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RESEARCH ARTICLE

Impact of medicinal chemistry integration in Pharm.D. programmes on first-time NAPLEX pass rates

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Abstract

Objectives: To address the impact of instructing medicinal chemistry in an integrated versus stand-alone fashion on three-year average of first-time NAPLEX (North American Pharmacist Licensure Examination) pass rates of all United States of America Pharmacy programmes. **Methods:** A review of each programme's publicly available curriculum on their official webpage revealed medicinal chemistry as integrated (horizontal or vertical), or standalone course forms. Fisher's exact and the ANOVA tests were performed to assess the primary outcome and covariates. **Results:** Out of a total of 136 eligible programmes, 80 programmes (61.5%) stated that medicinal chemistry content was integrated with other foundational sciences content ('horizontal integration'), while 38 (29.2%) stated that medicinal chemistry was a standalone course. Medicinal chemistry is integrated with pharmacotherapy courses ('vertically integrated') in remaining 12 programmes (9.2%). **Conclusion:** A conclusion could not be made regarding the impact of medicinal chemistry instruction on NAPLEX outcome due to other underlying factors; however, this study provided a framework for future research.

Introduction

Over the last decade, the idea of the 'practice readiness' of entry-level pharmacy graduates has gained traction (Bzowyckyj *et al.*, 2021). As practice readiness includes a myriad of roles and responsibilities and different workplace settings, educational emphasis on the provision of patient-centred care has sharply risen accompanied by multiple demands for appropriate skills-based trainings embedded in the curriculum. While enhanced practice readiness for patient-centred care has become the central goal of pharmacy education, a survey conducted by the AACP (American Association of Colleges of Pharmacy) Biological, Chemistry, and Pharmaceutics Sections captured concerns from foundational sciences faculty regarding the possible dilution or compression of the pharmaceutical and foundational sciences in Doctor of Pharmacy (Pharm.D.) curricula (Poirier, Fan & Nieto, 2016). Indeed, medicinal chemistry is an example of a foundational course that is often integrated with clinical or other foundational science courses (Poirier, Fan & Nieto, 2016). Although medicinal chemistry is listed in Appendix 1 of ACPE (Accreditation Council for Pharmacy Education) Standard 2016 as a required element of the didactic Pharm.D. Curriculum, its significance is now questioned by not mentioning it in the most recent NAPLEX competency

statements. A detailed account of medicinal chemistry, its impact on the pharmacy curriculum, and its role in the evolution of the pharmacy profession have been reviewed by Khan and colleagues (Khan, Deimling, & Philip, 2011). Additionally, medicinal chemistry remains a major component for Area 2 of the national standardised Pharmacy Curricular Outcome Assessment (National Association of Boards Of Pharmacy, n.d.). Taken together, compression of the curriculum or integrative approaches have changed the way medicinal chemistry is taught at pharmacy programmes in the United States (U.S.), raising questions about the impact of medicinal chemistry on the learning and performance outcomes of pharmacy graduates.

Foundational sciences including medicinal chemistry are integral to Pharm.D. curricula because they allow learners to develop a deeper understanding of the basic principles governing pharmacy practice and clinical decision making (Kulasegaram *et al*., 2015). The adult theory of education posits that adult learners value the 'why they need to learn' the most, (Cooperstein & Kocevar-Weidinger, 2010; Reed *et al*., 2014), incentivising the ability of the student pharmacists to deploy their foundational science knowledge, such as medicinal chemistry, to inculcate critical thinking and problem solving. For these reasons, the integration of foundational and clinical sciences is also emphasised in Standard 1 in ACPE's 2016 Standards and in Domain 1, subsection 1.1.3 of the 2013 CAPE Outcomes (Accreditation Council for Pharmacy Education, 2015; Medina *et al.*, 2013).

In their 2021 AACP white paper, Malhotra and colleagues (Malhotra *et al*., 2021) examined multiple aspects related to the integration of foundational and clinical sciences including the need and challenges for integration, the theoretical educational framework for integration, and several curricular models for effectuating integration currently employed by medical and pharmacy education programmes in the U.S. currently, three integration models are employed across pharmacy schools: H-shaped vertical integration, Z-stack 'sliding scale' integration, and spiral integration. Although the reader is referred to this paper for a detailed explanation, briefly, the H-shaped model follows a sequential curriculum with IPPE (Introductory Pharmacy Practice Experiences) clinical rotations and other experiential exposure providing opportunities for vertical integration, while the Z-stack model requires the incremental inclusion of clinical sciences throughout the Pharm.D. programme, starting in the first year of the curriculum. The authors also explain the use of the Harden Ladder for creating and assessing integration. The current work adapted definitions of integration models based on this AACP white paper.

The main objective of this study was to assess how the instruction of medicinal chemistry in an integrated versus stand-alone fashion into U.S. Pharm.D. programmes may have impacted pharmacy board exam pass rates. The authors hypothesised that method of instruction of medicinal chemistry in Pharm.D. curricula impact primary and secondary learning and programme outcomes such as first-time NAPLEX pass rates.

Methods

All pharmacy programmes listed by the NABP (National Association of Boards of Pharmacy) with publicly posted NAPLEX pass rates were included in the study. Programmes were assessed using data from 25th February 2020, and were excluded from the analysis if any one of the following conditions was true:

1) programmes were located outside of the 50 states,
2) their accreditation status was changed from 2018 to 2020, or
3) if NAPLEX pass rates were not reported for any year from 2018 to 2020.

The primary outcome measure was the three-year average of first-time NAPLEX pass rates from 2018 to 2020. As exact enrolment numbers were not captured in the data source, this was calculated by multiplying each school's reported first time NAPLEX attempts for each year by the school's first-time NAPLEX pass rate for that year to estimate the number of students who passed on first attempt at each school in each year, and then dividing the total number of first-time attempts across all years by the total number of students who passed on their first attempt all years.

The primary independent variable of interest was the integration strategy employed for each school's medicinal chemistry content in their curriculum. A preliminary exploration of the published curriculum of each U.S. pharmacy programme revealed three main styles for teaching medicinal chemistry:

1) a standalone medicinal chemistry course,
2) a horizontally integrated curriculum , or a
3) vertically integrated curriculum.

For the purpose of this analysis, a programme was defined as horizontally integrated if medicinal chemistry was co-taught with pharmacology, pharmaceutics, or other foundational science subjects. Programmes were defined

as vertically integrated if medicinal chemistry was being taught with clinical sciences such as pharmacotherapy. Medicinal chemistry was considered a standalone course if it was reported as an independent class in a programme's curriculum. For this analysis, each programme was only classified into one of these categories using publicly accessible information. Covariates collected for analysis were each school's public or private status, U.S. Census region (Northeast, South, Midwest, or West), use of an accelerated curriculum (such as a three-year programme). Additionally, the number of first-time NAPLEX attempts in the year 2020 was included as a measure of class size.

The three groups were characterised with respect to these variables, and were then assessed for differences in covariates using Fisher's exact test for categorical variables and the ANOVA test for continuous variables. A similar test was performed using the ANOVA for the primary outcome variable. As the dataset is believed to contain all relevant observations, these inferential tests were performed to better understand where real-world differences between the three groups may exist, rather than to facilitate comparison to any larger population.

A series of linear regression models was constructed using the three-year average of first-time NAPLEX pass rates as the dependent variable. The first was a univariate model that included only medicinal chemistry integration status as in the independent variable. The second model was a multivariable model that kept integration status as the primary independent variable, adding the covariates to adjust for potentially confounding effects: public or private programme status, regional variation in programmatic implementation, accelerated curricula, and class size. Finally, a sensitivity analysis was performed using a linear regression model that omitted the U.S. Census region as a test of the explanatory value of this variable. Categorical variables with more than two values (integration classification and U.S. Census region) were coded as dummy variables. In all cases, statistical significance was assumed to be present at the $\alpha = 0.05$ level. All tests were performed with SPSS version 26. This was an analysis of publicly available aggregated academic data and therefore did not meet the criteria of human subject research.

Results

A total of 136 programmes were eligible for inclusion. Two programmes were excluded for being outside of the 50 states, while one programme was excluded due to a change in accreditation status, and three programmes were excluded for missing first-time NAPLEX pass rates during this period, leaving 130 programmes for analysis. A summary of included programmes is presented in Table I; of these, 80 programmes (61.5%) stated that medicinal chemistry content was integrated with other foundational sciences content ('horizontal integration'), while 38 (29.2%) explicitly stated that medicinal chemistry was a standalone course. The remaining 12 programmes (9.2%) were classified as vertically integrated where medicinal chemistry is integrated with pharmacotherapy courses throughout the curriculum.

Statistically significant differences were found in the public/private status of schools between these groups, with almost two-thirds of schools with a standalone medicinal chemistry course being public schools, compared with 33.3% to 41.3% in the other groups. ANOVA analysis of first-time pass rates identified a statistically significant difference in the year 2018, but not in other years. The three-year average first-time NAPLEX pass rate was 90.6% for the standalone medicinal chemistry group, 87.7% for the horizontal integration group, and 87.8% for the vertical integration group. A graph of first-time NAPLEX pass rates for each group across all three years, as well as the overall rate, is shown in Figure 1.

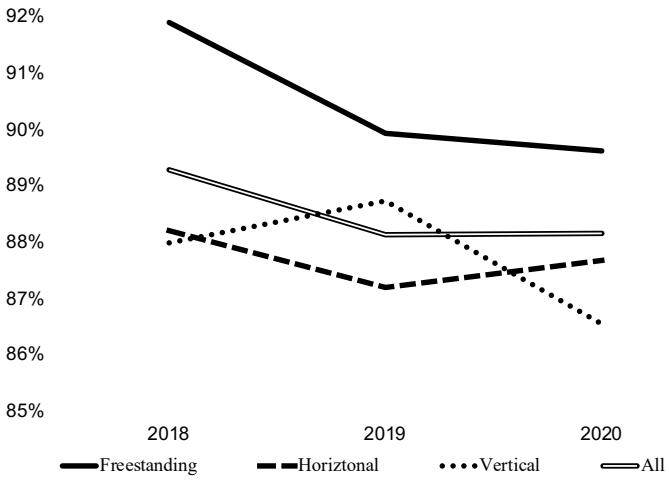

Figure 1: First-time NAPLEX pass rates for years 2018 to 2020 for all included pharmacy schools, combined and by medicinal chemistry integrated model

Results from the linear regression models are given in Table II. The group with medicinal chemistry as a standalone course was arbitrarily chosen as the reference group, as was the U.S. Census region in the Northeast. In the univariate linear regression model that only assessed

Table I: Summary of programmatic curricular data of U.S. Pharmacy Schools/Colleges in regards to medicinal chemistry components and NAPLEX outcomes

	Medicinal chemistry freestanding	Horizontal	Vertical	All included programmes	*p* value†
Count, n (%)	38 (29.2)	80 (61.5)	12 (9.2)	130 (100.0)	
Type of Programme, n (%)¶					0.047*
Public	24 (63.2)	33 (41.3)	4 (33.3)	61 (46.9)	
Private	14 (36.8)	47 (58.8)	8 (66.7)	69 (53.1)	
Census Region, n (%)¶					0.93
Northeast	7 (18.4)	15 (18.8)	1 (8.3)	23 (17.7)	
South	16 (42.1)	26 (32.5)	5 (41.7)	47 (36.2)	
Midwest	8 (21.1)	22 (27.5)	3 (25.0)	33 (25.4)	
West	7 (18.4)	17 (21.3)	3 (25.0)	27 (20.8)	
Three Year Programme, n (%)¶					0.064
Three Year	1 (2.6)	12 (15.0)	0 (0.0)	13 (10.0)	
Other	37 (97.4)	68 (85.0)	12 (100.0)	117 (90.0)	
First-time NAPLEX Attempts, median (IQR)					
2018	101.0 (68.50 - 135.75)	91.0 (70.25 - 125.75)	103.0 (68.50 - 188.50)	92.5 (69.75 - 131.50)	0.50
2019	103.5 (63.50 - 136.00)	93.5 (67.00 - 123.5)	92.5 (64.00 - 204.00)	94.5 (66.75 - 128.25)	0.34
2020	97.0 (58.50 - 130.00)	87.0 (65.00 - 122.5)	88.0 (134.00 - 57.25)	87.0 (65.00 - 122.5)	0.75
First-time NAPLEX Pass Rate %, mean (SD)					
2018	91.9 (5.9)	88.2 (8.1)	88.0 (8.5)	89.3 (7.7)	0.042*
2019	89.9 (7.4)	87.2 (9.0)	88.7 (5.5)	88.1 (8.4)	0.25
2020	89.6 (8.7)	87.7 (7.8)	86.5 (7.3)	88.1 (8.1)	0.37
Three-year First-time NAPLEX Pass Rate %, mean (SD)	90.6 (6.3)	87.7 (7.5)	87.8 (4.7)	88.5 (7.0)	0.11

¶Percentages are within-column for these rows.
†Assessed using Fisher's exact test for categorical variables (type of program, Census region, three year program) or ANOVA for continuous variables (first-time NAPLEX attempts, first-time NAPLEX pass rate, three-year first-time NAPLEX pass rate). Statistical significance was judged to be present if $p < 0.05$.
IQR = interquartile range
SD = standard deviation

Table II: Summary of Results from Linear Regression Models Used to Correlate Medicinal Chemistry Integration to Three-Year Average of First-Time NAPLEX Pass Rates †

	Univariate Model¶ Effect Size β, % (95% CI)	*p* value	Fully-Adjusted Model¶ Effect Size β, % (95% CI)	*p* value	Sensitivity Analysis¶ Effect Size β, % (95% CI)	*p* value†
Integration						
- Freestanding	REFERENCE	-	REFERENCE	-	REFERENCE	-
- Horizontal	-2.9 (-5.6, -0.1)	0.04*	-1.5 (-4.1, 1.2)	0.27	-1.3 (-3.9, 1.3)	0.32
- Vertical	-2.7 (-7.3, 1.8)	0.24	-2.2 (-6.5, 2.2)	0.32	1.9 (-6.2, 2.4)	0.38
First-time Attempts, 2020			0.0 (0.0, 0.1)	0.02*	0.0 (0.0, 0.1)	0.02*
Public School			3.3 (0.8, 5.8)	0.01*	3.6 (1.2, 6.0)	0.004*
Three Year Programme			-5.0 (-9.2, -0.7)	0.02*	-5.0 (-9.2, -0.9)	0.02*
Census Region						
- Northeast			REFERENCE			
- South			0.6 (-2.8, 4.0)	0.73		
- Midwest			2.0 (-1.7, 5.6)	0.3		
- West			1.6 (-2.2, 5.4)	0.41		
Intercept α, % (95% CI)	90.6 (88.1, 92.8)		84.4 (80.0, 88.8)		85.4 (81.9, 88.8)	
Model R^2	0.034		0.21		0.20	

¶All models are linear regression models correlating covariates to three-year average of first-time NAPLEX pass rates. Univariate model uses only medicinal chemistry integration as a covariate, coded using dummy variables with freestanding medicinal chemistry as a reference. Fully-adjusted model uses medicinal chemistry integration, number of first-time NAPLEX attempts in 2020, public school status, three year programme status, and U.S. Census region (coded as a dummy variable with the northeast region as a reference). The sensitivity analysis includes all of the covariates in the fully-adjusted model with the exception of U.S. Census region.
The model intercept and coefficient of determination, R^2, are included for each model for reference.
† Statistical significance for the correlation of each covariate was judged to be present if $p < 0.05$.

differences between the three groups on three-year average NAPLEX pass rates, the horizontally integrated group had a statistically significant correlation with the outcome. This integration model was correlated with average pass rates that were 2.9 percentage points lower (95% CI: -5.6%, -0.1%; p = 0.04) when compared to the freestanding integration model.

However, no integration model was associated with a statistically significant difference in first-time NAPLEX pass rates in either model that included other covariates. In the fully adjusted model, the number of first-time attempts was correlated with an increase in the average NAPLEX pass rates by 0.032 percentage points per additional student (95% CI: 0.006%, 0.058%; p = 0.02). Therefore, the model holds that —holding all other variables equal— each additional 32 students in a class may be correlated with a 1 percentage point increase in NAPLEX pass rates. Similarly, public school status was correlated with a 3.3 percentage point increase in pass rates (95% CI: 0.8%, 5.8%; p = 0.01), while accelerated programmes were correlated with reductions in pass rates by 5 percentage points (95% CI: -9.2%, -0.7%; p = 0.02). The effect sizes and results of statistical significance testing were consistent in the sensitivity analysis that excluded U.S. Census region, suggesting that this variable may not have contributed much explanatory power to the model.

Discussion

The investigation presented here is both timely and relevant, as both the 2013 CAPE Outcomes and the Entrustable Professional Activities (EPA) guidance are being reviewed by AACP task forces, in addition to the next version of the ACPE Standards being formulated. Thus, it is important to consider the impact that foundational sciences such as medicinal chemistry have on the learners' critical thinking abilities, overall growth and learning, and their ability to make sound, science-based clinical decisions. This ambitious undertaking of collecting and analysing multiple years of outcomes data from all schools and colleges of pharmacy in the U.S. was driven by the need to contextualise and critically examine aspects of pharmacy education related to Standard 1 of the 2016 ACPE Standards (Accreditation Council for Pharmacy Education, 2015).

As discussed in the introduction section, in view of the lack of a standard reference for integration that is uniformly employed across all pharmacy programmes, it is difficult to gauge the exact impact of integrating medicinal chemistry across the entire programme. This is further compounded by an often unclear or incomplete depiction of the curricular structure employed at pharmacy programmes. Consequently, in some instances, based on the information publicly available, the authors had to assign the possible degree of integration (or non-integration) of medicinal chemistry. Interestingly, in contrast to previous report that the majority of schools/colleges taught foundational sciences in therapeutics (Poirier, Fan & Nieto, 2016), this study identified more pharmacy curricula with horizontal integration of medicinal chemistry and very few curricula with vertical integration.

Beleh, Engels and Garcia (2015) evaluated the impact of integrating medicinal chemistry and pharmacology courses and alignment with a therapeutics series followed by an appropriate remediation process. This was found to be beneficial in terms of student performance and was viewed positively by both students and faculty. This is considered as partial and horizontal integration, as defined in this current research, and the positive impact was measured only within the institution by the course grades. However, no correlation with NAPLEX or PCOA performance was measured. Another cross-sectional study of a similar nature within a foreign Pharm.D. programme on the impact of multidisciplinary, vertically integrated pharmacotherapy curriculum by Alrasheedy (2020) reported positive student learning outcomes. Both participating students and faculty believed that this approach improved learners' problem-solving skills by achieving the required depth of the foundational knowledge and ability to apply those into therapeutic problem solving. However, this method requires careful design and implementation to get the full benefit of the integration. Nonetheless, the significance of medicinal chemistry and other foundational knowledge in clinical decision-making has been clear in these studies. The importance of medicinal chemistry in pharmacy education and practice has been further demonstrated by Fernandes (2018) by utilising clinically relevant medicinal chemistry case studies where medicinal chemistry concepts were found to be critical in clinical decision-making.

The significance of medicinal chemistry in pharmacy educational outcomes including foundational knowledge, essentials for practice and care, approach to practice and care and personal and professional development (ACPE Standards 1-4) and the inseparable and inherently bonded nature of these two scientific/professional areas are reviewed elsewhere in details (Alsharif, Theesen & Roche, 1997; Alsharif, Shara, & Roche, 2001; Accreditation Council for Pharmacy Education, 2015; Khan, Deimling & Philip, 2011). Importantly, most of the work cited in these

references provides only a conceptual framework based on theoretical aspects or research findings at a specific institution. However, the present study addressed this question using a comprehensive approach to examine the status of medicinal chemistry in the curriculum of all U.S. Pharm.D. programmes and the ultimate educational outcome defined by NAPLEX first-time passing rates. These may explain to some extent the current findings that the institutions with standalone medicinal chemistry curricula have slightly better NAPLEX passing performance compared to those with horizontal or vertical integrations. The results presented here are noteworthy to the extent that captured information on all relevant programmes in the U.S., and to the extent that the operationalisation of relevant variables is valid. Based on the findings of the current study, it is reasonable to opine that inclusion of multiple approaches of medicinal chemistry instruction in Pharm.D. education will positively impact learner performance on standardised national tests. However, the vital roles played by the factors such as programme maturity, resources, geographical locations cannot be ruled out.

The study discussed here is subject to several limitations. First, much of the information used to categorise programmes was collected from programme websites. However, data were presented in a limited fashion and in different ways. The authors attempted to address this by creating rigid rules for programme categorisation. For a few programmes, the authors reached out to the appropriate personnel to clearly understand the published curriculum on their web and appropriately categorise the programmes in one of those three groups. Second, programmes could only be effectively categorised at one time point, and programmes may have changed educational offerings in the years prior to the assessment. Some programmes may have been assigned on the basis of newer academic curricula that would not apply to first-time NAPLEX test takers, who may have been educated under older curricula. This miscategorisation may dilute the treatment effect, making results seem smaller than they are in reality. Third, these results were created from a near-total census of U.S. pharmacy programmes. While the authors were attempting to create comprehensive results, there is no larger 'whole' against which to compare or validate the present models. Finally, the authors only assessed the integration of one component of pharmacy sciences. Larger studies may be needed to create and test more comprehensive integration models, or to compare the present findings to findings from other time points or countries.

The new direction in pharmacy education increased the volume and rigour of clinical coursework. This has prompted the question of the relevance of medicinal chemistry in pharmacy education although it remains one of the required foundational components by the ACPE. In addition to drug design, development, and ADMET (absorption, distribution, metabolism, excretion, and toxicity) assessments, medicinal chemistry is vital in understanding the mechanism of action and structure activity relationship of medications. All these have a significant impact on therapeutic decision making and placing pharmacists at a unique position among health-care professionals in ensuring the safe, appropriate, and cost-effective use of medications. While a slightly better performance was observed in first-time NAPLEX pass rate in schools with standalone medicinal chemistry curricula compared to those with horizontal or vertical integration, no definitive conclusions can be made regarding the impact of degree of integration of medicinal chemistry content on pharmacy board exam pass rates due to multitude of other factors. Other factors such as programme maturity, resources, and geographical location may also have influence in first-time and overall NAPLEX pass rates.

This study highlights the challenge of assessing foundational science integration within the pharmacy curriculum and the need for a standard of reference for integration. The most recent NAPLEX Competency Statement identified six different areas for the examination. While Area 2 (Identify Drug Characteristics) covering approximately 14% of the test is directly related to medicinal chemistry and pharmacology as the foundational knowledge component, Area 3 (Develop or Manage Treatment Plans; ~35% of Test) and Area 5 (Compound, Dispense, or Administer Drugs, or Manage Delivery Systems; ~11% of Test) have integrated the medicinal chemistry concepts so that students can apply those to evaluate literature, solve therapeutic problems and provide evidence-based, patient centred, population-based care. The integration of knowledge may occur in both integrated or carefully designed and coordinated non-integrated curriculum. Here, the authors have provided a working framework for future research on detail curricular impact on NAPLEX and other educational outcomes.

Conclusion

This study is an initial analysis of the impact of medicinal chemistry on NAPLEX pass rate without a definitive

conclusion due to many compounding factors. However, it provides a compelling argument for a re-examination with new data and a framework for future research.

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