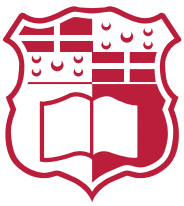

L-Università ta' Malta

DEPARTMENT OF PHARMACY

FACULTY OF MEDICINE AND SURGERY

DISSERTATION ABSTRACTS AND PROJECT DESCRIPTIONS 2019

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Foreword

Evidence of Excellence in Pharmacy Education

The presentations in the Annual Pharmacy Symposium organised by the Department of Pharmacy of the Faculty of Medicine and Surgery of the University of Malta, serve as a showcase of the research work which is expanding the evidence-base of the excellence of pharmacy education in Malta. Each year the Department acknowledges the students for their work by recognizing the highly successful results obtained through their efforts in producing original research with the supervision of their tutors.

The Pharmaceutical Journal Clinical Pharmacist December 2018 issue presents original research and evidence-based reviews as a means of identifying the expanding interventions of pharmacists. The areas covered in the Clinical Pharmacist 2018 issue include i) lower urinary tract infections (UTIs) where treatment provision of uncomplicated UTIs through community pharmacists is explained ii) medicines optimisation where an approach to medicines optimisation review is evaluated, iii) C-reactive protein testing where a study indicated that community pharmacists and GP clinics can deliver an effective service together with a high degree of patient satisfaction in this point-of-care test for respiratory tract infections which could in the long-term decrease bacterial resistance, iv) annual asthma reviews which intend to decrease the sub-optimal asthma care which is related to increased morbidity and mortality, v) instances of hypoglycaemia where an investigation is carried out to determine the presence of risks factors for recurrent hypoglycaemia and to identify whether these cases could be addressed by the pharmacist, vi) the care given to people living with HIV and how this care is continued in the older age now that people with HIV could have a normal life expectancy, vii) looking at the safety of new glucose lowering drugs on cardiology outcomes, viii) the contribution to public health which advocates the expansion of the role of community pharmacists particularly in relation to the provision of services that contribute to disease prevention and health improvement ix) combination inhalers in the treatment and management of chronic obstructive pulmonary disease and x) enhanced pharmacy care which looks at the impact of integrated pharmacy services on hospital admission cost.

This is the showcase given by the Royal Pharmaceutical Society of Great Britain of the way the UK has expanded its pharmacy evidence-base in 2018.

The Department of Pharmacy is celebrating this year the fifth intake of Doctorate in Pharmacy candidates. If one had to look at the eight projects presented by the Doctorate in Pharmacy 2019 prospective graduates one could easily compare the standard achieved in research in advanced pharmacy services in Malta with the above illustrated achievements in the UK. The titles and presenters of the projects are found on page 7 of this booklet and the abstracts showing the extent and breadth of this pharmacy practice research is published on pages 8 to 11. It is now time for pharmacy leaders to acknowledge this outstanding work as is done in the UK and to develop and invest in postgraduate training by working with Malta's Department of Pharmacy in placing this form of education as a priority in 2019 and beyond.

Graduates in the Doctorate in Pharmacy from the University of Malta should be in the first instance appointed as advanced clinical practitioners within the Government health services. This will help to stop the drain of highly qualified pharmacists to other areas where their capabilities and skills are well recognised.

The Doctorate in Pharmacy is now a showcase of excellence of pharmacy not only in Europe but in the international scenario. This postgraduate Professional Doctorate in Pharmacy, carried out in collaboration with the University of Illinois at Chicago College of Pharmacy, focuses on patient safety with regards to the development and use of innovative drugs. It is also providing a platform for supporting the development of leadership skills in topical issues in the pharmaceutical area for which there is also an increase of interest in the national scenario. These areas include stem cell therapy, medical devices, clinical trials and cannabis for medicinal use. This in addition to the practical placements which include the clinical rotations undertaken in different pharmaceutical scenarios including hospital pharmacy, community pharmacy, pharmacy health systems and pharmacovigilance settings.

The international family that is participating and exchanging good practice includes candidates from Germany, Ireland, Spain, Libya, Jordan, Italy, Hungary, Estonia, Serbia, Uganda, Oman, India and the Philippines.

It is time that the health authorities encourage, in a tangible and rewarding way, pharmacists working in the government services to join this successfully internationally-acknowledged doctorate programme.

Professor Anthony Serracino-Inglott
Pharmacy Practice Projects Co-ordinator

Introduction

The Department of Pharmacy has advanced in terms of academic, research and international outreach as a response to react to the national needs to cater for an expanding and advanced pharmacy workforce.

The course leading to a Bachelor of Science (Hons) in Pharmaceutical Technology prepares graduates who are focused towards pharmaceutical processes across the different settings of pharmacy including industrial, regulatory, administrative, hospital and community practice. The re-design of the Master of Science course offered by the Department of Pharmacy to provide the opportunity for graduates with a diverse background in science and healthcare areas to establish competences relevant to pharmaceutical regulatory sciences, pharmacoeconomics and pharmacy administration is a positive step to sustain further development of manpower required in the pharmaceutical sector.

The two-cycle programme leading to a degree in pharmacy offered by the Department of Pharmacy has evolved to present a model for pharmacy education that is followed and adopted by schools of pharmacy in Europe and Asia. The high quality pharmacy education programme equips students with relevant skills and competences that are essential to any pharmaceutical work setting. The emphasis in the programme is to support students to mobilise knowledge and apply science to practice in pharmaceutical settings. To complement the opportunity for pharmacy graduates to read for a doctoral level degree, a challenging and innovative step was taken five years ago with the commencement of the Doctorate in Pharmacy course that is offered by the Department in collaboration with the College of Pharmacy of the University of Illinois at Chicago, USA. This programme provides pharmacists with the opportunity to further their studies, empowering them to advance knowledge, practice and research through professional innovation and leadership. The course has attracted 65 students, of whom 25 hail from 14 countries around the globe including: Estonia, Germany, India, Ireland, Italy, Jordan, Lebanon, Libya, Oman, the Philippines, Serbia, Spain, Turkey, and Uganda. We are now witnessing Doctorate in Pharmacy graduates who are contributing to the expansion of pharmaceutical activities which focus on patient safety such as assessment and access to innovative pharmacotherapy, pharmacovigilance, and advanced clinical practitioners in hospital and community pharmacy settings.

Through the five undergraduate and postgraduate programmes offered by the Department of Pharmacy, research skills are developed at varying levels. The development of these research skills are considered to be a relevant transferable skill which graduates can put immediately to use once they join the real job market. During the Annual Pharmacy Symposium, students following the different courses present their work-in-progress or final results for their research project or dissertation. This experience imparts skills in disseminating research results through posters and oral presentations. Through pharmacy practice research within the Department, new pharmaceutical service models in our hospitals and community pharmacies have been designed, elaborated and launched. Research outcomes focus on processes that increase optimisation of therapeutics whilst striking a balance not to overburden the patient, achieving pharmacoeconomic stability, assessing medication quality, safety and efficacy, supporting equity and importantly access to treatment.

The international outreach enjoyed by the Department of Pharmacy contributes to the expansion of the network for staff and students. Through this network, around 90% of pharmaceutical technology and pharmacy students have the opportunity to participate in the Erasmus student mobility programme. The Department of Pharmacy has collaboration agreements with the College of Pharmacy of the University of Florida and through this agreement the Department hosts students from the University of Florida for rotations and for a short-study abroad clinical pharmacy course. This year, an agreement has been finalised with the Skaggs School of Pharmacy and Pharmaceutical Sciences at the University of Colorado, Denver to provide opportunity for postgraduate student exchange and to collaborate on research on cannabis for medicinal use. Five doctorate in pharmacy students have followed rotations in Chicago and Florida as part of their studies.

The Department of Pharmacy employs a rapid responsive planning as a reaction to innovation and advances in the pharmaceutical sector. This is achieved by maintaining a cooperative model with stakeholders.

Professor Lilian M. Azzopardi
Head, Department of Pharmacy

Doctorate in Pharmacy
Dissertation Abstracts

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Pharmacogenetics in Statin Use
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Marta Zuccarelli

Pharmacist-Led Transition of Care in Diabetic Patients

Charlene Camilleri

Background: It has been demonstrated that pharmacist-led interventions contribute to a decrease in drug-related problems (DRPs) and improve clinical outcomes.

Purpose: To develop and implement a pharmaceutical service at the outpatient setting for diabetic patients focusing on medicine reconciliation and effective transition of care.

Method: A prospective investigational study conducted at Mater Dei outpatient department was undertaken. Patients >18 years of age and having at least one antidiabetic medication were eligible to participate in the study. A Transition of Care Document, aimed at compiling all the necessary medicine information obtained during the medicine reconciliation carried out during this study, was compiled and disseminated to the patient's community pharmacist via e-mail. Three questionnaires were compiled. One was sent together with the Transition of Care Document to the community pharmacist to assess the effectiveness of the transition of care document. A second questionnaire was completed by the patients to assess the pharmacist intervention and the third questionnaire was disseminated to twelve health-care professionals.

Results: Eighty-seven patients were recruited for the study. One hundred eight-two drug related problems (DRPs) were identified during the medicine reconciliation and classified into six different categories. The two most prevalent DRPs were: Lack or misinterpretation of information (46%) and insufficient awareness of health and disease (37%). During the outpatient pharmacist session, 83 patients required verbal intervention from the pharmacist and 15 patients required both written and verbal interventions. A Transition of Care document was disseminated to 64 pharmacists together with a questionnaire, to assess the effectiveness of the document. Twenty-seven pharmacists completed the questionnaire and unanimously agreed that there is a need for better communication between hospital pharmacists and the community. Patients (98%) reacted positively to the clinical service offered by the pharmacist while all healthcare professionals encouraged the addition of a clinical pharmacist to the diabetic team.

Discussion: The implementation of this pharmacist-led transition of care service was shown to be relevant to the outpatient diabetic group as demonstrated by the identified DRPs. The effectiveness of the transition of care document needs to be further evaluated.

Harmonisation of a 24-hour Drug Information Service

Jeffrey Cassar

Background: The Pharmacy Department at Mater Dei Hospital (MDH) operates a drug information service (DIS) during normal working hours through its Medicines Information Department (MID). The after-hours DIS is provided by shift pharmacists and follows a different model to that made available by the MID.

Purpose: To achieve harmonisation between the DIS provided by the MID and shift pharmacists by addressing the needs of, and identify improvements required by the after-hours DIS.

Method: A three-week research observation placement was attended at the drug information centre at the University of Illinois in Chicago (UIC), USA, to detect the framework used. A gap-analysis comparing the DIS at MDH to that of UIC was performed. A focus group comprising of nine members was set-up to discuss improvements identified based on the observational framework and which are required in the after-hours DIS at MDH. An improvement framework with a timeline over four months for implementation was drafted and validated.

Results: Five categories of needs were identified from the improvement framework: communication, quality assurance, documentation, standardisation of workforce number and organisation of resources. A liaison pharmacist was introduced to enhance communication between the MID and after-hours DIS and performed fifteen interventions. Twelve training sessions were held by the MID for the two pharmacists forming part of one shift complement of the after-hours DIS. Seven and seventeen pharmacists attended the journal club and clinical-based discussion, respectively, organised by the liaison pharmacist. An electronic documentation form was developed, validated and used to document seventy-one after-hours DI requests, nine of which were audited by three pharmacists. An on-call system to keep staff levels constant was implemented in fourteen and nine cases of vacation and sickness leave, respectively, for one shift complement. Twelve out of twenty-four printed after-hours reference resources were outdated and were removed from circulation. Access information for four electronic reference resources was assembled.

Discussion: The improvements identified from the gap analysis and the focus group led to the development and implementation of the improvement framework. The outcomes of the framework laid down a harmonised system. Focus on enhancing communication needs to be emphasised.

Pharmacogenetics in Statin Use

Judith Cerdá Iñesta

Background: The *SLCO1B1* c.521T>C (rs4149056) genetic polymorphism is a predictor of simvastatin-induced myopathy.

Purpose: To identify presence of the *SLCO1B1* c.521T>C genetic polymorphism in a cohort of cardiac patients on simvastatin, correlate genotype results with myopathy risk and analyse EudraVigilance adverse drug reaction (ADR) reports for myalgia, myopathy and rhabdomyolysis with simvastatin.

Method: Patients on simvastatin were recruited by convenience sampling from the catheterisation laboratory at Mater Dei Hospital after ethics approval. An EDTA-blood sample was collected from each patient and genomic DNA was extracted using the QIAamp® DNA Blood Mini kit. Real-time polymerase chain reaction *SLCO1B1* c.521T>C genotyping was performed with the Sacace® Biotechnology kits and Rotor-Gene™ 6000/Q. Patients were classified into three genotypes (phenotypes): TT (normal *SLCO1B1* function), TC (intermediate *SLCO1B1* function) or CC (low *SLCO1B1* function). TC and CC patients were referred to cardiologists with Clinical Pharmacogenetics Implementation Consortium (CPIC)[1] recommendations and patients followed after 6 months. EudraVigilance ADR reports (2014-2018) for myalgia, myopathy and rhabdomyolysis with simvastatin were analysed.

Results: The 110 patients recruited (all Caucasian, 90 male, mean age 65 years) were genotyped as TT (78.2%, n=86), TC (20.0%, n=22) and CC (1.8%, n=2). Fifteen of the 24 TC and CC patients were prescribed simvastatin 40mg daily. At follow-up, 15 patients (12 TT, 2 TC, 1 CC) self-reported muscle stiffness (n=6; 5 TT, 1 TC - 20mg), cramps (n=4; all TT), pain (n=4; 3 TT, 1 CC - 40mg) or weakness (n=1; TC- 40mg). A total of 1,950 ADR reports were recorded in 5 years; myalgia (n=1450), myopathy (n=153), rhabdomyolysis (n=347). The dose was included in 1,294 reports; myalgia (≤20mg n=560, >20mg n=402), myopathy (≤20mg n=43, >20mg n=45), rhabdomyolysis (≤20mg n=99, >20mg n=145).

Discussion: Patients genotyped as TC and CC (22%) have mild and high myopathy risk respectively. The CPIC recommends a lower simvastatin dose (20mg/day) or consideration of an alternative statin (rosuvastatin) in patients genotyped as TC and CC. The observed findings are exploratory and warrant further investigation.

Reference: 1. Ramsey L, Johnson S, Caudle K, Haidar C, Voora D, Wilke R, et al. The Clinical Pharmacogenetics Implementation Consortium Guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update. Clin Pharmacol Ther. 2014;96(4):423-8.

Reducing Readmissions in Heart Failure Patients through Pharmacist-Facilitated Transition-Of-Care Interventions

Ivan Debono

Background: Consistent preventative pharmaceutical care interventions during care transitions with the aim of improving patient outcomes and quality care are imperative for a shift towards value-based care. The impact of pharmacist interventions on readmission rate of heart failure (HF) patients is a target outcome measure. Finding the most appropriate and practical intervention combination to be applied during transition from hospital to community is challenging.

Purpose: To determine and apply pharmacist interventions during transition-of-care (TOC) to a sample of HF patients and study impact on readmission rate.

Method: The study was conducted from 20th June, 2018 to 31st January, 2019, at Mater Dei Hospital. A multi-perspective focus group supported with surveys and literature was used to determine pharmacist interventions for a TOC pathway. Patients suffering from HF who followed the pathway were compared to a control group that followed the usual TOC. Recruitment involved prospective convenience sampling using eligible criteria. The study involved two phases starting with the control group (n=52). The proposed pathway was then piloted in the intervention group (n=27). The primary outcome was 30-day all-cause readmission. The secondary outcomes were all-cause readmission during the observation period from day 31-60 post-discharge and the number and type of interventions.

Results: The proposed pathway followed a ward-based pharmacist model with a case management approach that included medication reconciliation, medication-use education and telephone care management post-discharge. The 30-day all-cause readmission rate of the control group was 30.8% and that of the intervention group was 18.5% (p=0.242). The readmission rate between days 31-60 was 13.5% for the control group and 22.2% (p=0.211) for the intervention group. A total of 317 interventions with a mean of 11.7 per patient were performed as part of the pharmaceutical care pathway.

Discussion: The piloted TOC pathway is a quality improvement composite indicative that pharmacist interventions delivered at the right place and the right time may reduce readmission rate of HF patients during the immediate period after discharge and possibly beyond 30 days if interventions are continued. The results obtained remain exploratory and a study on a larger population with a randomised controlled approach is warranted.

Evidence Generation in the Clinical Development of Medicines for Leukaemia

Dylan Said

Background: Leukaemia accounts for the highest age-standardised mortality rate among haematological malignancies in Europe. Evidence of efficacy for antineoplastic agents may be valued differently by regulatory and health technology assessment (HTA) bodies in the European Union (EU), impacting decision-making and access to novel medicines.

Purpose: To analyse the evolvement of efficacy endpoints studied in leukaemia clinical trials (CTs), to explore scientific expert opinions on the quality of evidence generated for antineoplastic therapies and to determine core efficacy outcomes prioritised by EU decision-makers for leukaemia CTs.

Method: Part I data collection (trends in efficacy endpoints): (1) Phase II to Phase IV leukaemia CTs were identified from the EU Clinical Trials Register database throughout an 11-year period (2007-2017), (2) CTs were screened against inclusion criteria, (3) efficacy endpoints were extracted and grouped according to type of measurement, (4) data mining of trends was performed using descriptive and inferential statistics. Part II data collection (scientific expert opinions): (1) the Response Evaluation in Leukaemia (REVALEU) surveying tool was developed and tested for validity and reliability, (2) the tool was disseminated in an e-Delphi process with two independent panels composed of regulatory and HTA oncology experts, (3) core efficacy outcomes reaching consensus were determined.

Results: Thirty-six unique efficacy endpoints were identified from the final dataset of CTs (N=431) and grouped into clusters of survival (n=5), time-to-event (n=6), response rates and biomarkers (n=16) and other (n=9). Complete response rate was the most studied primary endpoint (CTs: 19%, n=81), with progression-free survival (PFS) and minimal residual disease (MRD) registering the highest frequency change pre- and post-2012 (PFS: 8%, p=0.01; MRD: 8%, p=0.003). Thirty-six panellists were recruited in the e-Delphi; 24 regulatory representatives from the European Medicines Agency (EMA) and 12 experts from HTA bodies in 9 EU countries. Opinions on the quality of pre-authorisation evidence generated were divergent (mean scores: 2.83 (HTA), 3.28 (regulatory), p=0.01). Six core efficacy outcomes reaching consensus were common to both decision-makers.

Discussion: Biomarker-based endpoints are emerging as primary efficacy measures in leukaemia CTs. Decision-makers perceive the quality of evidence generated differently. The identification of core efficacy outcomes optimises CT data packages for potential regulatory and reimbursement approvals.

Drug Information Access to Pharmacists' Bedside Decision Making

Timothy Scicluna

Background: The provision of drug information (DI) is a routine component of the daily practice of a pharmacist and has been associated with decreased drug cost and reduction in hospital stays.

Purpose: To evaluate DI requests for pharmacists' bedside service and assess access to DI systems.

Method: The study was set up in three phases. An observational study at the University of Illinois in Chicago (UIC), USA was carried out to undertake a comparative approach between US and local DI settings. The second phase consisted of a focus group made up of users and providers of DI which was aimed at identifying limitations and barriers for DI access at bedside. An 8-week prospective study at the Intensive Care Unit (ITU) at Mater Dei Hospital was carried out to identify challenges to offer a DI bedside service.

Results: The DI centre and bedside DI services at UIC are standalone, as opposed to those in Malta. At UIC, DI services at ward level by pharmacists is carried out using a mobile bedside computer with access to all the necessary resources. During the focus group discussion, it was concluded that the main challenges to DI bedside access are Wi-Fi access at ward level and lack of online resources. During the period at the ITU at MDH, 140 bedside queries were forwarded to the pharmacist at bedside with a mean of 7 queries daily. Forty-three percent of the queries were forwarded by medical officers and 32% by medical consultants. Pharmacists used DI to tackle 8% of queries which arose while reviewing drug treatment chart. Drug Interactions/Adverse Drug Reactions and Pharmacotherapy were the most common types of queries with 27% and 28% respectively. Fifty-nine percent of the queries were answered in less than 5 minutes at patient bedside, while only 1% of queries took more than 10 minutes to answer. Resources used to answer these queries were the mobile applications Micromedex and UptoDate. Seven percent were forwarded to the MDH DI centre.

Discussion: Pharmacist bedside DI services improve efficiency of turnaround time and provided that all the necessary resources and mobile DI applications are available, the majority of DI queries can be handled at bedside.

Social and Scientific Implications of Pharmacogenetic Testing

Althea Marie Xuereb

Background: Lack of awareness and confidence among healthcare professionals are barriers in implementing pharmacogenetic (PGx) testing in patient care.

Purpose: To assess awareness and attitudes of pharmacists and physicians regarding PGx testing.

Method: A self-administered questionnaire was developed, validated and tested for reliability. The questionnaire was disseminated i) online to pharmacists and physicians through social media groups ii) personally by the researcher by visiting pharmacies and clinics selected by convenience sampling iii) through the mailing list of the Malta College of Family Doctors and iv) during two local medical conferences. Descriptive statistics were performed and mean rating scores were calculated for Likert-type questions, 1 (lowest) to 5 (highest).

Results: The potential number of participants was 2,148 resulting in 292 (14%) responses (6% margin of error); 75% (n=220) completed online. The sample consisted of 179 pharmacists (64% female, 38% practicing >10 years) and 113 physicians (50% female, 54% practicing >10 years). Participants agreed that PGx testing guides personalised therapy selection and dosing (4.38 ±0.64), is useful in treatment resistance (4.34 ±0.68) and intolerance (4.22 ±0.71) cases, should be a government-funded service (3.88 ±0.80) and results in decreased healthcare costs (3.63±0.82). Oncology drugs were perceived as most important for PGx testing (58%, n=168). Challenges for implementation of PGx testing perceived highest by participants included lack of public (4.42 ±0.77) and healthcare professional (4.31 ±0.70) awareness and cost issues (4.32 ±0.68). Thirty-two percent (n=92) of participants perceived the need to order a PGx test at least once monthly, but only 4% (n=11) had ever ordered a test. Participants did not feel competent in PGx (1.82 ±0.88) and lacked confidence in recommending (2.30 ±1.13) and ordering (2.35 ±1.14) a PGx test, in interpreting test results (1.99 ±1.03) and in discussing results with patients (2.22 ±1.12). Participants agreed that more education is required to increase their competence and confidence (4.41 ±0.91). Seminars (73%, n=211) were the preferred approach for further education.

Discussion: Participants recognised the benefits of PGx testing. The need for further education is addressed through organisation of an online seminar for pharmacists and physicians on the practical aspects of PGx testing using case studies.

Developing Safe and Effective Medicinal Products to treat Rare Eye Diseases: Leber Hereditary Optic Neuropathy and Retinitis Pigmentosa. Clinical and Regulatory Challenges

Marta Zuccarelli

Background: Leber Hereditary Optic Neuropathy (LHON) and Retinitis Pigmentosa (RP) are two ocular rare-inherited diseases leading to blindness with only few treatments available within the European Union (EU).

Purpose: To understand emerging patterns being pursued by pharmaceutical companies when developing safe and effective innovative medicines to treat LHON and RP.

Methods: Investigational medicinal products (IMPs) to treat LHON and RP were retrieved from the EU Clinical Trials (EudraCT) Register and from the United States National Library of Medicines (USNML) database of clinical trials. The clinical trials included were (i) carried out between January 2007 and November 2018, (ii) interventional, (iii) related to a medicinal product (MP), (iv) registered as ongoing, recruiting or completed. Prospective treatment protocols for LHON and RP were developed. Emerging patterns in primary endpoints over time in relation to efficacy were identified and compared.

Results: Clinical trials related to IMPs studied for LHON were retrieved from USNML (31) and EudraCT (9). Clinical trials related to IMPs studied for RP were retrieved from USNML (147) and EudraCT (17). Sixteen clinical trials for 9 IMPs studied for LHON were selected according to the inclusion and exclusion criteria. Out of 9 IMPs, 6 were small molecules and 3 were advanced therapy products (2 gene therapy MPs and 1 somatic therapy MP). Among the small molecules, Raxone (idebenone) was authorised in the EU under exceptional circumstances. Thirty-five clinical trials for 18 IMPs studied for RP were selected according to the inclusion and exclusion criteria. Out of 19 IMPs, 10 were advanced therapy MPs (3 gene therapy and 6 somatic therapy MPs), 7 were small molecules and 2 were growth factors. Among the gene therapy products, Luxturna (voretigene neparvovec-rzyl) has an initial marketing authorisation within the EU for RP. Prospective treatment protocols for both LHON and RP were suggested.

Discussion: There is an increased interest in studying medicines to treat LHON and RP as shown by the increased number of clinical trials carried out and the number of drug classes explored. Medicinal products available on the market are still not sufficient for the treatment of LHON and RP and an unmet medical need is present.

M.Pharm. Students
Dissertation Abstracts

Pharmaceutical Care

Haemoglobin Point-of-Care Testing
Martina Scicluna

Transitional Care in Rheumatoid Disease Patient Management
Francesca Galea

Access to Antidiabetic Medication and Patient Self-Monitoring
Jessica Zarb

Supplementary Pharmacist Prescribing and Point-of-Care Testing in Community Pharmacy
Tricia Micallef

Older Person's Perception of Pharmacy Services
Nemanja Dodic

Haemoglobin Point-of-Care Testing

Martina Scicluna

Background: Various haemoglobin point-of-care testing (POCT) devices exist differing in size, blood sample volume and measuring methods.[1] In this study the suitability of two haemoglobin POCT devices namely Diaspect Tm and STAT-Site M Hgb was assessed.

Objectives: To compare diagnostic accuracy measures of two POCT devices against standard laboratory testing.

Design: Testing was first implemented on 72 participants who were undergoing a complete blood count test on the day and were suffering from Chronic Kidney Disease (CKD) (n=24) or diabetes (n=24) and on healthy patients (n=24 control group). Testing involved finger pricking with a lancet and using the second and fourth drop of blood to generate a result using STAT-Site MHgb and Diaspect Tm respectively. The test results generated by the POCT devices were compared to the results generated by automated analysers at MDH laboratories. Sixty new participants, 20 from each patient group were then tested once using Diaspect Tm only.

Setting: Patients were recruited from a Health Care Centre Setting.

Main Outcome Measures: Haemoglobin results generated by automated analysers at MDH and point-of-care devices.

Results: Diaspect showed a sensitivity of 89% whereas Stat-Site showed a sensitivity of 100%. Diaspect gave better results in terms of specificity as it showed 51% specificity compared to Stat Site's 15.5%. The mean Diaspect values for the three patient groups were 13.5 (healthy), 12.2 (diabetes) and 12.0(CKD) and the mean lab values were 14.7 (p=0.000), 13.4 (p=0.000) and 12.9 (p=0.007). On testing participants using Diaspect Tm only, the device showed a sensitivity of 100% and a specificity of 75%.

Conclusion: The higher accuracy, the balance between sensitivity and specificity, and the ease of use of Diaspect Tm render it a superior haemoglobin POCT device compared to Stat-Site M Hgb.

References:

1. Singh A, Dubey A, Sonker A, Chaudhary R. Evaluation of various methods of point-of-care testing of haemoglobin concentration in blood donors. Blood Transfusion. 2014;13(2):233-239.

Transitional Care in Rheumatoid Disease Patient Management

Francesca Galea

Background: Patients visit the Rheumatology Outpatients Department at Mater Dei Hospital every 6-12 months and any changes in drug therapy are decided by the caring consultant rheumatologist. Patients are collecting their chronic medications from their community pharmacy of their choice (POYC).

Objectives: To set up a transitional care service consisting of a transitional care letter and to evaluate feedback from pharmacists regarding this letter.

Design: The transitional care letter was developed and validated through an expert panel. The letter highlighted any treatment changes instituted during the rheumatology out-patient session. The letter was prepared for 13 patients who were then asked to submit it to their community pharmacist during the next POYC pick-up. An interview with community pharmacists participating in the POYC scheme chosen by stratified convenience sampling was undertaken.

Setting: Rheumatology out-patient clinic and community pharmacies

Main Outcome Measures: Development of a transitional Care Letter, perception of value of the Letter by community pharmacists.

Results: The letter was completed at the Rheumatology Out-Patient clinic for 13 patients. When the community pharmacies were contacted to follow-up on delivery of the letter by the patient, no pharmacists had received the letter. Community pharmacists lamented that on occasions patients themselves have inadequate information regarding changes in medication and added that the letter will help them notice any drug to drug interactions. The only negative comment by a pharmacist was that the advantage of the letter will be lost among the excessive number of documents that each patient would have. When offered the option of receiving the transitional care letter electronically or by hard copy, 20 pharmacists agreed that both would be acceptable.

Conclusion: The method used to convey the transitional care letter to the community pharmacists adopted in this study needs to be further streamlined.

Access to Antidiabetic Medication and Patient Self-Monitoring

Jessica Zarb

Background: Patient self-monitoring of blood glucose (SMBG) levels contributes to patient empowerment and optimisation of diabetes management.

Objectives: To investigate the perception of patients with type 1 diabetes mellitus (T1DM) regarding SMBG and Continuous Glucose Monitoring (CGM) and to identify problems encountered when carrying out BG monitoring.

Design: A questionnaire on SMBG in English and Maltese language completed by a semi-structured interview developed and validated in a previous study by Cassar[1] was updated with the inclusion of a section on CGM. The questionnaire was disseminated to T1DM patients ≥18 years recruited by convenience sampling after ethics approval. Descriptive statistics were calculated.

Setting: Fifteen community pharmacies; 3 from each of the 5 districts in Malta

Main Outcome Measures: Perception of T1DM patients on SMBG and CGM; challenges with BG monitoring

Results: The mean age of the 70 patients interviewed was 39 (range 18-69) years, 38 were female and 52 had been diagnosed with T1DM for more than 5 years. The most frequent problems encountered with daily SMBG were painful finger pricking (n=37) and high cost of buying extra test strips (n=33). Five patients currently use a CGM device and 30 patients are willing to use a CGM device in the future. Forty-seven patients stated that time was a barrier for SMBG.

Conclusion: Patients are not adhering to the recommended daily schedule for SMBG for various reasons including access to test strips and time limitations. T1DM patients are entitled to four test strips a day for free on the national health scheme. Improving awareness and access to CGM is warranted to overcome the problems identified with SMBG.

Reference:

1. Cassar J. Diabetic patient management [project]. Msida (Malta): Department of Pharmacy, University of Malta; 2009.

Supplementary Pharmacist Prescribing and Point-of-Care Testing in Community Pharmacy

Tricia Micallef

Background: Supplementary pharmacist prescribing (PP) was found to be an appropriate model for the local scenario.[1]

Objectives: To put forward a feasible model for point-of-care testing (POCT)-led supplementary PP.

Design: A questionnaire to assess local pharmacist and physician opinions on the introduction of PP in Malta, and POCT devices considered accurate was developed. Three treatment frameworks for the chronic conditions Type 1 and Type 2 diabetes mellitus in adults and hypertension in adults were developed based on NICE guidelines. The frameworks were also validated by means of the questionnaire. The frameworks were updated after considering participant suggestions, and validated again by a focus group consisting of 3 pharmacists and 3 other health care professionals.

Setting: Questionnaires were disseminated in community pharmacies to all community and locum pharmacists, and 250 physicians.

Main Outcome Measures: Analysis of local pharmacist and physician opinions on introduction of POCT-led supplementary PP.

Results: A response rate of 22.8% physicians and 65.14% pharmacies was obtained, yielding 57 physician and 205 pharmacist responses (178 community pharmacists, 27 locum pharmacists). When asked if pharmacists are competent to prescribe with their current level of knowledge and training, the overall mean rating score was in the positive (3.73 on a scale of 1 to 5). Pharmacists (community 3.84, locum 3.81) rated the statement significantly higher than physicians (3.33; $p = 0.002$). The main limitation identified by participants to the local introduction of PP was time restriction (3.75).

Conclusion: Pharmacist and physician opinions are in support of supplementary PP for hypertension and diabetes mellitus.

Reference:

1. Scerri M. Use of NSAIDs and Pharmacist Prescribing [Dissertation]. Msida (Malta): Department of Pharmacy, University of Malta;2013.

Older Person's Perception of Pharmacy Services

Nemanja Dodic

Background: Pharmacists' involvement in the care of geriatric patients contributes to optimisation of chronic disease management and polypharmacy use.

Objectives: To assess the perception of older persons about their care and of pharmacist services.

Design: A questionnaire developed by Zammit[1] was administered to patients ≥ 60 years as a semi-structured interview. The questionnaire collects patient demographics and information about living situation, support received with medication administration, comorbidities and medications, perception of pharmacist-patient relationship and pharmacist services. Descriptive statistics were performed.

Setting: Day hospital and medical outpatients, Karin Grech Hospital

Main Outcome Measure: Perception of older patients of pharmacist services

Results: Ninety-six patients were interviewed; 61 patients were ≥ 75 years old, 65 were female and 36 completed up to secondary education. Twenty-three patients live alone; 9 of whom are assisted by a private caregiver. Sixty-two patients have been visiting a community pharmacy to collect their medicines for ≥ 5 years and 75 patients received medication advice from the pharmacist. Fifty-two patients declared that they manage their daily tasks very well or well, while 23 require daily assistance. Most patients suffer from hypertension (*n*=46) and 85 patients take more than 1 medicine daily. Thirty patients were hospitalised more than once in the past year. Twenty-seven patients had a medication review performed by a pharmacist and 69 patients stated that they would feel comfortable with regular pharmacist-led medication review.

Conclusion: Patients in this study sought pharmacist advice about their medication, however medicine review by pharmacists was minimally performed. Patients were in favour of pharmacist-led medicine review, which has the potential to individualise pharmaceutical care to improve patient safety and quality of life.

Reference:

1. Zammit R. Community Pharmacist Intervention in the Management of Older Persons [dissertation]. Msida (Malta): Department of Pharmacy, University of Malta; 2018.

Pharmacy Information

Evolvement and Evaluation of the Maltese Medicines Handbook
Renita Busuttil

Medicine Information and Patient Discharge
Thomas Zammit

Education in Chronopharmacology
Onyinyechi Chesa

Medicine Acceptability and Drug Delivery Routes
Maria Bartolo

Evolvement and Evaluation of the Maltese Medicines Handbook

Renita Busuttil

Background: The British National Formulary (BNF) is a popular reference book used by professionals in Malta. Certain products found on the Maltese market are not included. The Maltese Medicines Handbook (MMH) is a formulary developed to include these preparations.

Objectives: To update the MMH to its fifth edition and to analyse and follow-up the present system of publication.

Design: A list of all the products, having a marketing authorization and available on the Maltese market until July 2017 was obtained from the Maltese Medicines Authority (MMA). The trade name and active ingredient of each entry in this list was reviewed through the BNF (edition 73) and the MMH (4th edition). A list of non-cited preparations was established and included in the formulary. Using Scicluna's[1] questionnaire as a guide, a questionnaire to evaluate the efficacy and utilisation of the previous edition of the formulary, both the book and the online versions was developed. An online questionnaire was distributed among 81 pharmacists.

Setting: Local pharmacy practice setting

Main Outcome Measure: Evaluation of the updated MMH

Results: Out of the 6240 products, 3359 were found in the BNF, 623 were found in the MMH and 2258 entries did not have their active ingredient and/or trade name in neither the BNF nor the MMH. These 2258 entries were sub-classified under 654 active ingredients, each having their corresponding branded and generic products. Fifty-six pharmacists replied that they use the MMH in their daily practice. The introduction of an online version, released in 2015 was an improvement but only 23 pharmacists were aware of this availability.

Conclusion: When comparing the 4th edition of the MMH to the 5th edition that will be published, the number of non-cited products has increased from 1550[1] to 2258.

Reference:

1. Scicluna T. Formulary for non-BNF cited items. [Dissertation] Msida (Malta): Department of Pharmacy. University of Malta; 2016.

Medicine Information and Patient Discharge

Thomas Zammit

Background: Medicine reconciliation is vital to the discharge process and can be improved by evaluation, reducing errors and readmissions, saving resources and improving quality of life.

Objectives: To analyse prescribing trends and to identify patient awareness of the changes and to evaluate patient perspective of pharmacist medicine reconciliation service.

Design: The 30 patients chosen were over 18 years of age, had a chronic disease and were currently taking two or more drugs, had no severe cognitive impairment, and were discharged back to their private residence. Medication forms were compiled from the patient's file and medicine reconciliation for that patient was observed. A patient questionnaire was filled and an evaluation of patient discharge SOP compliance was carried out. A questionnaire aimed at healthcare professionals about the medication reconciliation process at discharge was carried out. A Likert scale of 1-5, with 5 being the highest, was used for the questionnaires.

Setting: Karin Grech Rehabilitation Hospital (KGRH).

Main Outcome Measures: Medicine use in elderly patients, knowledge about medication changes at discharge, healthcare perception of medicine reconciliation.

Results: Twenty-nine out of 30 patients were aware of medicine changes. The mean patient rating of effectiveness of medicine reconciliation was 4.5. The experts (n=7) rated the process feasibility as 4.3, effectiveness as 4.7, and were willing to spend 20 minutes on patient reconciliation. The most common class, regimen and route were antihypertensives (13.4%), daily administration (41.6%) and oral route of administration (88.1%) respectively.

Conclusion: Both patients and professionals are satisfied with the process. Emphasis must be made during reconciliation, especially on antihypertensive changes.

Education in Chronopharmacology

Onyinyechi Chesa

Background: Chronopharmacology contributes to the optimisation of drug effects in disease management because the timing of drug administration is significant. Study of persons and health professionals knowledge of chronopharmacology with regards blood pressure, blood cholesterol and rheumatoid arthritis showed room to improve the knowledge of chronopharmacology.

Objective: To expand the knowledge of health professionals on chronopharmacology.

Design: Education sessions are organised to target doctors, pharmacists and pharmacy students. Each education session is to be based on a PowerPoint™ presentation and questionnaire which are validated by an expert panel of pharmacists. The knowledge of participants will be assessed before and after the education session through a questionnaire. Microsoft Excel® and IBM® SPSS® Statistics can be used to collate questionnaire responses and the t-test used to compare the difference in participant responses.

Setting: Education sessions: (1) Students at the Department of Pharmacy, University of Malta, (2) Pharmacists at the Medicines Authority and (3) Doctors at the seminar organised on issues related to Adverse Drug Reporting.

Main outcome measures: Questionnaire responses to assess effectiveness of the education session.

Results: Study of 55 doctors in Mater Dei Hospital, 25 community pharmacists and 23 persons on blood pressure medication, 16 on cholesterol medication and 31 on both medications' understanding of chronopharmacology with regards blood pressure, blood cholesterol and rheumatoid arthritis by means of the self-administered questionnaires, 'Chronopharmacology Questionnaire' and 'Time to Take Medicine Questionnaire', showed that there is room to improve the knowledge of chronopharmacology, to optimise disease management in these areas. Three education sessions have been organised and a PowerPoint™ presentation on chronopharmacology and questionnaire prepared.

Conclusion: Health professionals empowered with knowledge of chronopharmacology can in turn educate their patients.

Medicine Acceptability and Drug Delivery Routes

Maria Bartolo

Background: The dosage form and route of drug administration affect patient acceptability of pharmacotherapy.

Objectives: The aims of the study were to establish a link between dosage forms and medicine acceptability and to assess patient preferences in dosage forms in Malta.

Design: Patient preferences were assessed using the adapted Medication Delivery Route Preferences questionnaire for an international project by UCL, London. The questionnaire asked consumers to give a number between 1(none) to 10(a lot) to rate the discomfort, efficacy, speed of action and acceptability for medicine taken by different administration routes. Data was inputted in SPSS® version 25. The Kruskal Wallis and Chi-squared tests were used to statistically analyse the data.

Setting: The questionnaire was self-administered to consumers identified from; a Day Care Centre, the University of Malta, a community pharmacy, Junior College and to the personnel of a school.

Main Outcome Measures: Perception of consumers for different drug dosage forms and delivery routes

Results: Three hundred and eight hard copy questionnaires were distributed to participants and 237 answered questionnaires were collected. Thirty-nine online questionnaires were answered. The response rate from hard copy questionnaires was 77%. The online response rate was 0.33%. The mean rating score provided for discomfort caused by medicine when swallowed by mouth is significantly larger for participants aged between 21-40 years (2.79) compared to their younger (2.11) and older counterparts (2.21). The mean rating score provided for acceptability when medicine is swallowed by mouth is significantly larger (8.98) for participants aged over 40 years compared to their younger counterparts (8.38). There were no significant differences in mean rating scores given by different age groups for efficacy and speed of action.

Conclusion: This study sheds light on the expectations and perceptions of consumers for different pharmaceutical forms.

Pharmacy Administration and Regulatory Sciences

Extended Pharmacist Services in Community Pharmacy Practice
Rand Abdulrahman

Student Perception of Professional Development Programmes for Pharmacists
Catherine Anne Busuttil

Pharmacy of Your Choice Out-Of-Stock Medications: Perception, Facts and Implications
Charlene Bartolo

Access to Medicines Acting on Cardiovascular System
Jelena Tadic

Public Perceptions on Drugs and Driving
Abigail Calleja

Extended Pharmacist Services in Community Pharmacy Practice

Rand Abdulrahman

Background: Community pharmacy practice is continuously evolving particularly to include aspects of pharmacist intervention in extended services. It is imperative to establish the view and gain understanding of perception of community pharmacists and consumers in Malta on extended community pharmacy practice.

Objectives: To evaluate perception of accessibility of community pharmacists at all times and to identify areas for development of extended services.

Design: Two self-administered questionnaires were distributed to stratified random sampling. Fifty questionnaires were distributed to community pharmacists and 300 questionnaires to consumers. Pharmacists were asked to rate agreement on a number of extended services on a 5-point Likert scale ranging from 1 (least agree) and 5 (most agree). A total of 3600 minutes of direct observation was carried out during after-hours using a time and motion technique. The study was conducted in 5 community pharmacies for 8 weeks, each pharmacy located in a different district.

Setting: Community Pharmacy Setting

Main Outcome Measures: Perception of pharmacists and consumers regarding access to community pharmacy services.

Results: Mean rating scores for extended services show that pharmacists were in favour of various extended services including programs such as smoking cessation (mean rating score, 4.33), weight management (4.17) and alcohol intervention (4.13). The least agreed extended services were asthma care (3.35) and hyperlipidaemia monitoring (3.76) respectively. The majority of patients (greater than 50% in all districts) agreed that pharmacies should open from 09.00 until 21.00. Some respondents (30%) agreed that pharmacies should still remain open after 21.00. The difference between the proportions of district and longer pharmacy hours is not significant. Mean values for time-motion study show that during after-hours in a 120 minutes session, most time is dedicated on professional services (70 minutes) followed by communication (32 minutes) and administration (18 minutes).

Conclusion: Pharmacists are in favour of extended services and consumers are after accessibility to community pharmacists at all times.

Student Perception of Professional Development Programmes for Pharmacists

Catherine Anne Busuttil

Background: Medical data is constantly updated by virtue of advancements in technology and new findings. In order for healthcare systems to be in line with relative progress, healthcare professionals must keep themselves up to date with such advancements in retaining their professional validity.[1]

Objectives: To review professional development programmes for pharmacists which are implemented internationally and to assess the understanding and perception of fourth year B.Sc (Hons) Pharm Sci students with respect to Continuing Professional Development (CPD).

Design: A variety of professional development programmes carried out globally were assessed. A focus was made on CPD, discussing the use of different media in fulfilment of the CPD cycle. A logbook following the structure of the CPD cycle was identified as a prototype programme which is currently introduced to 4th year B.Sc (Hons) Pharm Sci students during an experiential placement. A questionnaire which assessed the users' understanding and perception of CPD programmes was drawn up, validated and disseminated.

Setting: University of Malta

Main Outcome Measures: Perception of CPD programmes in undergraduate pharmacy education

Results: Preliminary results from a pool of 25 respondents have been analysed to date. The use of a logbook portfolio during the placement increased interest in 20 participants, having an effect on the career path of 15 of them. The main reasons attributed to non-adherence to CPD proposed programmes are cost (*n*=14) and time management (*n*=13). Thirteen participants were in agreement that the taking up of such programmes during a professional career are necessary, and only 8 participants believed that such programmes should be made mandatory.

Conclusion: The implementation of professional development models within undergraduate pharmacy education supports graduates in grasping the value of this educational activity.

Reference:

1. International Pharmaceutical Federation (FIP). Pharmacy Education Taskforce - A Global Competency Framework Version 1 [Internet]. The Hague; 2012 [cited 2019 Jan 05]. Available from: https://www.fip.org/files/fip/PharmacyEducation/GbCF_v1.pdf

Pharmacy of Your Choice Out-Of-Stock Medications: Perception, Facts and Implications

Charlene Bartolo

Background: Medicinal shortages impose a crucial threat to all health care professionals, which often lead to the disruption of patient care. All stakeholders involved in the pharmaceutical service should act to prevent the occurrence of out – of – stock medications (OOS).

Objectives: This study identified the current instances of OOS medications in the POYC scheme and the negative outcomes of OOS medications on the patients and pharmacists. Occurrence of this problem was also evaluated. The effect of OOS medications on the POYC scheme and measures to prevent the occurrence of this situation were also considered.

Design: The first part of the study was the circulation of a questionnaire to patients entitled to the POYC scheme. The second part consisted of conducting interviews to community pharmacists registered with the POYC and running focus groups with the Central Procurement and Supplies Unit (CPSU) and the POYC staff. Data collected from the questionnaire was analysed through 'IBM SPSS Statistics 24'. Data collected from the focus groups was documented into 'Microsoft Office Word 2016'.

Setting: Ten community pharmacies chosen by convenience sampling. The focus groups were conducted in the CPSU offices at Mater Dei Hospital and at the POYC offices in Pieta.

Main Outcome Measures: Perception and implications of POYC OOS medications**.**

Results: Currently there are 2000 items on the procurement scheme. Patients specified 8 OOS medications during January-June 2017. Ten pharmacists reported 11 OOS medications during January-June 2018. POYC reported 5 OOS medications in January-June 2017 and 8 OOS medications in January – June 2018. Forty-one (46%) patients admitted to hoarding their medications while only 31 patients (16%) are willing to pay for their medications when they are OOS.

Conclusion: Regular episodes of OOS medications can lead to a possible threat to the quality, safety and efficacy of treatment. Joint efforts are essential to bring awareness and valid solutions to OOS medications. Non-compliance to treatment may be a result of OOS medications.

Access to Medicines Acting on Cardiovascular System

Jelena Tadic

Background: In Malta medicines used for chronic conditions, such as cardiovascular diseases can be attained from the community pharmacy, hospital pharmacy and through the "Pharmacy of Your Choice" scheme.

Objectives: To identify medicines acting on the cardiovascular system which are registered and marketed in Malta and to determine reasons why some registered medicines are not available to the public.

Design: A list of medicines available in Malta was found and downloaded from the Malta Medicines Authority website[1] and from this list the registered drugs acting on the cardiovascular system available to the public were identified.

Setting: Local community pharmacy

Main Outcome Measures: Medicines registered in Malta, medicines withdrawn in Malta, medicines marketed in Malta

Results: A total of 816 medicines acting on the cardiovascular system are registered in Malta. The majority of medicines acting on the cardiovascular system *(n*=212) which are registered act directly on the renin angiotensin system. For most medicines (*n*=52) which were withdrawn from the market, alternative medications were available.
Conclusion: It is important for patients with chronic conditions to have alternative medications available when medicines are withdrawn from the market.

Reference:

1. Malta Medicines Authority. Advanced search. National products [cited 2018 November 10]. Available from: URL: http://www.medicinesauthority.gov.mt/advanced-search

Public Perceptions on Drugs and Driving

Abigail Calleja

Background: Drug driving is one of the 'three killers' in terms of road fatalities. The lack of awareness among the public about the dangers of driving under the influence (DUI) of legal drugs is of great concern.

Objectives: To increase awareness among the public about the impairing effects on driving caused by certain legal drugs and to obtain a better understanding of the existing legal approaches and drug driving policies with reference to other EU member states.

Design: A self-administered questionnaire was developed in paper format and electronically in Maltese and English and aimed at individuals 18 years or older. Validation was carried out through discussion with a panel of five experts. The questionnaire was disseminated to the public through convenience sampling and social media. Maltese and other European drug driving policies and legal approaches on DUI of legal drugs were reviewed online. Data analysis was carried out using IBM SPSS software version 24.

Setting: Social media and general public

Main Outcome Measures: Perception of the general public on drugs having negative effects on driving ability.
Results: Two hundred and fifty-five individuals answered the questionnaire. Ninety percent (*n*=230) of the participants strongly agreed and agreed that they would want to know whether a medicine will affect their driving ability, 82% (*n*=208) were aware that certain medications may cause dizziness, drowsiness and sedation and 59% (*n*=151) of the participants would temporarily stop driving and take their medicine. In Malta, drivers will be punished only if their driving ability is visibly impaired but in Slovenia, Poland, Belgium a 'zero tolerance' policy is enforced in which detected DUI is always penalised.

Conclusion: Participants are aware that certain medications may impair their driving ability. Pharmacists are in an ideal position to advice patients about specific medicines side effects, for example drowsiness, dizziness and sedation. There is need for data at a national level to be gathered and disseminated.

Pharmaceutical Analysis and Formulations

Validation of Methods for Testing Drugs of Abuse
Michaela Cini

3D Printing in Pharmacy
Christopher Johnson

Validation of Methods for Testing Drugs of Abuse

Michaela Cini

Background: Several methods of drug testing, for cases of seized drugs and drugs in biological fluids have been developed. All methods of analysis need to be validated before being used in a laboratory.

Objectives: To validate methods for the identification and quantification (percentage purity) of illegal drugs using Gas Chromatography-Mass Spectrometry (GC-MS).

Design: The method was developed, calibrated and validated, according to standards set by the United Nations Office on Drugs and Crime (UNODC) for cocaine, diacetylmorphine (DAM) and 3,4-methylenedioxymetam phetamine (3,4-MDMA) at 1mg/ml using Diphenylamine as an internal standard. The retention time, qualifier ions and relative abundance were tabulated and used to set up a quantification method to estimate the percentage purity of the drug in the tested sample.

Setting: The forensic laboratory in BioDNA Laboratory services at Life Sciences Park.

Main Outcome Measures: Chromatographs obtained through a Varian 450 GC-220 MS and results generated through Varian Inc. MS Workstation.

Results: The results for the validation parameters tested for cocaine, DAM and 3,4-MDMA were as follows. The method was linear from the limit of detection (LOD) to the highest calibration point, with R^2 values >0.99 (0.9982, 0.9961, 0.997). The LOD was 1% for all drugs. The limit of quantification (LOQ) was 1% for cocaine and 3,4-MDMA, and 12.5% for DAM. The method was successfully validated for accuracy and precision (% CV: -5.361, 2.445, 1.346 and %E: 9.257, 14.448, 13.550). Samples of cocaine and 3,4-MDMA were stable at room temperature for 36 hours and for 6 hours for DAM. No carry-over was observed between samples.

Conclusion: All the validated parameters were within the limits set by the UNODC. This shows the applicability of the methods in a forensic laboratory.

3D Printing in Pharmacy

Christopher Johnson

Background: 3D printing is a tool that is being harnessed in the pharmaceutical industry and new implementations and concepts are being developed especially in the tailored dose industry. 3D printing is used in dosage form manufacturing.

Objectives: To give an overview of 3D printing in pharmacy. To find the best tablet shape with the best dissolution results. To compare times for loading of amitriptyline on Polyvinyl alcohol (PVA). To analyse amount of amitriptyline loaded on PVA via High Performance Liquid Chromatography.

Design: Different shapes for tablets to be used for 3D printing were compared according to their surface area to volume ratio. HPLC analysis of amitriptyline was carried out. Loading of amitriptyline in ethanol is performed on PVA for 24 and 48 hours. Determination of amitriptyline drug loading in a PVA tablet via HPLC analysis is carried out.

Setting: Department of Pharmacy Laboratory at the University of Malta.

Main Outcome Measures: Best tablet shape for 3D printing. Loading time and amount of amitriptyline on PVA.

Results: Dissolution time of differently shaped tablets and tablets with different dimensions was determined. Tablet with the shortest dissolution time was cylindrical in shape. When using HPLC amitriptyline eluted at 6 minutes. PVA cannot be analysed using reversed-phase HPLC with Ultraviolet detection due to lack of solubility in buffer.

Conclusion: The study will give more information about the best shape for 3D-printed amitriptyline tablets and time needed to load amitriptyline on PVA.

Medicinal Chemistry

Design and Identification of Liver X Receptor Modulators for the Management of Pancreatic Cancer using the Agonist GW3965 Scaffold as a Lead
Nicole Bonello

Design and Identification of Novel Protein Kinase Inhibitors Using the Naturally Occurring Isojacareubin Scaffold as a Lead
Jeanelle Caruana

Design and Identification of Steroid Receptor Co-Activator Modulators for the Management of Neoplastic Disease
Ruth Fiorentino

Design and Identification of Novel Protein Kinase Inhibitors Using the Naturally Occurring Staurosporine Scaffold as a Lead
Elena Maria Mallia

Design and Identification of Kappa Opioid Receptor Modulators for the Treatment of Addiction
Maria Mangion

Design and Identification of Novel Androgen Receptor Inhibitors Using the Experimental Small Androgen Receptor Modulators (S)-11 and (R)-9, and R-bicalutamide Scaffolds as Lead Molecules
Simona Svetlozarova Neykova

Design and Identification of Beta Cell Lymphoma-2 Receptor Modulators for the Management of Leukaemia and Other Solid Tumours
Yvonne Savona-Ventura

Design and Identification of Partial Peroxisome Proliferator Activated Receptor-γ Agonists Using the Synthetic Analog of Tetrahydrocannabinol, Ajulemic acid Scaffold as a Lead
Kirby Zammit

Design and Identification of Liver X Receptor Modulators for the Management of Pancreatic Cancer using the Agonist GW3965 Scaffold as a Lead

Nicole Bonello

Background: Liver X Receptors (LXR) are important members of the nuclear receptor family making the LXR a suitable target for the development of agonist molecules. Experimental molecules GW3965 and 4-(3-Aryloxyaryl) quinoline sulfone are suitable lead molecules for the design of novel structures which could successfully modulate the target.

Objectives: To probe LXR and to identify critical interactions between it and experimental molecules. To identify through virtual screening and *de novo* design novel structures with potential to act as LXR agonists.

Design: PDB crystallographic depositions 3IPQ[1] and 3KFC[2] describing the synthetic agonists GW3965 and 4-(3-Aryloxyaryl) quinoline sulfone were used as templates. The small molecules were separated from the complex and baseline binding affinity determined. Construction of seed structures, with seed modelling being based on two-dimensional topology maps were generated for 3IPQ.[1] *De novo* growth was subsequently sustained using LigBuilderv1.2 and the generated structures evaluated for Lipinski Rule compliance.

Setting: Department of Pharmacy, University of Malta.

Main Outcome Measures: Molecular display, modelling, seed generation.

Results: Five seed fragments modelled for 3IPQ[1] sustained molecular growth, resulting in a total of 30 new molecules. These have been grouped into families with a shared pharmacophore and assessed for Lipinski's Rule compliance.

Conclusion: Molecules generated were only for 3IPQ[1] which must be assessed and ranked in order of affinity. The top ranked molecules will be studied and optimised further.

References:

1. Bernotas R, Singhaus R, Kaufman D, Travins J, Ullrich J, Unwalla R, *et al*. 4-(3-Aryloxyaryl)quinoline sulfones are potent liver X receptor agonists. Bioorg Med Chem Lett. 2010;(20)1:209-212.
2. Fradera X, Vu D, Nimz O, Skene R, Hosfield D, Wynands R, *et al*. X-ray structures of the LXRalpha LBD in its homodimeric form and implications for heterodimer signaling. J Mol Biol. 2010;399(1):120-32. PubMed PMID: 20382159.

Design and Identification of Novel Protein Kinase Inhibitors Using the Naturally Occurring Isojacareubin Scaffold as a Lead

Jeanelle Caruana

Background: Protein Kinase C (PKc) is a target for chemoprevention, as increased activation of PKc is implicated in cancer.[1]

Objectives: To identify and to design and optimise novel ligands capable of selective PKc modulation using the isojacareubin (ISJ) scaffold as a lead.

Design: In the first part of the study, X-ray crystallographic deposition 2I0E describing the bound coordinates of the bisindolylmaleimide (BIM) inhibitor with PKc was used as a template. The bound coordinates of BIM were used to dock ISJ into the PKc active site, resulting in the generation of binding conformers. In the second part of the study, VS and *de novo* design were performed. From the virtual screening (VS) exercise the four highest affinity hits were identified, and are proposed for further optimisation. In *de novo* design, the best conformers were edited to create seeds and were allowed to undergo growth, generating new molecules.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Accelrys Discovery Studio(®): Molecule Display; Sybyl(®): Molecular modelling; X-Score(®): Ligand Binding Affinity (LBA) calculation; LigandScout v3.12: Consensus pharmacophore construction; ZINCPharmer: Purchasable chemical space search; LigBuilder(®): Ligand Binding Pocket elucidation.

Results: The total score of the entities generated from VS ranged from 0.04 to 7.16. The binding affinities (pKd) of the *de novo* designed molecules ranged from 8.21 to 10.00.

Conclusion: The molecules identified through VS and *de novo* design which had the optimal LBA and propensity to oral bioavailability combination, were identified for further validation and optimisation.

Reference:

1. Mochly-Rosen D, Das K, Grimes KV. Protein kinase C, an elusive therapeutic target? Nat Rev Drug Discov. 2012; 11(12): 937–957.

Design and Identification of Steroid Receptor Co-Activator Modulators for the Management of Neoplastic Disease

Ruth Fiorentino

Background: This project derives from data that indicates that paradoxical agonism of the Steroid Receptor Co-activator (SRC) normally associated with cancer progression actually has a mitigating effect on tumour growth.[1]

Objectives: To use the MCB-613 scaffold for the design of novel structures capable of agonist modulation of SRC-1 receptor with clinical utility in the management of neoplastic disease.

Design: The small agonist molecule MCB-613 was docked into the apo SRC ligand binding pocket (LBP) obtained from Protein Data Bank (PDB) crystallographic deposition 2SRC. Conformational analysis was performed. The molecule with the lowest ligand binding energy (LBE) and highest ligand binding affinity (LBA) was identified as the optimal conformer, and its critical interactions with the SRC were used in a dual approach of virtual screening and *de novo* ligand growth. The modelled seed fragments generated by the *de novo* approach were planted within the generated SRC_LBP map and fragment growth was performed which resulted in a cohort of structures. A consensus pharmacophore was modelled and used for analog identification using MCB-613 best conformer. A protomol was generated and structures were identified for virtual screening.

Setting: University of Malta

Main Outcome Measures: *De novo* approach and virtual screening

Results: *De novo* growth using all fragments yielded a total of 402 Lipinski Rule compliant molecules whose average LBA (pKd) ranged between 5.44 and 5.80, whereas virtual screening yielded 17,863 hits filtered for molecular weight up to 500 and rotatable bonds between 2 and 12 per molecule.

Conclusion: The optimal structures will be further validated through molecular dynamic studies and *in vitro* assays.

Reference:

1. Wang L, Yu Y, Chow DC, Yan F, Hsu CC, Stossi F, *et al*. Characterization of a steroid receptor coactivator small molecule stimulator that overstimulates cancer cells and leads to cell stress and death. Cancer Cell, 2015;28(2): 240-52

Design and Identification of Novel Protein Kinase Inhibitors Using the Naturally Occurring Staurosporine Scaffold as a Lead

Elena Maria Mallia

Background: Protein Kinase C (PKc) inhibitors are important anticancer drugs. Staurosporine has recognised PKc inhibitory ability[1] and will be used as a template for the design of clinically useful high affinity PKc inhibitors.

Objectives: To use the bioactive coordinates of staurosporine, to identify, through Virtual Screening (VS) and *in silico de novo* techniques, novel PKc modulators.

Design: Two strategies were adopted for this study: VS - The bioactive conformation of staurosporine was used to query the molecular database ZincPharmer® to identify small molecules similar to the query. A protomol was modeled in Sybyl®-X v1.1 and the Lipinski Rule compliant molecules identified were uploaded into the protomol and their affinity quantified. *De novo* - The Ligand Binding Affinity (LBA) of staurosporine was calculated. Two-dimensional topology maps were used to guide modeling of seed structures in Sybyl®-X v1.1. The designed seed fragments were planted into the restricted pharmacophoric space in LigBuilder® v.1.2 and novel molecular growth was driven. The resultant molecular cohort was assembled into a molecular database and ranked in order of affinity.

Setting: Department of Pharmacy, University of Malta.

Main Outcome Measures: Sybyl®-X v1.1: Molecular modelling, X-Score® v1.3: LBA calculation, LigandScout® v3.12: Consensus pharmacophore construction, ZINCPharmer®: Chemical space search, LigBuilder® v.1.2: Ligand Binding Pocket elucidation.

Results: The total score of the entities generated from VS ranged from 6.78 to 9.65. The binding affinities of the *de novo* designed molecules ranged from 7.47 to 10.00.

Conclusion: The affinities of the optimal molecules exceeded that of staurosporine, and these molecules will be proposed for further study.

Reference:

1. Marengo B, De Ciucis C, Ricciarelli R, Pronzato MA, Marinari UM, Domenicotti C. Protein kinase C: an attractive target for cancer therapy. Cancers. 2011 1;3(1):531-67.

Design and Identification of Kappa Opioid Receptor Modulators for the Treatment of Addiction

Maria Mangion

Background: The Kappa Opioid Receptor (K-OR) was traditionally a druggable target for analgesia. Recent studies have demonstrated its association with the reward pathway. Salvinorin A, derived from *S. divinorum*, is the only non-nitrogenous (alkaloidal) and selective K-OR full agonist making it a valuable lead for the development of more potent drugs in the management of pain and addiction without dependence or tolerance.[1]

Objectives: To use the Salvinorin A scaffold for the design of lead molecules to probe the K-OR ligand binding pocket (LBP) and to model novel structures capable of its modulation using *de novo* techniques.

Design: PDB crystallographic deposition 4DJH describing the K-OR:JDTic small molecule agonist complex guided this study. Salvinorin A was modeled *de novo* and docked into the K-OR LBP. The 20 optimal conformers were isolated, and the best one was selected on the basis of maximum peak height difference between the ligand binding affinity and energy. Three seed fragment structures were created using the optimal Salvinorin A conformer, retaining the structural moieties fundamental to agonism. Growing sites were designated as H.spc hydrogens. User directed growth could be sustained at these loci. The novel structures generated, were filtered to ensure Lipinski rule compliance for molecules capable of blood brain barrier (BBB) penetration.

Setting: The study is carried out *in silico*.

Main Outcome Measures: Sybyl-X®, X-score®, LigBuilder® v.1.2, and Biovia AccelerysDraw®

Results: Forty percent of the *de novo* generated structures conformed (*n* = 33) to the pre-designated inclusion criteria. The molecules with the highest binding affinity will be further validated.

Conclusion: This study provided *in silico* evidence that the salvinorin A scaffold is suitable for the design of high affinity molecules capable of BBB penetration.

Reference:

1. Wang Y, Sun J, Tao Y, Chi Z, Liu J. The role of k-opioid receptor activation in mediating antinociception and addiction. Acta Pharmacol Sin. 2010;31(9):1065-70.

Design and Identification of Novel Androgen Receptor Inhibitors Using the Experimental Small Androgen Receptor Modulators (S)-11 and (R)-9, and R-bicalutamide Scaffolds as Lead Molecules

Simona Svetlozarova Neykova

Background: Current pharmacological treatment of prostate cancer centres around Androgen Receptor (AR) inhibition or Androgen deprivation.[1] Eventually the AR mutates and becomes resistant to treatment.

Objectives: To carry out Virtual Screening (VS) in order to identify structures capable of mutant AR inhibition.

Design: Evidence in literature[2] has shown that novel molecules (S)-11 and (R)-9 are capable of mutant AR inhibition, so they were chosen as leads to probe the mutant AR for this study. PDB crystallographic deposition with ID 1Z95[3] describing the holo (R)-bicalutamide:AR complex was used as a template.

Setting: University of Malta

Main Outcome Measures: Sybyl®-X[4], X-Score®, LigandScout® and ZINCPharmer® were the software tools used to probe the AR mutant and to screen for molecules capable of its inhibition.

Results: Nine hundred and five hit molecules were obtained and sorted according to their affinity for the mutant AR in the following order: by the highest Total Score, followed by the highest CScore and then by the highest Global CScore. The six molecules with the highest Total Score were selected.

Conclusion: The molecules obtained though VS are structurally diverse. They will be further optimised and proposed for computational validation and for *in vivo* signalling assays.

References:

1. Banerjee PP, Banerjee S, Brown TR, Zirkin BR. Androgen action in prostate function and disease. Am J Clin Exp Urol. 2018 1;6(2):62-77.
2. Tesei A, Leonetti C, Di Donato M, Gabucci E, Porru M, Varchi G et al. Effect of Small Molecules Modulating Androgen Receptor (SARMs) in Human Prostate Cancer Models. PLoS ONE. 2013;8(5):e62657.
3. Protein Data Bank [Internet]. New Jersey: Rutgers, The State University of New Jersey. 1971 - [cited 2019 Jan]. Available from www.rcsb.org.
4. Sybyl®-X: molecular modelling suite. Version 1.1. Missouri: Tripos (DE), Inc. USA; 2010

Design and Identification of Beta Cell Lymphoma-2 Receptor Modulators for the Management of Leukaemia and Other Solid Tumours

Yvonne Savona-Ventura

Background: Literature indicates that navitoclax and venetoclax have potential in the management of malignant tumours and leukaemia. These molecules mimic the structure of pro-apoptotic proteins and act as antagonists to pro-survival receptors found on the mitochondria of cancerous cells.[1] This at the expense of unacceptable side-effects including thrombocytopenia.

Objectives: The Beta Cell Lymphoma-2 (BCL-2) receptor regulates apoptosis and is a target in the design of tumour mitigating drugs.[2] The navitoclax and venetoclax antagonist scaffolds will be used as lead molecules for the *in silico* identification and design of improved high affinity antagonists.

Design: Virtual screening (ligand based drug design) and *de novo* (structure based drug design).

Setting: University of Malta

Main Outcome Measures: The hits obtained from the ZINCPharmer®[3] database were docked inside a protomol, modelled within BCL-2 receptor and ranked in relation to their physicochemical properties and Lipinski Rule[4] compliance.

Results: A total of 8 lead-like hits were obtained from virtual screening.

Conclusion: The optimal structures obtained are candidates for optimisation, synthesis and *in vitro* validation to assess potential clinical efficacy.

References:

1. Cummings J, Ward TH, Ranson M, Dive C. Apoptosis pathway-targeted drugs—from the bench to the clinic. Biochim Biophys Acta. 2004 10;1705(1):53-66
2. Lindsay J, Esposti MD, Gilmore AP. BCL-2 proteins and mitchondria—specificity in membrane targeting for death. Biochim Biophys Acta. 2011; 1813(4):532-9
3. Koes DR, Camacho CJ. ZINCPharmer: pharmacophore search of the ZINC database. Nucleic Acids Res. 2012; 40(W1):W409-W414
4. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev. 2001;46(1-3):3-26.

Design and Identification of Partial Peroxisome Proliferator Activated Receptor-γ Agonists Using the Synthetic Analog of Tetrahydrocannabinol, Ajulemic acid Scaffold as a Lead

Kirby Zammit

Background: Peroxisome proliferator-activated receptor gamma (PPARγ) is a druggable target for the management of diabetes and inflammatory disease. Total agonism of this receptor produced clinically significant adverse effects, resulting in the withdrawal of entire drug classes specifically the glitazones from the market.[1]

Objectives: To use the bioactive conformation of ajulemic acid (AJA) as lead molecule to probe the PPAR Ligand Binding Pocket (LBP). To identify critical interactions responsible for affinity and stability at this locus, identify optimal structures and validate their utility through molecular dynamics simulation.

Design: PDB crystallographic depositions, 20M9 and 4XUM describing bound coordinates of PPARγ bound to AJA and indomethacin respectively were recruited. The small molecules were extracted, and their bioactive coordinates were superimposed to generate a consensus pharmacophore. This was submitted as a query to the ZincPharmer® database. The idealised PPARγ LBP was modelled. The hits from the virtual screening (VS) exercise were filtered for Lipinski Rule compliance, docked and ranked in order of affinity. A de novo approach was carried out where seeds retaining the critical fragments were modelled computationally.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: The study incorporated results from the VS exercise which will be further compared with the *de novo* method carried out *in silico*.

Results: A cohort of 44,276 high affinity Lipinski Rule compliant hits with known synthetic pathways were identified and grouped according to pharmacophoric similarity. The highest ranked structures (n=5) were proposed for molecular dynamics.

Conclusion: The selected structures provide guidance to understanding of partial agonism, suggesting a rational approach to the design of molecules capable of activating the receptor at levels that avoid undesirable side effects.

Reference:

1. Tyagi S, Gupta P, Saini AS, Kaushal C, Sharma S. The peroxisome proliferator-activated receptor: A family of nuclear receptors role in various diseases. J Adv Pharm Technol Res. 2011; 2(4): 236–240.

M.Sc. Pharmacy
Dissertation Descriptions

The Valsartan Saga: Science, Myths and Realities
Stephania Baldacchino

Risk Assessment in Pharmaceutical Processes
Abigail Bezzina

Training in the Pharmaceutical Industry
Maria Calleja

Risk of Data Integrity of Electronic Records in the Pharmaceutical Industry
Andrew John Cauchi

Physicochemical Properties of Products Obtained from the Local Carob Tree Varieties
Luca Galea

Development of Characterisation Process for Active Pharmaceutical Ingredients
Júlia Mušková

Extractability of Polyphenols from Local Herbs using Different Traditional Extemporaneous Preparations
Nicholas Rapa

Software Validation in the Pharmaceutical Industry
Chris Sammut

The Valsartan Saga: Science, Myths and Realities
Stephania Baldacchino

In Malta, over 27,000 patients (6% of the total population) were taking Valsartan through the Pharmacy-of-Your-Choice Scheme at the time when the Valsartan Saga erupted. The stakeholders involved in resolving the issue of the N- Nitroso-dimethylamine contaminating valsartan products included the Malta Medicines Authority, CPSU, the POYC Department, Superintendent of Public Health and healthcare professionals. SWOT analysis resulting from data gathered through the focus group, interviews and questionnaires will shed light on useful improvements in handling similar situations.

Risk Assessment in Pharmaceutical Processes
Abigail Bezzina

The pharmaceutical supply chain is an integral aspect of the health system. Risks involved in the pharmaceutical supply chain are to be assessed through a risk-based approach to encourage better and proactive decisions. A Failure Mode and Effects Analysis approach is adopted with the objective to identify, assess, control, communicate and review risks during the flow of goods at a local pharmaceutical company. Shortcomings in the management of the supply chain are identified and risk minimisation strategies for each process are proposed.

Training in the Pharmaceutical Industry
Maria Calleja

Training programs help employees learn specific knowledge or skills to improve performance in their current roles. The study aimed to gather perspective on training from local pharmaceutical manufacturing companies through a set of questionnaires. EMA and FDA guidelines were compared. EMA Eudralex Volume 4 GMP Guidelines and FDA 21 Code of Federal Regulations Part 211 emphasise that all personnel should receive appropriate training in the particular operations assigned and continuous training in Current Good Manufacturing Practice relevant to their needs.

Risk of Data Integrity of Electronic Records in the Pharmaceutical Industry
Andrew John Cauchi

Pharmaceutical companies use complex software as part of their quality systems with inherent high level of risk directly related to the integrity of data. The aim is to perform a risk assessment protocol, investigate the capabilities and outline the limitations of the Batch Tracker Software and minimise the risk of breaches. Corrective and preventive actions to correct gaps indicated through misuse are then put forward.

Physicochemical Properties of Products Obtained from the Local Carob Tree Varieties
Luca Galea

Various products are derived from the carob pod, including, carob syrup, carob honey and carob candy. The rationale for this research is to valorise the local carob tree for the variety of products that are obtained from it, which have a potential use for medicinal purposes. The physicochemical properties of carob products will be analysed spectrophotometrically and data will be evaluated to determine any significant differences between means for different samples for various parameters.

Development of Characterisation Process for Active Pharmaceutical Ingredients
Júlia Mušková

This study aims to describe the active pharmaceutical ingredient (API)-related characteristics that will be evaluated when a new active ingredient which is not characterised in the relevant pharmacopoeia, is being developed. Following the identification of methods used for the characterisation of APIs, interviews or focus groups are conducted with professionals from various fields in the pharmaceutical industry, and a guideline for API characterisation is developed.

Extractability of Polyphenols from Local Herbs using Different Traditional Extemporaneous Preparations
Nicholas Rapa

The search for naturally-occurring antioxidants as a replacement to synthetic ones in medicine has increased considerably due to their association with various health benefits. This study aims at optimising the extraction conditions and determining the effect of steep time and temperature on eight different locally available herbal tea infusions. The polyphenolic content and antioxidant activity are investigated by the Folin-Ciocalteu test and the DPPH assay, respectively. MP-AES is also used to determine the heavy metal content in the herb material, herbal infusion and residual herb.

Software Validation in the Pharmaceutical Industry
Chris Sammut

Users responsible for validation of computer systems to be used in the pharmaceutical industry may rely upon vendor-supplied documentation. When users generate their own validation documentation, it is easier to ensure that the functionality of the system is tested against the intended use. The study aims to compile a validation protocol to assess and document the performance of software for use in a pharmaceutical laboratory.

B.Sc.(Hons) Pharm.Tech.
Project Descriptions

Quality Audits in Medical Devices
Michaela Abela

Green Chemistry along the Years
Peter Azzopardi

Pharmacogenomic Information in Drug Labels
Yasmine Azzopardi

Different Dosage Forms of Cannabis
Ingrid Bonello

Techniques for the Identification of Pharmacogenetic Markers
Leanne Camilleri

Analysis of Amitriptyline
Yana Chircop

Chemistry of Cannabis
Daniel Cini

Evolvement of Compounding Processes
Ian Farrugia

Quality Systems for Online Medicines Information
Gabriel Leon Galea

Perception of Risk among Pharmaceutical Stakeholders
Steve Grech

Inspection of Pharmaceutical Packages
Jake Pace

The Unique Identifier and Authentication of Online Pharmaceutical Purchases
Alaa M M Suwan

Registration Process for Medical Devices used in Hospital
Julian Vella

Pharmaceutical Technologist Emerging Roles
Christ Xerri

Synthetic Drugs of Abuse exhibiting Kinetic and Non-Kinetic Toxicology
Sarah Xuereb

Understanding Risks in Pharmaceutical Processes
Melanie Zahra

Quality Audits in Medical Devices
Michaela Abela

The project focuses on developing a risk assessment tool after observing cases and identifying gaps with respect to medical devices, related accessories and consumables. The objective is to improve the performance of medical devices through surveillance from the various stages of procurement until medical devices are supplied to the end user. The requirements for good quality medical devices are being evaluated to ensure their safety and effectiveness to reduce possible risks.

Green Chemistry along the Years
Peter Azzopardi

An ever-growing concern on the negative impact of the chemical industry on the environment is driving the pharmaceutical industry to rethink its processes. This has led to the creation of an environmental oriented chemical discipline called green chemistry. An extensive, qualitative literature review was carried out using online journal databases to determine major developmental stages of this discipline such as the publishing of the twelve principles of green chemistry. Focus was made on the pharmaceutical industry's adaptations over the years in response to green chemistry.

Pharmacogenomic Information in Drug Labels
Yasmine Azzopardi

The aim is to compare pharmacogenomic (PGx) information in drug labelling by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Drugs (N=70) with PGx implications available in the Maltese Government Formulary were identified. Label annotations by each regulatory body listed in Pharmacogenomics Knowledge Base and PGx information in the FDA label and EMA-approved Summary of Product Characteristics of each drug are compared. A PGx information quality scoring scale consisting of nine criteria is applied in this comparative analysis.

Different Dosage Forms of Cannabis
Ingrid Bonello

The different ways in which cannabis is presented for medical use is collated. Reports on the availability, distribution, efficacy, manufacturer, price, quality, regulation, safety, technical properties, use and user preference are critically analysed. The advantages and disadvantages of each cannabis product identified are assessed. Prescribers and public perceptions on the various products are gathered through an interactive seminar and a questionnaire.

Techniques for the Identification of Pharmacogenetic Markers
Leanne Camilleri

The aim is to analyse and compare testing methods for the identification of pharmacogenetic (PGx) markers. Five drugs with PGx implications (abacavir, azathioprine, warfarin, codeine, fluorouracil) were selected for this comparative analysis. These drugs have a different PGx marker, are available on the Maltese Government Formulary and have genotype-guided therapy recommendations by the Clinical Pharmacogenetics Implementation Consortium. Test principle and performance, sample type and handling, quality assurance, sensitivity and specificity to reference method, robustness and costs are analysed.

Analysis of Amitriptyline
Yana Chircop

Amitriptyline is metabolised into nortriptyline, E- and Z-10-hydroxynortriptyline and E- and Z-10-hydroxyamitriptyline. A method of analysis using Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) is developed for the identification and quantification of amitriptyline and its metabolites. A C18 column is used for the stationary phase while two mobile phases are investigated: water-methanol with formic acid and ammonium formate buffer; and water-acetonitrile with formic acid buffer. Electrospray ionisation (ESI) is used for ion generation with preference given to positive ions.

Chemistry of Cannabis
Daniel Cini

A comprehensive literature review on *Cannabis sativa* is carried out to obtain information on chemistry, mechanism of action, pharmacokinetic properties and pharmacological effects. Different active constituents in the plant are studied. Methods for determination and analysis of synthetic and natural cannabinoids and their metabolites are described and compared. Analytical methods involve screening and confirmatory tests.

Evolvement of Compounding Processes
Ian Farrugia

The aim of the study is to identify the standards and skills required to perform compounding processes, whilst exploring the practical application of the tech-check-tech in hospital. A scenario analysis of the current compounding processes was carried out. A skill competency checklist for reconstitution officers and pharmaceutical technologists was compiled and validated. Based on findings, a proposed restructuring of the compounding process was compiled and validated. The proposed process maximises the role of pharmaceutical technologists whilst releasing pharmacists to perform clinical duties.

Quality Systems for Online Medicines Information
Gabriel Leon Galea

The study investigates online sources of medicines information and tools to assess their quality. The methodology included identification and classification of online medicines information sources and development and validation of a quality system. Out of a total of 66 sources identified, the majority (40) provided general drug information, and healthcare professionals were the most popular intended audience (38). Timeliness of information and source of information were the most frequently observed criteria within evaluation tools studied.

Perception of Risk among Pharmaceutical Stakeholders
Steve Grech

The aim of this project is to evaluate the perception of risk among pharmaceutical stakeholders by conducting structured interviews with community pharmacists and procurement officers within the Central Procurement and Supplies Unit. Interview questions were validated by four individuals through an evaluation questionnaire. The questionnaire assesses whether the stakeholder's perception of risk affects risk management planning and whether new legislation affects the current perception. Risk minimisation strategies for community pharmacies and procurement services are put forward.

Inspection of Pharmaceutical Packages
Jake Pace

This project looks into the components of the pharmaceutical package with a particular interest on the packaging of solid dosage forms. By identifying critical aspects of the packages that are important for inspection, a detailed literature review is conducted explaining how and why inspections are carried out in the pharmaceutical industry from a manufacturing and distribution point of view. This study aims to assess the inspection systems employed by local pharmaceutical companies and establishing better knowledge and improvements in the inspection of packaging.

The Unique Identifier and Authentication of Online Pharmaceutical Purchases
Alaa M M Suwan

The role of the unique identifier is to prevent the entry of counterfeit medicines to the pharmaceutical supply chain from illegal pharmacies through online purchase. The outcome of the study addresses the danger of unregulated online pharmacies as well as the implementation of the process as referred to in the Falsified Medicines Directive, which includes the application of the unique identifier. The study also reflects the opinions and level of awareness of pharmacists and persons working in the pharmaceutical industry on the subject from their response to questionnaires.

Registration Process for Medical Devices used in Hospital
Julian Vella

The project involves the setting up of a registration system for medical devices which ensures that devices received are scrutinised from the quality aspect. Review of current process used for medicines registration is undertaken to identify gaps. The system that tackles medical devices, including consumables is reviewed to find the best way to set up the new system in the light of the new Medical Devices EU-Directive.

Pharmaceutical Technologist Emerging Roles
Christ Xerri

The study focuses on extending the roles of pharmaceutical technologists working within a hospital setting. Gap analysis was carried out to identify roles that can be performed by pharmaceutical technologists. A questionnaire on the extended roles of pharmaceutical technologists was compiled, validated and implemented to capture the perception and expectations of pharmacy technicians and technologists working at Mater Dei Pharmacy. By extending the roles of pharmaceutical technologists within a hospital more pharmacists can move to patient bedside resulting in an improved holistic pharmacy service.

Synthetic Drugs of Abuse exhibiting Kinetic and Non-Kinetic Toxicology
Sarah Xuereb

An extensive literature review was carried out on the kinetic and non-kinetic toxicology of cocaine, N-methyl-1-(3,4-methylenedioxyphenyl)-propan-2-amine and the synthetic cannabinoid JWH-018. Literature published between January 1998 and December 2018 was included. Kinetic effects of the drugs following absorption, distribution, metabolism and excretion and non-kinetic effects which included local effects following exposure to drugs were researched. Clinical cases related to these drugs of abuse are compared to kinetic and non-kinetic toxicological effects.

Understanding Risks in Pharmaceutical Processes
Melanie Zahra

The aim of this study is to understand the different risks faced by various pharmaceutical processes by conducting structured interviews with pharmaceutical industries and wholesale dealers. Interview questions were validated by four individuals by conducting an evaluation questionnaire. A comparative analysis on deviation handling is carried out to compare standard operating procedures from a local pharmaceutical company with that found in literature. Recommendations for risk minimisation in the pharmaceutical industry are put forward.

B.Sc.(Hons) Pharm. Sci. Fourth Year Students

Project Descriptions

Rational Design of Novel Acid Ceramidase Inhibitors
Gabriel Abela

Literature indicates that acid ceramidase enzyme drives melanoma proliferation. The pyrimidine analogue carmofur has been shown to be an acid ceramidase antagonist with demonstrable shrinkage of tumour size *in vivo*. Carmofur was designated in this study as a lead scaffold. It was modelled and after conformational analysis the optimal conformer was used as a query to identify similar structures which are currently being analysed for utility.

Rational Design of Novel μ-opioid Antagonists Based on the PZM21 Scaffold
Stephanie Attard

The identification of PZM21 as a selective, potent and biased μ-opioid agonist shows its significant potential of providing opioid level analgesia without the typical concomitant side effects. PZM21 was used as a lead, docked into the μ-opioid receptor ligand binding pocket and conformational analysis performed. The best conformers in terms of ligand binding energy and ligand binding affinity were derived. These will be used for optimisation in *de novo* design for the generation of novel μ-opioid antagonists.

Pharmacist Recommended Medicines for Paediatric Patients
Chiara Baldacchino

Scenario analysis of pharmacist-recommended medications available on the market for paediatric patients was undertaken. In total, there are 34 over-the-counter medications available for paediatrics. A statistical model to capture safety and efficacy of these products is developed through the use of SPSS. Safety is based on the side-effect profile, contra-indications and cautions. The pharmacokinetic and pharmacodynamic profiles are used to assess efficacy. Guidelines with respect to the updated use of non-prescription medicines in paediatric patients are developed.

Rational Design of Glutathione-S-Transferase Pi1 (GSTP1) Antagonists Based on the Novel LAS17 Scaffold
Gabriel Borg

Evidence from literature shows that the GSTP1 receptor is a target for triple negative breast cancer and that experimental LAS17 is a high affinity antagonist. LAS17 was modelled and used as a lead in a Virtual Screening exercise to identify analogous structures. Specifically, the critical interactions forged between the optimally binding LAS17 conformer, and the GSTP1 receptor were submitted to ZincPharmer and high affinity low molecular weight hits were identified, ranked in order of affinity, and the best structures selected for optimisation.

Rational Design of Proto-Oncogene Tyrosine-Protein Kinase SRC Antagonists Based on the Novel ECF506 Scaffold
Lara Maria Busuttil

Triple negative breast cancer is not susceptible to conventional chemotherapy and is the subject of significant research. Literature shows that kinase SRC inhibition by experimental molecule ECF506 retards tumour growth. The ECF506 molecule was modelled, docked into the tyrosine kinase SRC receptor and conformational analysis performed. The optimal conformer was identified. This conformer will be used in virtual screening and its interactions used in a *de novo* approach to create an analog series of molecules, with the potential to treat triple negative breast cancer.

Rational Design of Dual PPARγ/α Agonists Based on the Novel SR10171 Scaffold
Justin Cassar

The PPAR γ and α subtypes have been implicated in the mediation of diabetes mellitus and osteoporosis. PPARγ agonists exert a hypoglycaemic effect and reduce bone mass, while PPARα agonists maintain bone mass. This study modelled the experimental PPARγ/α agonist SR10171 to generate consensus pharmacophores that represented the binding requirements of both subtypes. This was used as a query for virtual screening. The hit structures are being evaluated to assess potential for dual agonist activity.

Use of Antibacterial Drugs in the Intensive Care Unit
Julia Catania

Data on antimicrobial consumption in acute care hospitals is necessary to assess the magnitude, the reasons and determinants of antimicrobial use. The use of antibacterial drugs in the intensive care unit (ICU) was reviewed by analysing trends in antibiotics administered between 2009-2017. Forty-nine different types of antibiotics were used. The most common antibiotic administered in 2017 was meropenem. An 'Antibacterial information Sheet' is completed for patients currently in the ICU, where information related to the type of antibiotic, reason for use and route of administration is included.

Rational Design of Novel Structures Based on the Leiodermatolide Scaffold Capable of Tubulin Inhibition
Graziella Chetcuti

Leiodermatolide, through its high affinity for tubulin, has been classified in the literature as a novel microtubule targeting agent suitable for pancreatic cancer management. Leiodermatolide was modelled. Three binding sites on tubulin were identified and probed. The best conformer of leiodermatolide at the optimal binding site was selected. It was used as a query for Virtual Screening and de novo design for the identification of orally bioavailable analogs.

Rational Design of Novel Histone Deacetylase (HDAC) Inhibitors based on the AR-42 Scaffold
David Gatt

Cachexia is characterized by skeletal muscle breakdown and is co-morbid in cancer. Experimental molecule Ar-42 has been shown to mitigate cachexia through Histone Deacetylase (HDAC) inhibition. The Ar-42 molecule was modelled and its optimal binding conformation was used together with cognate vorinostat to generate a consensus pharmacophore. This was the query for virtual screening. A cohort of lead-like hits was identified and is being analysed for suitability for molecular database inclusion.

Use of the UM-164 scaffold to Design Tyrosine-Protein Kinase SRC Inhibitors
Thomas Sammut

Experimental molecule UM-164 was modelled and docked into the SRC receptor, a driver of triple negative breast cancer. Conformational analysis was performed. Critical interactions made by the optimal UM-164 conformer and the SRC receptor will be used in the *de novo* design and identification, through Virtual Screening, of SRC antagonists with potential clinical utility in the management of this condition.

Repurposing Fluphenamic Acid and Glibenclamide for the Design of AKR1C1 Receptor Inhibitors
Matthew Scicluna

In this repurposing study, fluphenamic acid and glibenclamide were successively docked into the AKR1C1 receptor. The best binding conformations were selected and will be used to identify and design analogues capable of modulating the AKR1C1 receptor with potential utility in the management of bladder cancer.

Rare Diseases and Orphan Medicines
Sharon Vassallo

In Malta there are 25000 rare disease (RD) patients. Awareness about RDs in Malta is increased by updating the RD registry template belonging to National Alliance for Rare Diseases Support Malta and designing an information booklet. Two questionnaires are developed, one for healthcare professionals (HCPs) and one for the public to analyse the knowledge, and awareness about RDs. Two hundred and three people answered the public questionnaire and 61% (n=124) were aware of organisations for RDs. Seventeen out of 59 participating HCPs encountered problems while trying to obtain orphan drugs for patients.

Methods for Determination of Water Content in Tetrahydrofuran
Maria Xiberras

A method to quantify the water content in tetrahydrofuran (THF) using cobalt chloride ($CoCl_2$) as an indicator and UV-Vis spectrometry is developed and validated. The maximum absorbance of THF and $CoCl_2$ was determined. Samples of THF and $CoCl_2$ containing different concentrations of water were prepared in triplicates. The water content in THF was determined by observing variations in absorbance at 548-721nm, which is the absorbance of $CoCl_2$. The developed method is an advancement on traditional methods for water determination such as Karl Fischer, oven-drying method and azeotropic distillation.

Use of Newer Generation Statins in Cardiovascular Disease
Maia Zarb

The aim is to compare the effectiveness and safety of simvastatin and atorvastatin in terms of attainment of target low-density lipoprotein cholesterol (LDL-C) goals and occurrence of side-effects. Patients with ischaemic heart disease and on statin therapy are recruited (t1) from Mater Dei Hospital, matched for age, gender, hypertension and diabetes, and followed up after 6-12 months (t2). Eighteen patients (9 simvastatin, 9 atorvastatin, 10 male, 8 female, mean age 70 years) were recruited. Mean LDL-C simvastatin t1/t2 = 2.2/2.4 mmol/L, mean LDL-C atorvastatin t1/t2 = 2.86/1.52 mmol/L.

B.Sc.(Hons) Pharm. Sci. Third Year Students

Project Descriptions

Repurposing the Methotrexate Scaffold to design Novel Janus Kinase inhibitors
Francesca Borg

This study repurposed methotrexate to design Janus kinase (JAK) modulators having potential clinical utility in myeloproliferative neoplasm. Methotrexate was modelled, docked into the JAK ligand binding pocket (pdb ID 3EYG) and conformational analysis was performed. The optimal methotrexate conformer and cognate JAK-inhibitor were used to yield a consensus pharmacophore used for virtual screening for similar molecules.

Repurposing the Anthelmintic Drug Niclosamide for the Rational Design of PTEN-induced Putative Kinase 1 Agonists
Abigail Buttigieg

This study repurposed the anthelmintic niclosamide to design high efficiency pten-induced putative kinase 1 (PINK1) modulators for Parkinson's disease management. Niclosamide was modelled, docked into the PINK1 ligand binding pocket (pdb ID 5YJ9) and conformational analysis performed. The optimal niclosamide conformer and cognate ubiquitin were used to yield a consensus pharmacophore used for virtual screening for similar molecules.

Cultivation of Cannabis
Miriana Cachia

Conditions required for indoor cultivation of medicinal cannabis (MC) to obtain a standardised product under Good Manufacturing Practice are studied. A review of validated methods for the analysis of MC is carried out. A high-performance liquid chromatography method for determination of active ingredients in medicinal cannabis are developed and validated.

Outcomes of Pharmacist-Led Medication Use Review for Patients with Respiratory Disease
Christy Caruana

This study analyses the impact of a pharmacist-led medication use review in the optimisation of treatment in patients with respiratory conditions. A medication use review is conducted for patients with chronic respiratory disease who obtain medication through the Pharmacy of your choice (POYC) scheme. A pre- and post- medication review patient assessment on knowledge and adherence is undertaken.

Risk of Cannabis for Medical Use
Michael Cini

The perception of health care professionals on Cannabis for Medical use is analysed through focus groups and questionnaires. A two-dimensional risk matrix is used to rank the side-effects according to probability of occurrences and severity of consequences.

Identification of Potential Endogenous Targets for Maltanedienol
Ella Coppini

Maltanedienol mediates *in vivo* calcium deposition through a hitherto unidentified target. A bioinformatics software used a ligand-based approach to identify potential targets for Maltanedienol. The potential targets were divided into two groups- those with calcium deposition association and those without. Comparative affinity studies are being carried out for the development of a predictive *in silico* tool.

Rational Design of Phosphoinositide 3-Kinase Modulators
Hannah Coppini

Phosphoinositide 3-kinase (PI3K) inhibition mitigates the rare spinal neoplasm chordoma. The crystal structure of a quinazoline inhibitor:PI3K complex (pdb ID 5ITD), has been resolved. The critical ligand:receptor contact points were elucidated in this study and used to create a pharmacophoric query molecule in Ligand Scout® which was submitted to ZincPharmer® for virtual screening of similar molecules.

Pharmaceutical Care for Stem Cell Transplant Patients
Krysta Cutajar

A stem cell pharmaceutical care service is implemented at Sir Anthony Mamo Oncology Centre. Pharmaceutical care issues are identified by the researcher and a multidisciplinary team to ensure safe and effective care. The service considers medicine access and patient concordance. A database is developed from data obtained through interviews and records. Patient leaflets are compiled to address compliance.

The Unique Identifier on Drug Products
Mireille Debono

The impact envisaged by stakeholders from the pharmaceutical sector of the unique identifier on accessibility, distribution and dispensing of medicines in Malta is compared with the impact after the Falsified Medicines Directive is enforced. This is carried out by questionnaires to pharmaceutical stakeholders validated though focus groups.

Pharmaceutical Interventions During Labour
Rebecca Marie Falzon

Oxytocin use in labour within MDH Obstetrics and Gynaecology unit is evaluated. Utilisation data is extracted from patient files and compared and contrasted to local protocols and international guidelines. Correlation of use with effects on the new-born is also carried out. Findings will influence training material prioritisation for healthcare professionals working within the delivery room.

Pharmaceutical Care in Paediatric Oncology
Sarah Marie Falzon

A protocol for the empiric management of febrile neutropenia in paediatric cancer patients is developed. Retrospective analysis of blood cultures of paediatric cancer patients admitted with febrile neutropenia is carried out and the protocol is put forward to rationalise the use of selected empiric antibiotics in our local scenario. The protocol is validated and audited.

Pharmaceutical Care Interventions in Obstetrics and Gynaecology
Naomi Fiteni

Antibacterial drugs are useful medications for the treatment and prophylaxis of interventions in Obstetrics and Gynaecology. Analysis of the usage trends of antibacterial agents in a hospital setting for the past two years is carried out. Common antibacterial drugs and duration of treatment are identified. Auditing of use against local protocols and international guidelines is performed.

Design of BRD9 Receptor Antagonists Based on the BI-7273 Scaffold
Paula Gambin

BRD9 is a novel druggable target for the treatment of acute myeloid leukaemia. The crystal structure of BRD9 bound to lead molecule BI-7273 (pdb ID 5EU1), has been resolved. The critical contact points between BI-7273 and BRD9 were elucidated in this study and used to create a pharmacophoric query probe which was submitted to ZincPharmer® for virtual screening of similar molecules.

Design of Androgen Receptor Inhibitors Using the Naturally Occurring Capsaicin Scaffold as a Lead Molecule
Johan Grech

This study aimed to design molecules based on the capsaicin scaffold capable of androgen receptor (AR) modulation & anti-prostate cancer activity. Capsaicin was modelled, docked into the testosterone ligand binding pocket (pdb ID 2AMA) and conformational analysis was performed. The optimal capsaicin conformer and cognate testosterone were used to yield a consensus pharmacophore used for virtual screening for similar molecules.

Design of BU10119 Analogs for the Management of SSRI Refractory Depression
Matthew Grech

This study used BU10119, a dual opioid κ/μ antagonist to design analogs with potential in refractory depression. A consensus pharmacophore predisposing affinity for both subtypes was modelled by performing conformational analysis with BU10119 at both κ & μ receptors (pdb IDs 4DJH & 4DKL) and using the cognate ligands and the optimal conformer at each subtype to create an average used for virtual screening.

Risk-based Processes in Pharmacy Practice
Emily Magro

The study is divided in two phases. Phase I identifies pharmacy practice risk factors via a questionnaire addressed to community pharmacists. Phase II evaluates management risks at the POYC Unit via a structured interview. Two focus groups are set up to validate the questionnaire and interview. Two-dimensional risk matrices are developed to classify risks according to probability and severity of consequences.

Evaluation of Anaesthetic Drugs in the Intensive Therapy Unit
Julia Micallef

The study evaluates the use of celecoxib in the intensive care setting. Protocols and procedures particularly those adopted in day surgery are reviewed and audit of compliance is undertaken. Availability of COX-2 inhibitors in different dosage forms and limitations with access are established. A reflection on potential use of parecoxib and dexmedetomidine in this setting is carried out.

Outcomes of a Pharmacist-Led Medication Use Review for Diabetics
Mathea Montebello

This study aims to develop a service and evaluate the outcome of a pharmacist-led Medication Use Review for diabetic patients by conducting patient sessions in a community pharmacy. Patients are monitored at baseline, at four months and six months where HbA1c, random blood glucose and body weight are measured. Patients` views on the pharmacist intervention are evaluated.

Smoking Cessation in Post-Hospitalisation Rehabilitation
Gabrielle Scicluna

Smokers attending the initial assessment session at the cardiac rehabilitation unit at Mater Dei Hospital are recruited into this prospective study. A pharmacist-led smoking cessation intervention is developed and implemented at initial assessment. Patients are followed up after six weeks, three months and one year, and the impact of pharmacist intervention on smoking cessation is evaluated.

Design of 6-Phosphogluconate Dehydrogenase Inhibitors Using Parietin, and its Semi-Synthetic Derivative S3 Scaffolds as Lead Molecules
Daniel Sinagra

This study aimed to design novel parietin-based 6PGD modulators with anti-proliferative potential. Parietin was modelled and conformational analysis performed. Two pharmacophores; one derived from endogenous inhibitor S3 (pdb ID 2IZ1) and one derived from the optimal parietin-6PGD-bound conformer were modelled and used for virtual screening using ZincPharmer® for similar molecules.

Simplification of the Experimental Molecule FR900359
Brandon Sultana

This was a simplification study that used novel lead FR900359 to design low molecular weight analogs capable of G protein inhibition and bronchodilation. FR900359 was modelled, docked into the Gqa-ligand binding pocket (pdb ID 3AH8) and conformational analysis performed. The optimal FR900359 conformer and cognate YM-254890 were used to yield a consensus pharmacophore used for virtual screening.

Patient Education and Medication Compliance in Osteoporosis
Michaela Vella

Osteoporosis prophylaxis and management rely on patient understanding of the consequences of the condition and medication compliance. Questionnaire A will assess the knowledge pre-menopausal women have regarding osteoporosis. Questionnaire B will assess how compliant osteoporotic patients are and their access to medications. Patient education initiatives are proposed.

Rational Design of Glutaminase c Modulators
Lara Zammit

Glutaminase c (Gc) inhibition mitigates lung tumours through Glutaminate depravation. The crystal structure of the novel Gc inhibitor CB-839:Gc complex (pdb ID 5ITD), has been resolved. The critical ligand:receptor contact points were elucidated in this study and used to create a pharmacophoric query probe in Ligand Scout® which was submitted to ZincPharmer® for virtual screening of similar molecules.

B.Sc.(Hons) Pharm. Sci. Second Year Students

Pharmacy Practice Project Descriptions

Pharmacy Evolvement and Workforce Development
Nicole Agius Markham

Local pharmacist manpower, evolvement of pharmacy systems and impact on manpower needs are studied. The local pharmacy scenario is compared to international settings. Proposals for opportunities of improvements are put forward.

Perception of Green Practices in Community Pharmacy
Michela Baldacchino

Perception of pharmacists and pharmacy technicians working in community pharmacies towards green practices is evaluated using a questionnaire. The developed questionnaire is validated through a focus group and distributed to community pharmacies around Malta.

Evolvement of Systems for the POYC Scheme
Luke Cassar

This study aims to explore and analyse the local National Health System identifying strengths, weaknesses, opportunities and threats underlying the POYC scheme. The perception and experience of healthcare professionals using this scheme are analysed.

Facing Brexit: The Impact on Medicines
Andrew Felice

The accessibility to medicines in Malta depends substantially on the UK market supply, with the local government pharmaceutical services sourcing about 800 products. This project assesses the impact of Brexit by analysing problems of accessibility, registration and increase in medicine cost.

Radiopharmaceuticals
Yasmine Fenech

Evolving therapeutic and diagnostic uses of radiopharmaceuticals (RP) are reviewed. Proposals for pharmaceutical interventions in the procurement, handling, use and safe disposal of RPs are elaborated and frameworks for professional development are developed.

Development of a Quality System for the Analysis of Medicinal Cannabis
Oksana Friggieri

A laboratory quality system for the sample preparation and analysis of medicinal cannabis is setup. This system includes Standard Operating Procedures related to methods for determination of compounds and active constituents (THC and CBD) in the cannabis plant.

Point-of-care Testing for Infections
Laurent Grech

Availability of point-of-care testing for infections for different infective conditions is analysed. Implementation of kits in different settings, focusing on reliability and patient ease-of-use is evaluated. Novel tests and current local uses are proposed.

Direct Acting Oral Anticoagulants in Older Patients
Kevin Kirkop

Direct oral anticoagulants (DOACs) have emerged as promising alternatives to warfarin in the management of atrial fibrillation and venous thromboembolism. Since more older patients are prescribed DOACs, a review of prescribing practices and patient experience is warranted.

Myths, Science and Realities of Medicines Wastage
Roderick Micallef
Medicines wastage is a problem with profound economic and environmental implications. This project discusses the various myths and assesses the realities of local medicinal wastage. The stability, environmental and psychological scientific aspects of this problem are analysed.

Biosimilars: Perception and Awareness among Healthcare Professionals
Sephora Scicluna Bugeja

Biologics and biosimilars target the management of chronic conditions. The high cost of biologics' production places pressure on healthcare systems. Biosimilars are cheaper and thus preferred by policymakers. Perception of healthcare professionals regarding their use is sought.

Consumer Perception of Risk of Pharmacist Prescribing
Emma Theuma

Risks of pharmacist prescribing as perceived by the general public are evaluated through a self-administered questionnaire. Common conditions identified by the general public through the questionnaire are used to develop a framework for community pharmacist prescribing.

Clinical Audit of Pharmacotherapy in the Management of Hypertension
Francesca Vassallo

Appropriate hypertension (HTN) management reduces risk of associated complications. This audit assesses pharmacotherapy in patients with HTN according to the 2018 European Society of Cardiology guidelines selected as audit standards. Blood pressure measurement is performed.

Notified Bodies for Medical Devices
Mariah Vella

Conformity assessments on medical devices can only be conducted by Notified Bodies (NB). This project assesses the importance of NB for medical devices by analysing their roles, their various establishments in Europe, and ways to implement a NB in Malta for mutual benefit.

B.Sc.(Hons) Pharm. Sci. Second Year Students

Medicinal Chemistry Project Descriptions

Probing the Thioredoxin Reductase (TrxR) ligand binding pocket computationally
Nicole Agius Markham

Mammalian TrxR inhibition mitigates tumour cell growth *in vitro*. Motexafin gadolinium selectively targets tumour cells leading to cell death and apoptosis through TrxR inhibition. It will be used as a lead for this study to model novel analogs capable of similar TrxR modulation.

Gephyrin modulation using the artemisinins- a rational drug design study
Michela Baldacchino

Gephyrin has been implicated in the mediation of Alzheimer's disease, epilepsy and schizophrenia. Artemisins modulate gephyrin, slowing down disease progression. Artesunate is the lead molecule in this study that aims to design and identify high affinity gephyrin modulators.

Design and identification of selective Foetal Liver Tyrosine Kinase 3 (FLT3) inhibitors for the management of Acute Myeloid Leukaemia (AML)
Luke Cassar

Patients with recurring AML develop a mutation driven by a protein-FLT3 Kinase, making the condition more aggressive. Alkynyl aminoisoquinoline and alkynyl naphthyridine, inhibit FLT3 Kinase and will be used as leads for the rational design of high efficiency analogs.

Drug design at the Cyclin Dependent Kinase (CDK) receptor using Palbociclib as a lead
Andrew Felice

CDKs 4 and 6 have been shown to drive breast tumour growth. Palbociclib is a novel orally administrable inhibitor of these enzymes. It will be used as a lead in this study for the modelling of analogs with the potential to provide non-hormonal alternatives to patients.

Repurposing Efavirenz as a CYP46A1 agonist to decrease Tau levels- a viable route for Alzheimers Disease (AD) management
Yasmine Fenech

Evidence using pluripotent stem cells from AD patients show an increase in cholesteryl esters (CE) which increases intra-cerebral tau levels. Efavirenz lowers CE and tau levels by agonism of the neuronal enzyme CYP46A1 and will be used as a lead in the identification of analogs.

Design and identification of selective Casein Kinase 2 (CK2) inhibitors for modulation of circadian rhythyms and cancer cell growth
Oksana Friggieri

Over-expression of CK2 enzyme leads to uncontrolled Circadian rhythms that perpetuate abnormal cell growth. The experimental molecule G0289, selectively inhibits tumour CK2 and promotes apoptosis. It will be used as a lead in the *in silico* modelling of high efficiency analogs.

Rational Design of Heat Shock Proteins (HSP70) inhibitors
Laurent Grech

HSP70 is a target for triple negative breast cancer therapy. Its inhibition reduces intra-tumour tissue necrosis factor α levels. The interactions between HSP70 and the novel inhibitor VER-155008 will be used as leads for the identification of molecules with similar activity**.**

Investigating the role of Sirtuins computationally in Type 2 Diabetes Mellitus (TTDM)
Kevin Kirkop

Sirtuins are metabolic receptors. Their modulation results in a hypoglycaemic effect, making them viable targets in the management of TTDM. The resveratrol-bound SIRT1 serves as template for the modelling of high affinity competitive inhibitors for this enzyme.

The rational design of MEK inhibitors using the experimental TAK-733 scaffold as a lead molecule for the management of neoplastic disease
Roderick Micallef

Literature indicates that the experimental molecule TAK-733 exerts an *in-vivo* anti-tumour activity through MEK kinase inhibition. This study will model the TAK-733 scaffold and use the critical interactions that it forges with its receptor to identify analogs of clinical use.

Rational Drug Design at the *Helicobacter pylori* (*H. pylori*) Carbonic Anhydrase (CA) Enzyme
Sephora Scicluna Bugeja

Evidence shows that *H.pylori* expresses 2 CA isoforms- a and b. Their inhibition represents a new approach to treatment. This study will probe the *H.pylori* CAs ligand binding pockets and use their inhibitor-bound conformation in the design of selective analogs.

Investigating the role of Nutlin 3 in Mouse Double Minute 2 Homolog (MDM2) inhibition
Emma Theuma

Nutlins are cis-imidazolines. Clinical trials show that they can promote tumour cell senescence though MDM2 inhibition. The Nutlin-3 scaffold will be used as a lead in the identification of novel structures capable of similar interaction with the MDM2 receptor.

Design of Mouse Double Minute X and 2 homologs (MDMX/MDM2) modulators with potential in breast cancer treatment
Francesca Vassallo

Researchers have found a direct correlation between over-expression of MDMX and MDM2 receptors and triple negative breast cancer. This study will probe the ligand binding pockets of these receptors and use the scaffolds of existing experimental inhibitors for analog design.

The rational design of novel neutrophil elastase inhibitors for the management of muscular dystrophy
Mariah Vella

Muscular dystrophy is a currently incurable degenerative condition. Dystrophic muscle over-expresses neutrophil elastase (NE), which breaks connective tissue. NE inhibitor GW475151 will be used for the design and identification of high affinity, Lipinski Rule compliant analogs.

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