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Research

Creation and evaluation of a two-/three-dimensional molecular database for drugs used to target the respiratory system

Sara Jo Cassar, BSc Pharm Sci (Hons) (Melit), MPharm (Melit)*,
Claire Shoemake, BPharm (Hons), MPhil, MA (Diplomatic Studies), PhD (Nott), Dip (SBDD) (Nott), Dip (Arabic Studies),
Lilian M. Azzopardi, BPharm (Hons), MPhil, PhD, MRPharmS

Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Msida, Malta

Abstract

Introduction: Pharmacy undergraduate education has seen many changes throughout the years in order to provide a holistic approach to meet the needs of the current pharmacy profession. Nowadays educators are recognizing that molecular databases serve as a valuable reference point for clinical, physicochemical, and structural information.
Aims: The aim of this study was to compile an electronic molecular database of drugs used in respiratory conditions and to assess its utility by carrying out a randomized control study on a pharmacy student cohort of 125 students.
Method: To carry out this study, structures and representations of drugs acting on the respiratory system were created, compiled in a database, and uploaded onto the university's web site. An intervention lecture focusing on the molecular database was carried out with the experimental group, and students' individual performance at different stages in the study was assessed and statistical results were then generated.
Results: A drug repository of 51 entries was created. It was concluded that a significant improvement in the marks was attained in the experimental group ($n = 5.525$ points) with respect to the control group. A general trend can be noticed whereby student performance increased following the intervention and then diminished with time, as evidenced by the scores attained later in the study.
Conclusions: This study provides evidence that student understanding and knowledge is enhanced when teaching practices take on an innovative approach. The cohort gave high ranking scores when asked about the various aspects of the database, thus shedding light on the need of its implementation within the course as a lecturing and studying aid.

Keywords: Molecular database; Undergraduate pharmacy education; Medicinal chemistry; Respiratory pharmacology; Visualization

Introduction

With time, collating two- and three-dimensional structural information of small molecules within a molecular database has led to the latter's increase in number and availability. This development has led to an increased predictive power in medicinal chemistry, as well as to an abundance of information, which has enabled the enhancement our understanding of a drug's pharmacokinetic characteristics.[1]

An ideal database is one that is created around the needs of the user, thus providing the basic functions such as data retrieval, viewing functions, and drug structure

* Corresponding author: Sara Jo Cassar, BSc Pharm Sci (Hons) (Melit), MPharm (Melit), Department of Pharmacy, Faculty of Medicine and Surgery, University of Malta, Msida, Malta.
E-mail: scas0025@um.edu.mt, sarajocassar@gmail.com

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manipulation with maximal efficiency. This will prove to be very useful within a structure-based drug design (SBDD), automated synthetic progression, similarity testing, and substructural retrieval. Furthermore, the database must reach a level of detail that would make it a reliable and complete source of information, consequently enhancing its relevance both as a research and as an educational tool.[2]

Simultaneous enhancements with respect to visualization, computer science, and the World Wide Web have led to gradual modifications in the discipline of cheminformatics to include structure representation, search ability, and prediction of molecular properties. Due to the ever-increasing numbers of drugs that have been synthesized or are considered to be synthesisable, there has been an increasing need for cheminformatics to process and manage this data in order to make it available to researchers, students, and educators alike.[3]

Courses are continuously being introduced and revised to meet the needs of today's advancements in the fields of chemistry and informatics. Reforms in pedagogical practices are being carried out not only to strengthen students' skills during their current course of study but more importantly to create a sound basis for more advanced curricula that relies heavily on the initial bachelor coursework.[4]

Incorporating computational methods with medicinal chemistry education has led to the exploration of new skills that are necessary for related research programs. Literature has in fact shown that concepts in medicinal chemistry and more specifically in drug discovery are best conferred to students through visual aids and practical experiences that are deemed to be effective and attractive to students. Exposing students to such an approach will result in the appreciation of how concepts described in the lecture room can be applied to the pharmaceutical and biotechnological sectors.[5]

When introducing an educational tool, one must keep two goals in mind, namely, students' acquisition of key concepts and their participation when applying this information.[6] Computer technology has made it possible to facilitate not only students' appreciation of a drug's chemistry and properties but also their ability to contribute to the search of a drug-like molecule and its modification to make it more ideal for its role *in situ*.[7]

The link between medicinal chemistry, biochemistry, and the clinical setting can be improved by means of computerized cases. The latter can enable students to develop their skills in terms of structure–activity relationship studies, serving as a basis for their understanding of drug action at a molecular level. A holistic approach can be met if students are taught how to apply these skills to therapeutic situations, thus increasing its clinical relevance.[8]

A study carried out in 2013 by Edginton et al. concluded that student understanding of clinical biochemistry was enhanced during the initial stages of an approach encompassing self-assessment tests and case studies with lectures. This improved performance was seen as a promising start for further additions of this nature to the curriculum.[9]

The main objectives of this study which formed part of a larger research project being carried out by the Department of Pharmacy at the University of Malta were the following:

- To identify those drugs acting on the respiratory system as outlined by the British National Formulary (BNF)[10] and construct them in two- and three-dimensional form and deduce their physicochemical properties.
- To carry out a search for crystallographic depositions in the Protein Data Bank (PDB)[11] and create various representations using Visual Molecular Dynamics® (VMD),[12] consequently highlighting key interactions and spatial arrangements.
- To collate all the constructions, representations, and information in one searchable user-friendly database made available on the World Wide Web.
- To create, validate, and disseminate questionnaires to a student cohort to generate feedback about the database through the cohort's performance.
- To suggest methods by which this repository could serve as a learning and study aid.

Methods

Section 3 of the BNF 64 was used to identify drugs acting on the respiratory system together with their relevant clinical information. Structures were constructed in two dimension using Accelrys®[13] and in three dimension using Sybyl.®[14] Accelrys® was also used to generate the physicochemical properties of each drug. OCA browser® was utilized to identify PDB entries of drugs pertaining to this section. Interactions occurring between drugs and their cognate receptor were highlighted through depictive representations using VMD.® Jmol®[15] was used to create and embed interactive properties to three-dimensional structures and PDB entries. The structures, representations, physicochemical information, and clinical information were compiled in a searchable database framework using Zoho.com.® The database was then uploaded onto the University of Malta's web site.

In order to assess the utility of the database, a randomized control study was carried out on students reading for a Bachelor of Science degree in Pharmaceutical Sciences. The students were to be assessed at baseline (pre-test), after two weeks (post-test), and after four weeks (delayed). Initially, a 34-point questionnaire was created by extracting items from previous questionnaires[8,17,16] (Harrold, 1998) and by researching the syllabus covered by the students in these fields of study. The questionnaire was validated by a panel of experts, that included five clinical pharmacists, one respiratory medicine consultant, one respiratory senior registrar, one pharmacist specialized in regulatory affairs, and three pharmacists, two of whom specialized in respiratory pharmacology and one of whom specialized in medicinal chemistry. An information session regarding the stages of the study was given to the entire cohort prior to the dissemination of the pre-test questionnaire.