhance students' comprehension of core pharmacological concepts. Active learning, like flower diagrams in Antimicrobial Spectrum Activity, proved effective. These diagrams, reduce cognitive load, fostering a deeper understanding (MacDougall, 2017). Hybrid diagrams merging concept and mind maps facilitate meaningful learning (Ying et al., 2017). Conceptual animations simplify core pharmacology concepts by transforming drug pharmacokinetics, pharmacodynamics, and interactions into visuals. This leverages cognitive load theory, reducing extraneous load and optimizing generative/germane load (Khurshid et al., 2018).

Furthermore, integration of core pharmacological concepts in the curriculum, as proposed by Islam and Schweiger (2015), emphasizes real-world applications for a cohesive learning experience. Nursing education suggests that an integrated curriculum, blending core pharmacological concepts with nursing care theory offers students a holistic perspective through practical applications (Bhardwaj et al., 2015).

Moreover, innovative strategies like Piazza and technology integration illustrate how leveraging technology fosters active academic discussions, reinforcing crucial pharmacological concepts (Kolluru and Varughese, 2017). These multifaceted interventions contribute to a comprehensive understanding of core pharmacological concepts, promising enduring benefits for students. The synthesized approaches provide efficient and captivating teaching methods, enhancing students' learning journey.

Through this realist inquiry, we unveil that prior to implementing any pedagogical interventions in pharmacology learning, identifying the core and essential concepts is of utmost importance. This pivotal step holds the potential to refine learners' ways of thinking and practicing within the discipline. Spearheading this effort is the International Union of Basic and Clinical Pharmacology (IUPHAR) Pharmacology Education Project, which supports a standardized knowledge curriculum with a specific focus on core concepts. Beyond identification, the project emphasizes the importance of focusing on essential concepts. This empowers educators to tailor their teaching to key knowledge areas, avoiding overwhelming students with unnecessary details. The goal is to streamline teaching efforts for a

targeted and impactful learning experience, creating a transformative journey for pharmacology students (White et al., 2021a,b, 2023).

One significant finding in this realist review is how scaffolding can assist students in overcoming challenges associated with complex pharmacological knowledge, including its extensive terminology (Alton, 2016; MacDougall, 2017). Complex problem-solving in the context of troublesome knowledge of pharmacology is closely linked to constructivism, which views knowledge as constantly evolving through learner interaction with others and the environment (Fosnot and Perry, 1996; Cobb, 2005). Vygotsky's constructivism highlights instructional scaffolding, where teachers guide students to expand their cognitive schema, leading to improved development potential (Vygotsky and Cole, 1978). This approach engages learners in purposeful, learner-centered activities such as idea reflection, case discussions, self-assessment of confidence, simulation, and gamebased activities (Fidalgo-Neto et al., 2014; Vana and Silva, 2014; Jones et al., 2015; McLaughlin et al., 2015; Hermanns et al., 2017; Remington et al., 2017; Sanko and McKay, 2017; Zuna and Holt, 2017; Al-Sallami and Loke, 2018; Bernaitis et al., 2018; Patrick et al., 2018; Kirsch et al., 2019). Pedagogical support through active learning strategies may foster lifelong learners with enhanced confidence, critical thinking, and collaborative skills.

Interdisciplinary collaboration, a well-structured curriculum, and scaffolded experiences are essential for vertically and horizontally integrating basic and clinical sciences to foster student knowledge encapsulation (Gorman et al., 2015). Encapsulation is defined as process of grouping interconnected pieces of information into higherlevel units, treating them as single elements in working memory (Kalyuga, 2013). This realist review highlights the use of multidisciplinary integration through integrated modules, online platforms, and educational software that incorporate graphics, animations, and simulations (Fidalgo-Neto et al., 2014; Gaikwad and Tankhiwale, 2014; Beleh et al., 2015; Yadav et al., 2016; Ambwani et al., 2017; Kolluru and Varughese, 2017). Integrated courses spanning medicinal chemistry, biochemistry, pharmacology, pharmacotherapeutics promote active learning, emphasizing the relevance of core concepts to clinical practice. This multidisciplinary approach enhances students' conceptual understanding and prepares them for the effective application of integrated knowledge in optimizing patient care (Beleh et al., 2015; Islam and Schweiger, 2015; Kolluru and Varughese, 2017; Kurup et al., 2017).

Pedagogical interventions encompassing active learning significantly enhance students' learning through effortful engagement and the reinforcement of core concepts, promoting the connection, synthesis, and understanding of challenging constructs and ideas (McLaughlin et al., 2015; Chan et al., 2018). These active learning strategies include case-based learning, flipped classroom (Persky and Dupuis, 2014), team-based learning (TBL), discussion-based learning, blended learning (McLaughlin et al., 2015), interactive e-learning module (Gaikwad and Tankhiwale, 2014; Patel et al., 2018) gamification (Aynsley et al., 2018; Patrick et al., 2018) and patient simulations (Zuna and Holt, 2017). For instance, simulations, as a straightforward active learning strategy, integrate lecture material into real-life clinical settings, fostering communication skills and peer collaboration among pharmacy students (Dang, 2017). Pharmacology, as a fundamental medical sciences course, is well-suited for interprofessional education, given its relevance to multiple health professions (Javadi et al., 2017; Meyer et al., 2017). Interprofessional education enhances collaborative skills, attitudes, and practice for improved patient care. A study by Meyer et al. (2017) demonstrated higher satisfaction among nursing and pharmacy students with a simulation activity, highlighting the benefits of an interprofessional, realistic, and team-based approach to pedagogy.

In this context, these interventions yield diverse outcomes for students at different stages of their undergraduate education. For instance, pedagogical support aimed at addressing challenging knowledge and didactic lectures improves students' understanding and knowledge retention, reflected in enhanced exam scores (Karbownik et al., 2016; Islam et al., 2017; Arcoraci et al., 2019). For students in transition years, the interventions yielded improved competence in solving pharmacokinetic problems and transferability of skills for patient care (Dang, 2017; Zuna and Holt, 2017; Al-Sallami and Loke, 2018). Advanced students exhibit a high level of confidence in identifying, preventing, correcting, and communicating drug errors, particularly with prescription writing, fostering a more rational approach to prescribing (Kirsch et al., 2019). Furthermore, a shift toward a learner-centered approach in elective and capstone pharmacotherapy courses actively engages students, enhancing their learning, confidence, and competence (Trujillo et al., 2015; Remington et al., 2017).

Tailoring pedagogical guidance to learners' expertise levels, employing a scaffolding approach, can alleviate cognitive load (Kalyuga et al., 2003; Van Merrienboer and Sweller, 2005; Kalyuga, 2007). While many pedagogical interventions address characteristics of the cognitive framework, they often overlook cognitive load reduction as a fundamental mechanism underlying their effectiveness. To address the challenges in pharmacology education, educators should promote student-centered learning through innovative pedagogy that aligns with cognitive load theory principles, motivating and engaging students in meaningful learning (Kaylor, 2014; Mauldin, 2021).

The cognitive load theory provides design principles and strategies to enhance learning by reducing extraneous, managing intrinsic, and optimizing germane load (van Merrienboer and Sweller, 2010). The integration of these principles and strategies in pedagogical interventions sheds light on how this support is effective. For example, medical educators have introduced innovative tools like 3D printed molecular models, two-and three-dimensional visualizations, and computer-based multiscale models of the Pharmacology Inter-Leaved Learning-Cells environment to teach molecular modeling concepts related to drug-receptor and enzyme interactions (Hall et al., 2017; Dubovi et al., 2018; Hanson et al., 2019). Pharmacy students found the activity valuable, describing it as an "A-ha" moment that illustrated how molecules fit together and how binding sites work, significantly enhancing their understanding of essential pharmacological concepts for medication management. Additionally, it expanded their understanding of biochemical processes, improving their pharmacology learning beyond specific topics (Hall et al., 2017; Dubovi et al., 2018; Hanson et al., 2019). Visualization methods utilizing animation can eliminate barriers to understanding by simplifying complex cognitive processes and reduces the cognitive effort of mentally working out the interactions involved (Beyond, 2001). This realist review observes how pedagogical support as molecular modeling tools or computational models optimizes cognitive load to improve students' understanding of complex pharmacological concepts.

Simulation as a pedagogical tool enhances clinical reasoning and decision-making while preparing students for applying theoretical knowledge in a safe environment. Fidelity, representing the simulator's resemblance to real clinical practice, is an essential concept (Dieckmann et al., 2007; Cook et al., 2011; Benedict et al., 2013; Smith et al., 2014; Arcoraci et al., 2019). The beginner/junior students need learning in a relatively low fidelity environment that help to reduce the cognitive load (Reedy, 2015). This realist review observes second-year nursing students' use of low-fidelity simulation for time management improved confidence and readiness for clinical drug administration (Aggar et al., 2018). Meyer et al. (2017) found that nursing and pharmacy students' experience with high-fidelity simulation improved their pharmacology knowledge and application and emphasized the importance of interprofessional teamwork (Meyer et al., 2017). Although the design principles and strategies endorsed by Cognitive Load theory states that working from low to high fidelity environments can help to manage the intrinsic load (van Merrienboer and Sweller, 2010), this experience deviated from cognitive load theory's recommended transition from low to high fidelity, indicating the context of interprofessional learning positively influenced students' perception of pharmacology knowledge and interprofessionalism while managing intrinsic load.

This review identified emotional responses as the underlying mechanisms for translating pedagogical interventions into intended outcomes. Emotions significantly impact learning and cognitive processes, including perception, attention, memory, and reasoning (Clore and Palmer, 2009; Kensinger, 2009; LeBlanc et al., 2015). Emotions can either enhance memory and future recall or hinder information retrieval during moments of anxiety and stress, as seen in paramedics' drug dosage calculations (LeBlanc, 2009). Learners' experiences of satisfaction, enjoyment, enthusiasm, and interest can lead to a state known as "Flow" or "Flow experience" within an optimal balance between task challenge and skill level (Chang et al., 2018). Achieving this balance enhances learning, while an imbalance may lead to anxiety or boredom (Csikzentmihalyi, 1975, 1997). For example, final year pharmacy students' engagement in creating wellcrafted multiple-choice questions (MCQs) for an advanced clinical pharmacy program led to a constructive learning experience. A workshop on MCQ development helped them overcome the challenge of writing quality questions, improving their skills and making learning enjoyable in a less stressful environment. This not only boosted their satisfaction, motivation, and knowledge but also enhanced their assessment grades (Saba et al., 2019). The balance achieved in writing MCQs aligns with the flow experience observed in this flipped exam model.

The flow framework, which provides design principles for creating engaging elements in games, is an effective tool for studying the learning process in game-based learning (Kiili et al., 2012). High flow during gamification is linked to increased learner enjoyment, comfort, focused attention, and control of learning, resulting in better performance (Chang et al., 2018). Research has shown that adding gamification elements to online courses enhances learner engagement and performance (Hanus and Fox, 2015; Buckley and Doyle, 2016). This realist review observed comparable learners' experiences associated with game-based learning ranging from enjoyment, engagement, satisfaction, knowledge gain, to yielding better performance. Although the game designers consider factors contributing to flow experience, they usually do not refer to it directly with flow theory (Perttula et al., 2017). Utilizing a participatory design

approach based on the proposed principles of flow theory can enhance the effectiveness of gamification (Kiili et al., 2012).

A strong inverse correlation exists between flow experience and cognitive load, significantly impacting learning outcomes (Chang et al., 2018). The student's experience in the zone of proximal development shares similarities with the intrinsically satisfying flow experience, characterized by challenges slightly exceeding skills (Csikszentmihalyi and Rathunde, 1992, 2014). Flow theory highlights the importance of balancing challenge and skill for optimal learning. Moreover, balancing cognitive load, as argued by Sewell (2021), effectively navigates intrinsic and extraneous demands, safeguarding working memory for germane load, thus integrating optimal alignment between challenge and skill conditions for an ideal learning experience. This underscores a crucial equilibrium for successful learning navigation. This realist review illuminates pedagogical interventions facilitating student interest and enjoyment in the discipline in addition to reducing the cognitive load (Kaylor, 2014; Tankel, 2015; Khurshid and Noushad, 2017; MacDougall, 2017; Khurshid et al., 2018).

Finally, the realist focus determines "why" the pedagogical interventions are effective. Understanding the challenges gives us insight into the "why." Interventions primarily targeted the troublesome discipline of pharmacology, emphasizing complex concepts, content delivery, integration, and application. The majority of the interventions were effective since they were aimed at minimizing the gap between theoretical knowledge and clinical application (Vana and Silva, 2014; Kurup et al., 2017; Meyer et al., 2017; Sanko and McKay, 2017; Bernaitis et al., 2018), thus eliciting improvised practices and ways of thinking. Moreover, their effectiveness lies in the fact that they reinforce students' knowledge (McLaughlin et al., 2015; Eachempati et al., 2016; Kolluru and Varughese, 2017; Remington et al., 2017; Tinnon and Newton, 2017) and prepare them as selfdirected learners (Gaikwad and Tankhiwale, 2014; Persky and Dupuis, 2014; Patel et al., 2018; Saba et al., 2019). These interventions were included in the course curriculum to improve student learning in conjugation with the provision of clinical application of the knowledge. In conclusion, the desired outcomes of most of these interventions were favorable for students' cognitive gain and knowledge application.

The realist lens we applied provides a unique insight into pedagogical interventions focusing on three critical variables in pharmacology education: content, learners' motivation (self-drive), and the learning environment. These interventions fall into two broad categories, digital (online) and in-class approaches, each playing a significant role in shaping the learning experiences of undergraduate medical professional courses.

In terms of content, in-class approaches often adopt an integrated curriculum, capstone courses, small group discussions, teamwork, role-play games, and mind mapping. These methods deliver immediate results, enhancing test scores, promoting teamwork, critical thinking, and, importantly, boosting motivation. Learners are driven to engage with challenging content, which aligns with principles of social constructivism, emphasizing interaction and collaboration (Choudhury et al., 2015; Gorman et al., 2015; Jones et al., 2015; Karpa et al., 2015; James et al., 2016; Nguyen et al., 2016; Kurup et al., 2017; Ying et al., 2017).

Conversely, online interventions leverage technology to create an environment that can impact motivation. They employ diverse molecular modeling techniques, visual learning approaches, e-learning modules, gamification, and low to high fidelity simulations,

providing a deep understanding of complex concepts related to drug-receptor and enzyme interactions, biochemical processes, and essential pharmacological knowledge (Hanson, 2016; Hall et al., 2017; Meyer et al., 2017; Coons et al., 2018; Hanson et al., 2019). These tailored and personalized learning environments not only optimize cognitive load, preventing learners from feeling overwhelmed, but also foster a state of flow where students are fully engaged and motivated throughout their learning journey, making the experience highly effective.

In the context of the modern, technology-driven world, in-class pedagogical interventions and digital/online approaches harmoniously complement each other, forming the foundation of blended learning. This approach significantly enhances learners' ways of thinking and practicing, particularly in challenging subjects like pharmacology. Grounded in constructivism and viewed through the realist lens, this holistic approach strikes a balance between cognitive load, motivation, and effective learning strategies. As we evaluate the effectiveness of online and in-class interventions, it's crucial to consider the preferences and needs of pharmacology students. Understanding their learning styles and inclinations can guide us in tailoring the pedagogical approach that best suits their educational journey and how they can operationalize the domains of knowing, acting, and being.

Strengths and limitations

We undertook an innovative approach, marking our first attempt to identify why pharmacology interventions work, for whom, and in what contexts. It provided us with valuable insights about context and outcomes, offering practical information for educators and policymakers, especially in the field of pharmacology education. Our iterative and triangulated analysis fostered consensus and uncovered previously unreported outcomes, addressing a gap in scientific papers. We believe it adds depth to our understanding of the causal mechanisms behind these interventions, making it a valuable tool for evidence-informed decision-making.

Conducting a realist review proved resource-intensive for us, demanding substantial time and expertise for extensive data collection and analysis. The complexity of implementing this approach, particularly for researchers new to realist methods, posed a challenge. The process involved selecting educational theories to define causal mechanisms, which required our careful consideration. The iterative data collection added to the time-consuming nature of our research process. While we acknowledge these limitations, the insights we gained have the potential to inform future research and practice in the field of pharmacology education.

Conclusion

Pedagogical innovations aid medical and allied health sciences students in acquiring an understanding of core to complex concepts in pharmacology. These innovations impact students 'ways of thinking and practicing, foster interprofessional education, reduce cognitive load, and enhance learning experiences, ultimately improving exam performance. The review emphasizes the interplay between constructivism, cognitive load, and flow theories to enhance

pedagogical effectiveness, making it a valuable design principle for future implementation. By seamlessly integrating these pedagogical innovations over time, educational institutions can create a sustainable framework or design principle that consistently nurtures student engagement and performance in pharmacology. This holistic approach contributes to producing well-prepared professionals committed to patient-centered care and safety.

Practical implications

The practical implications of this research underline how educators can enhance the curriculum and redefine effective teaching and learning in pharmacology. By adopting pedagogical interventions centered around scaffolding and active learning strategies, educators empower students to grasp troublesome pharmacological concepts and improve their engagement. Effective teaching involves managing cognitive load and cultivating an atmosphere of enjoyment and satisfaction, ultimately leading to enhanced ways of thinking and practicing. Armed with these insights, educators can revitalize their instructional approaches, optimizing the learning journey for pharmacology students.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

FK, EO'C, RT, and IH collaborated on formulating the review question and establishing eligibility criteria. The team generated a protocol that was registered with PROSPERO. FK conducted the exploratory search, resulting in 70 papers from regular databases and 5 additional records for final screening. The team conducted an iterative process of examining primary studies and data synthesis using CMOc, leading to the refinement of the program theory. FK carried out data extraction using the CMOc spreadsheet, and IH, EO'C, and RT examined the consistency and patterns generated and their relationship with the program theory. FK presented the findings and conclusions derived during the process of data synthesis to the review team. Finally, FK drafted the manuscript, which was revised meticulously by IH, EO'C, and RT for content, ultimately giving their approval to the final submission. The exploratory search helped devise the initial program theory and CMOc, while the iterative process enabled the refinement of the program theory. Overall, the collaborative efforts of the team members allowed for a thorough and thoughtful review of the literature. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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