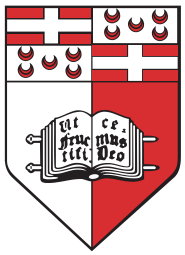

University of Malta

Dissertation Abstracts and Project Descriptions

Department of Pharmacy
Faculty of Medicine and Surgery
University of Malta

2017

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Foreword

Pharmaceutical Regulatory Affairs to Regulatory Sciences

During the last half a century pharmacy witnessed several evolvements which changed the dimensions of pharmacy practice. These included the movement towards a more patient-centred profession rather than product-oriented. We witnessed the contribution of drug intelligence to clinical pharmacy and later to pharmaceutical care and the evolvement of the sciences of biopharmaceutics and pharmacokinetics. Concepts dealing with bioavailability and bioequivalence, drug structure activity relationships, potency and efficacy, pharmacokinetic parameters, biological half-life, volume of distribution, drug clearance, protein binding, absorption and elimination constant were tackled by the Department in the early 1970s. The latest developments involve Regulatory Affairs. Today we are witnessing the full development of Regulatory Affairs into the latest acknowledged Regulatory Sciences, with the addition of the science of Pharmacovigilance.

The Department of Pharmacy within the Faculty of Medicine and Surgery of the University of Malta has always been at the forefront of the development of these pharmaceutical sciences. A casual look at the previous symposium abstracts for the last thirty years show that the students in the Department of Pharmacy have followed through their projects, an array in these developments in the pharmacy scenarios.

This year the Department of Pharmacy is celebrating a historical milestone in the development of the profession of pharmacy. The evolvement of the subject of Regulatory Affairs to Regulatory Sciences could be mainly attributed to pharmacy scientists. The Department of Pharmacy in Malta has contributed in no small way to this historical development. One may consider that Regulatory Sciences now form a substantial area of special interest not only in our teaching and research but also in the contribution of academics to the regulatory scenarios both in Malta and in the international scenario through contributions at the international front and the publication of peer reviewed scientific papers. The subjects covered in this recently acknowledged science in the pharmaceutical field include Pharmacovigilance, Quality Assurance of Regulatory Processes, Good Manufacturing Practice, Harmonisation of Pharmaceutical Processes, Accreditation of Sciences Related to Processes such as Production, Quality Control, Clinical Trials, Inspectorate, Licensing, Registration, Assessment of Dossiers, Standard Operating Procedures, Quality Assurance through Change Control, Deviations, and other Documentary Records . This input by Malta into the education and scientific needs in the training and research aspects of Pharmaceutical Regulatory Sciences was recognised last month during the Presidency Meeting of the Heads of Medicines Agencies. Malta is to run a pilot project to ensure the courses within the area of Regulatory Sciences fall within the European Credit Transfer Systems (ECTS) and in accordance with the Bologna Agreement on structuring tertiary level education systems in Europe. Such advanced tertiary education structures in pharmacy from social, teaching and research aspects serve to increase recognition of our Alma Mater. They also provide strong arguments to support Malta in its bid to host the European Medicines Agency. The MHRA, the UK agency that supports Regulatory Sciences in the UK is a major leader in the area. The MHRA is at present pivotal in the provision of access to good quality, safe and effective medicines in Europe. With Brexit, the United Kingdom will no longer form part of the European Union. Malta needs to come forward to fill the empty spaces left by the UK. This can be assisted if academia prepares the workforce of experts required in this area through its state-of-the-art teaching and research in the field. The Department of Pharmacy is ready to take up this challenge and it would be a very sad day if the authorities do not support the Department in ensuring that facilities are available to provide for such an innovative science especially through the recruitment of adequate academic staff.

The Department has proven its worth by disseminating its student work. This year's symposium where pharmacy students present their scientific work, is another feather in the hat of the Department. This year we do have an additional reason to be proud and celebrate because for the first time the Department is presenting the Level 8 Doctorate in Pharmacy candidates. The gist of their hard and rewarding scientific work is presented in this symposium. Other enthusiastic and intellectually gifted candidates reading for degrees offered by the Department of Pharmacy, namely the Bachelor of Science in Pharmaceutical Technology, Bachelor of Science in Pharmaceutical Sciences, Master of Pharmacy and Master of Science in Pharmacy are presenting their work at the symposium.

Congratulations to all! You have done great work! Thank you for disseminating your results to your colleagues, friends and families. This week is a great week for all of us professors, lecturers, supporting staff, family and friends. The protagonists are the students without whom this week would not only be meaningless but non-existent. Finally, an appeal to all to disseminate your work. By disseminating our work we would be contributing to society at large to benefit and ultimately meet the needs of our patients who are always in the centre of our work.

Professor Anthony Serracino-Inglott
Pharmacy Practice Projects Co-ordinator

Introduction

The Department of Pharmacy has evolved over the years into a pharmacy-centred institution that is focused on high-levels of excellence in education and research. The Department today offers five courses at undergraduate and postgraduate level.

The three year programme leading to a degree of Bachelor of Science (Hons) in Pharmaceutical Technology attracts students who have an aptitude towards developing competence in pharmaceutical processes and quality aspects. This course was developed as a means to satisfy the needs of the pharmaceutical industry and the pharmaceutical services. Pharmaceutical technology graduates have the opportunity to take up the Master of Science (Pharmacy) course to develop areas of specialisation in pharmaceutical regulatory sciences, pharmacoeconomics and industrial pharmacy. The two-cycle programme leading to a degree in pharmacy comprises the four year course leading to a Bachelor of Science (Hons) in Pharmaceutical Sciences and the three semester Master of Pharmacy course.

The Department offers the postgraduate course leading to a Doctorate of Pharmacy Level 8 degree. The course is offered in collaboration with the College of Pharmacy of the University of Illinois at Chicago. In this Symposium, the first cohort of students completing their doctorate studies are presenting their research dissertation. The Doctorate of Pharmacy course is an opportunity for pharmacists to develop advanced skills in pharmacotherapy and patient management, in the assessment of innovative therapies and in leadership. The course consists of three components: the didactic part that is composed of online lectures and tutorials and patient-case based sessions, the professional part that involves six periods of practice rotations in different settings including hospital pharmacy, community pharmacy and pharmacovigilance, and the research part that consists of an applied research dissertation. Currently, 34 students from 9 countries are enrolled in this international programme.

Through these courses, the Department is providing 645 ECTS credits. A highlight of the courses offered are the inclusion of academic-led experiential placements where students have the opportunity to immerse in the 'real-life' scenarios in different aspects of pharmacy ranging from manufacturing industry, quality control, distribution of medicines, regulatory affairs, hospital pharmacy and community pharmacy. This experience engages the students to merge knowledge with relevant practice and to reflect on contemporary practice. The success of these placements is due to the excellent collaboration which the Department enjoys with the different experiential sites and to the academic input provided by the academic staff during specific tutorials. This academic input is focused to support the student in approaching the three domains of learning namely the cognitive, psychomotor and affective, within the practice settings.

These academic-led placements are also offered as part of the student mobility activity within the Erasmus programme, where students take up one semester of study in a partner University in Europe. During this academic year, all the students following the Bachelor of Science (Hons) Pharmaceutical Science course and 42% of the students following the Bachelor of Science (Hons) in Pharmaceutical Technology course took up a student mobility. The Department is hosting 17 students from partner universities who are either following credits within the courses, or taking a placement or undertaking their research dissertation within the research groups of the Department.

A recent paper by Nunes-da-Cunha et al published in the American Journal of Pharmaceutical Education in June 2016 has established that Malta has the highest percentage of clinical studies in the pharmacy curriculum at 12. 3% in Europe and is second to the United States which stands at 16.7%. Through the regular reviews and updates of the curriculum in the pharmacy programme, the Department is taking a lead in pharmacy education that is aiming to prepare the pharmacist graduate with a skill set and competences base as required by the changes in the pharmaceutical industry, in pharmaceutical regulatory sciences and in handling complex drug therapies in complex patients.

The establishment of the Pharmaceutical Technology programme with the elaboration of the Master of Science (Pharmacy) course to address more specifically pharmaceutical regulatory affairs has led to increasing the manpower required in the rapidly developing pharmaceutical industry that is driven by ensuring quality, safety and efficacy in medicinal products.

The Doctorate of Pharmacy programme, which was the latest evolvement within the courses provided by the Department, is empowering pharmacists to elaborate innovative pharmaceutical services in our hospitals and health systems and to contribute in the European and international platforms in aspects of innovative drug therapy evaluation and policy developments.

Professor Lilian M. Azzopardi
Head, Department of Pharmacy

Doctorate in Pharmacy
Dissertation Abstracts

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Self-Management of Insulin in Type I Diabetic Patients

Khaled Abdelmaula

Background: Flexible intensive insulin therapy (FIT) permits the patient to adjust the timing and the amount of insulin administered by using long-acting insulin which is injected once or twice daily and rapid acting insulin which is taken according to carbohydrate intake. This therapy allows patients to have greater dietary flexibility.

Purpose: The aims of this study are 1) to evaluate the impact of how educating patients on combining FIT (insulin dose adjustment) with dietary flexibility improves glycaemic control in type 1 diabetes (T1DM) and 2) to investigate the impact of FIT on HbA1C levels.

Method: A questionnaire about carbohydrate counting was adapted from 'The Heart Healthy Carb Quiz'. This questionnaire was validated by an expert panel (1 diabetologist, 2 pharmacists, 1 diabetic nurse specialist, 1 diabetic educator). The study took place in November 2016 at the 'Diabetes and Endocrine Centre' at Mater Dei Hospital. Patients were chosen by convenience sampling and asked to complete this self-administered questionnaire. Two groups of patients completed the questionnaire- one group who was taking insulin according to their carbohydrate count (Group 1) and the other group on conventional insulin therapy (Group 2).

Results: Forty patients (29 female; mean age=36 years; range=14-65 years) were in Group 1 and 40 patients (18 female; mean age=40 years; range=(16-66 years) were in Group 2. When the HbA1c values of the 2 patient groups were compared, the mean HbA1c value of patients in group 1 (8.09%) was significantly lower (p=0.02) than the mean HbA1c value of patients in group 2 (8.73%).

Conclusion: Patients who were taking insulin according to the carbohydrate count were associated with better glycaemic control than those who were using conventional insulin therapy.

Evolvement of EU Regulations on Innovative Medicines

Roberta Agius

Background: Regulatory requirements are a major reason affecting access to innovative medicines (IM).

Purpose: To study the impact of EU regulation regarding IM by investigating authorisation procedures.

Method: Analysis of EU regulatory tools developed to facilitate access to IM was undertaken. Conditional (CMA) and exceptional circumstances (EC) authorisations were studied using the European Public Assessment Reports as the data source. Challenges faced by the National Health Service (NHS) in Malta were identified through interviews with the Medicines Authority, Pharmaceutical Affairs Directorate (DPA) and Government Central Procurement and Supplies Unit (CPSU). Existing legislative tools were explored to identify challenges and optimise IM access in Malta.

Results: Since 2001, 65 IM products were centrally authorised for the European market using CMA and EC procedures (35 CMA, 30 EC). Seven products were withdrawn due to commercial reasons (5), lack of efficacy (1) and lack of requested additional data (1). Forty-three percent (28) of the authorised products or EC were given a new active substance status and 51% (33) were given orphan designation. In 2015, there were a total of 822 centrally authorised products (CAPs) covering 522 Anatomical Therapeutic Chemical (ATC) Codes. The Maltese NHS formulary does not include 322 (61%) CAP ATC codes. Identified challenges with importation of CAPs in Malta are the low volumes required and costs of IM. Regulatory pathways such as approval for use as unlicensed medicines on a named patient basis (2015: 3 CAPs) and use in exceptional cases according to Article 20 (1) of the 2003 Medicines Act (2015: 14 CAPs) are used to improve access. Parallel distribution (PD) was explored as another tool to increase access. Together with the European Medicines Agency (EMA), a one-year pilot project with fee reductions for PD notifications for CAPs in the Maltese language was launched in 2016, during which PD of Neulasta® (pegfilgrastim) and Erbitux® (cetuximab) was authorised.

Conclusion: Regulatory tools such as CMA and EC authorisations are used successfully to improve access to IM, particularly in rare diseases. Targeted regulatory initiatives, as exemplified by the special pilot PD project involving notification fee reductions specifically authorised by the EMA for Malta, may help to overcome accessibility barriers especially in small countries.

Glucagon Use in Paediatric Type 1 Diabetic Patients: An Innovative Approach to Improve Outcomes

Danika Agius Decelis

Background: Hypoglycaemia is the most common acute complication and is considered a major problem amongst children with Type 1 diabetes mellitus. Hypoglycaemia is very often undetected, under-reported and poorly understood by patients and their carers. The lack of confidence in detecting, reporting and understanding hypoglycaemia puts the patients at risk of consequences of untreated hypoglycaemia.

Purpose: To develop and evaluate the impact of educating carers of paediatric patients suffering from T1DM, on the emergency use of glucagon in hypoglycaemia in a safe and effective way.

Method: A Tool Kit in both Maltese and English was developed, consisting of information on hypoglyceamia, a chart and a video on how to reconstitute and use glucagon. This was disseminated to all pharmacists and a self-administered questionnaire was completed to analyse the knowledge and confidence on the use of glucagon before and after the intervention. The same Tool Kit was also given to carers of children with T1DM. Carers were recruited after their visit to outpatients' clinic. A questionnaire was completed with the help of the researcher, at baseline to evaluate carer knowledge. Subsequently the carers received the information and the Tool Kit. Four weeks after the pharmacist intervention, carers were contacted by phone to complete the questionnaire for the second time to evaluate the impact of the intervention.

Results: One hundred thirty-nine pharmacists submitted a response to the questionnaire. Using the Wilcoxon sign test a significant difference is noted in both confidence (Mean before: 2.0; after: 4.0) and knowledge (Mean before: 2.2; after: 4.3) of use on glucagon when before to after intervention is compared ($p>0.001$). One hundred forty patients with diabetes attend the paediatric diabetes outpatients service at MDH and of these 80 successfully participated in the study. When comparing before intervention to after for confidence (Mean confidence before: 2.5; after: 4.1) and knowledge (Mean before: 2.7; after: 4.7) on reconstituting glucagon, both parameters resulted in statistical significant improvement ($p>0.001$).

Conclusion: The educational material had a significant impact on the knowledge and confidence the pharmacist and carers have on the use and reconstitution of glucagon. This will empower pharmacists with better tools to educate patients and also instill confidence in carers to make use of glucagon appropriately when required.

Therapeutic and Economic Implications of Regulating Stem Cell Therapy and Blood Components

Alison Attard

Background: Malta is in the process of studying a possible structure for regulation of blood products and stem cell therapies (SCT) analogous to the rules applied for medicinal products on the basis of quality, safety and efficacy.

Purpose: (1) To establish a network of stakeholders in the area of blood components and SCT facilities, (2) To address requirements for setting up an SCT unit and identify economic implications, (3) To identify regulatory sciences norms for regulators of blood and SCT facilities.

Method: Collaborations with academia, industry, technical specialists in regulatory sciences and European regulatory authorities are established through site studies. Business models for developing an SCT unit are analysed through the collaborations. Requirements and costs for set-up, maintenance and treatment are identified. A quality manual for regulators of blood and SCT facilities is developed following shadowing of inspections with a regulatory body.

Results: Collaboration with King's College, London (academic), Holostem Terapie Avanzate, Modena (industry), the first biotechnology company in Europe granted a marketing authorisation for SCT (Holoclar®), CTP System, Florence (technical specialists) and Health Products Regulatory Agency, Ireland (regulatory authority) was established. A private-public business model for setting up a SCT facility was identified as a partnership. Two laboratories were designed: A research laboratory ($36m^2$) at the Biomedical Sciences Centre, University of Malta and a Good Manufacturing Practice laboratory ($300m^2$) as a production facility at the Malta Life Sciences Park (MLSP). In addition to the facilities already available, the following are some examples of expenditures involved to set up and run an SCT: Rent of MLSP (€100/m^2/year), setting up a Class B processing laboratory (€5,000/m^2), equipment (c€500,000) and personnel (€93,000/year). On the income side, it is envisaged that therapy charges range from €3,000/treatment for hepatocyte transplantation to €50,000/patient for adipose stem cells for aesthetic medicines. A quality manual for regulatory authorities describing the mission, responsibilities, applicable standards and regulations, standard operating procedures and 'Aide Memoire' as a practical guidance for auditing blood establishments and SCT facilities is drafted and validated.

Conclusion: Collaborative partnerships served to up-skill knowledge in SCT and blood components. The results point to the need of a feasibility study which in itself costs €15,000- €25,000.

Pharmacoeconomics of Innovative Medicines in Cardiovascular Disease

Mark Cardona

Background: Compared to warfarin, novel oral anticoagulants (NOACs) have a much higher retail cost. Advantages of using NOACs include uncomplicated dosing with no need for INR monitoring and fewer possible drug interactions.

Purpose: To compare the NOAC rivaroxaban to warfarin with respect to medication adherence and the incidence and severity of bleeding.

Method: Following ethics approval, 100 patients (50 on rivaroxaban and 50 on warfarin) were recruited by convenience sampling from Mater Dei Hospital outpatients and community pharmacies. Patients included were 18 years or older, on anticoagulation therapy for 3 years or more, with no cognitive impairment and no hepatic or renal impairment. The validated Morisky Medication Adherence Scale (MMAS-8) was used to assess adherence to treatment, with each patient categorised as 'high' (score 0), 'medium' (score 1-2) or 'low' adherence (score 3-8). Bleeding complications were classified according to the Bleeding Academic Research Consortium (BARC) criteria. Data was analysed using the chi square, independent samples t-test, Kolmogorov-Smirnov, Shapiro-Wilk and Mann-Whitney tests.

Results: Patients in the warfarin and rivaroxaban groups were comparable ($p>0.05$) with respect to mean age (64.5 years, range 27-85 years), gender (53 female and 47 male), indication for anticoagulation (59 for atrial fibrillation, 30 for deep vein thrombosis) and mean duration for anticoagulation use (10 months, range 1-33 months). Total MMAS-8 scores for warfarin were: 'high' (n=17), 'medium' (n=24) and 'low' (n=9) adherence, while total MMAS-8 scores for rivaroxaban were: 'high' (n=37), 'medium' (n=9) and 'low' (n=4) adherence ($p<0.001$). Mean MMAS-8 score was 1.35 for warfarin and 0.50 for rivaroxaban ($p<0.001$). Twenty-four patients reported BARC Type 1 bleeding (18 warfarin and 6 rivaroxaban) and 10 patients reported BARC Type 2 bleeding (6 warfarin and 4 rivaroxaban) ($p<0.001$).

Conclusion: Results indicate that rivaroxaban has the advantages of higher adherence and lower bleeding rates compared to warfarin. A cost-effectiveness analysis will sustain or reject the pharmacoeconomic rationale for including rivaroxaban (NOACs) in the local National Health Service Formulary.

Pharmaceutical Issues and their Impact on the Efficacy and Safety of Biosimilar Therapeutic Products

Mark Cilia

Background: Patent expiration of biologics heralded a new category of medicinal products referred to as biosimilars, approved on the basis of similarity to their reference biological products. Pharmaceutical issues during development and manufacture of biosimilars can affect the safety and efficacy profile of biosimilars.

Purpose: To identify and analyse pharmaceutical issues encountered during development and manufacture of biosimilars, to assess how these issues are addressed and mitigated through risk minimisation measures (RMMs) and to determine the effect of these issues through the safety and efficacy profile changes of biologics with the advent of biosimilars.

Method: The adopted Day 120 list of questions on the quality module of marketing authorisation applications of 22 biosimilars is analysed, frequencies of deficiencies calculated and summarised descriptions included. Pharmaceutical issues are classified as either Major Objections or Other Concerns, collectively referred to as deficiencies. Review of whether any of these deficiencies were reflected as safety concerns and analysis of RMMs related to biosimilars and their reference products is carried out. Any change in the safety and efficacy profile of biologics with the advent of biosimilars is explored via a data mining exercise of adverse events reported in Eudravigilance database using its inbuilt Eudravigilance Data Analysis System (EV-DAS) for signal detection.

Results: Deficiencies' frequencies and trends were recorded for 22 biosimilar marketing authorisation applications. Identified Major Objections (n=32; mean 1.45 per application, range 0-12) and Other Concerns (n=1042; mean 47 per application, range 44-131) were analysed. Analysis of RMMs of biosimilars and their reference products revealed no differences in identified safety risks, whilst the data mining exercise of all adverse events associated with biosimilars and their reference products using EV-DAS signal detection (95% Confidence Intervals) did not result in any signal showing a changing safety and efficacy landscape.

Conclusions: This study contributes towards an in-depth understanding of pharmaceutical issues related to biosimilars and can help to improve dossiers and reduce approval timelines. The study indicates that the advent of biosimilars did not impact the safety and efficacy profile of biologics, encouraging the safe and effective use of biosimilars and leading to enhanced equity in availability of advanced biotechnological remedies to patients.

Classification of Herbal Medicines: What is Safe for the Patient?

Alexandra Curmi

Background: Plant and plant derivatives have been used for their medicinal properties for centuries. An example of this is St John's Wort used by Hippocrates in the 5th century BC. The use of herbal medicines is on the increase with market values expected to reach 105$ billion in 2017. One of the possible reasons for the vast use of herbals is due to the misconception that herbals are 'natural' and hence safe.

Purpose: To evaluate knowledge and confidence of pharmacists and health food shops employees with regards to use of herbal medicines, to evaluate perception and attitudes of patients towards herbals and to analyse classification of herbals within the EU from a regulatory aspect.

Method: Two questionnaires were developed and validated. The first questionnaire was disseminated to pharmacists and health food shop employees to determine knowledge and perception on herbal products and classification of herbal medicines. The second questionnaire was disseminated to the general public and was intended to determine their perception and attitudes towards the use of herbal products. A review was carried out to highlight the regulatory aspect of how herbal medicines are classified including latest updates and whether these reflect requirements of safety of the patient.

Results: A total of 121 respondents (107 pharmacists and 14 health shop employees) answered the questionnaire. Preliminary results show that there is need to support pharmacist and health shop employees' with knowledge on herbal products. A total of 150 people responded the general public survey. The majority of public interviewed (80%), prefer to consume herbal products from health shops and pharmacies but there is lack of concern regarding co-administration with conventional drugs. Fifty-six percent of respondents co-administer herbal and conventional medicines. The different opportunities for registration of herbal products and herbal medicines have been reviewed and strengths and weaknesses identified.

Conclusion: The results obtained show that consumers co-administer herbal products with medications and this may highlight safety issues. Pharmacists are in a privileged position to empower patients to co-ordinate safe use of herbal products when used in combination with other medicinal products.

Reducing Medication Errors through Better Prescribing

Clifton Curmi

Background: The healthcare system is a complex system which is susceptible to high risk in occurrence of errors. Medication errors are the most common type of medical errors. They can occur at any stage of drug provision and can occur at various settings within the health system. Medication errors can have a significant impact not only on the patient but also could result in an increased economic burden due to costs associated with re-hospitalization.

Purpose: To analyse prescriptions in a community pharmacy in terms of prescription content and whether these are in conformity with prescribing legislation. To evaluate frequency and nature of prescribing errors in prescriptions in a community pharmacy setting. To assess severity of potential adverse events of intercepted prescribing errors in a community pharmacy and to provide the framework for implementation of e-prescribing in a local scenario through the identification of a number of recommendations

Method: Incoming prescriptions within a community pharmacy were analysed in terms of prescription content according to local legislation. A data collection tool was developed and a pharmacist interventions related to interception of medication errors was documented and medication errors identified were classified. Severity of potential adverse events resulting from intercepted prescribing errors was assessed. A number of randomly selected potential errors were judged by members of an independent research panel according to 'Safety Assessment Code Score'. Also a number of recommendations related to e-prescribing implementation were identified and put forward within a framework.

Results: The majority of prescriptions have one or more missing data as requested by local legislation. 222 prescribing errors were identified by the community pharmacists. Error of omission (48%) was found to be the most common type of prescribing error within the community pharmacy, 75% of which were due to missing information regarding strength or dose of medication.

Conclusion: Most medication errors may not be harmful to patients and eliminating all medication errors is absolutely impossible, however understanding the causes of medication error is important so to improve patient safety and health care quality through better policies and strategies.

Risk Assessment of Medication Safety in Pharmacotherapeutic Practice

Richard Despott

Background: Approximately 2% of hospitalisations are associated with preventable adverse drug events, estimated to cost more than €2million annually for our national healthcare service.

Purpose: The research identifies key areas for improving medication safety and evidence-based strategies for reducing the margin of error in pharmacotherapeutic practice.

Method: The type of medication error is classified from a quality risk management perspective based on clinical stage and cognitive psychology of task-oriented behaviour**.** The severity of medication errors identified from reports of adverse drug events recorded in the EudraVigilance System between June 2012 and September 2015 is assessed using the WHO Severity index, and predetermined case variables are also noted. (Setting, Patient Age, Gender, Number of Drugs, Route of Administration and Pharmacological Group). Hypothesis testing of univariate analysis is carried out using the Pearson Chi-squared test to determine the correlation between the severity and explanatory variables, and the Kruskal-Wallis one way analysis of variance to compare the mean severity rating scores. A Multinomial logistic model for ordinal data is used to establish the relative significance of the predictors**.**

Results: From 2294 adverse drug events reported to the European Medicines Agency, (84%) were confirmed cases of medication error and 1300 (57%) were considered preventable. Most cases of medication error were encountered in the prescribing (28%) and the administration (27%) of medicine, compared to the dispensing (14%) stage. The majority of human errors were case based in the prescribing stage (60%), skill based in the dispensing stage (66%) and rule based during administration of drug treatment (75%). The severity of harm showed a strong positive correlation with the pharmacological group, number of drugs and route of administration ($p < 0.001$), type of error and patient age ($p < 0.003$).

Conclusion: The research supports a quality risk management approach to safeguard against patient harm in ways that are complementary to the existing pharmacovigilance activities required by law. The results provide evidence for significant improvements in medication safety through treatment review and screening of at risk patients, and point towards strategies for reducing margin of error based on promotion of Patient-Centred Prescribing, Dispensing Standards of Pharmacy Practice and In-line checks during Administration of Drugs.

The Implication of Monitoring Tumour Markers: A Personalised Medicine Approach

Charyl Fava

Background: The availability of tumour markers in managing oncology patients contributes to developing personalised pharmacotherapy.

Purpose: To develop a pharmaceutical personalised approach through the design and implementation of a pharmaceutical care plan (PCP) incorporating tumour markers for patients suffering from ovarian, pancreatic or prostate cancer.

Method: Guidelines, recommendations and standards of care for the management of ovarian, pancreatic and prostate cancer were reviewed. The classification systems for drug therapy problems developed and validated by Cipolle et al[1] and the Pharmaceutical Care Network Europe version 6.2[2] were considered. These classifications were used in the development of a newly designed PCP template. The PCP template presented specific pharmaceutical oncology care requirements and trending of tumour marker results. Subsequently the developed PCP was implemented at Sir Anthony Mamo Oncology Centre.

Results: The developed PCP template consists of two sections. The first section records patient's details, carer's details, diagnosis, past medical history, previous cancer treatments, current medications including non-oncologic therapy, chemotherapy cycles prescribed, relevant laboratory investigations and tumour marker results. The second section of the PCP template categorises individualised pharmaceutical care issues (PCIs) identified. The pharmacist's actions are also documented in this section. A total of 67 patients (35 male, 32 female) were enrolled in this study. The mean age was 65 years (range: 26-83 years). Forty-five patients had a family history of cancer while 22 did not. Oncologic patients suffering from ovarian, pancreatic and prostate cancer were 19, 27 and 21 respectively. A total of 238 PCIs were identified, ranging from 2 to 5 PCIs per patient. The most common PCIs identified were classified as counselling needs (65), adverse drug reactions (65) and additional medication needs (47).

Conclusion: The developed individualised PCP was intended as a helpful tool for the clinical pharmacist who can update patient pharmaceutical care records according to the PCIs identified whilst at the same time taking into consideration relevant tumour marker trends as well as other laboratory investigations.

References

1. Cipolle RJ, Strand LM, Morely PC. Pharmaceutical Care Practice. USA:McGraw Hill Co;2004.
2. Pharmaceutical Care 2. Network Europe (PCNE) Foundation: PCNE Classification for drug related problems. V6.2. 2010. Available from: http://www.pcne.org/upload/files/11_PCNE_classification_V6-2.pdf

Optimising Patient Self-Medication through the Community Pharmacist

Andrew Fenech

Background: Self-care with 'Over-the-Counter' (OTC) medicines is a widespread practice. Patients consider OTC medicines to be safe and frequently ignore patient information leaflets. This incurs certain risks such as drug interactions, masking of warning symptoms and inappropriate treatment. An innovative concept which addresses this issue is facilitated self-medication, whereby the pharmacist is directly involved by providing advice and care with self-medication products.

Purpose: The aim is to optimise patient safety and pharmacotherapy related to self-medication through the community pharmacist's intervention. The objectives are to investigate quantitatively the nature and frequency of drug-related problems (DRP's) occurring in relation to self-medication and to document the interventions carried out by pharmacist in relation to the identified DRP's.

Method: The approach towards the study was divided into two phases. The first phase consisted of compiling and validating the tool required to run the research. Ethics approval was sought and granted from the University of Malta Research and Ethics Committee (UREC). During the second phase, 203 patients presenting at a community pharmacy asking for OTC medications, who were over 18 years of age and able to understand English and Maltese were included in the study. The pharmacist-researcher recorded data on patient characteristics and the nature of the OTC request. Any identified DRP's were documented, together with the action taken by the pharmacists to resolve the identified DRP's. The time needed for resolving the problem was recorded.

Results: A total of 40 DRPs were detected in 18.71 % of patients presenting with requests for OTC medicines. The most common DRP (32.5%) was 'requested medicine is not optimal for symptoms presented', followed by 'requested medicine is contra-indicated' (27.5%) and 'duplication of medicines' (12.5%). The most frequent intervention (57.50%) was to change to a more suitable drug, followed by referral to a physician (22.5%).

Conclusion: The results from this study highlight the importance of the presence of a pharmacist when dispensing OTC medications, since a DRP was detected in nearly one of five encounters.

Pharmacotherapy in the Treatment of C*lostridium difficile:* Impact on Clinical Practice

Noelia Holgado Sanchez

Background: *Clostridium difficile* is a pathogen accounting for 20-30% of cases of antibiotic-associated diarrhoea and is the most common cause of hospital-acquired diarrhoea. Screening for *C. difficile* is recommended in the presence of diarrhoea and following recent or current antibiotic treatment.

Purpose: To propose a framework for *Clostridium difficile* culturing and antibiotic sensitivity testing in a clinical setting, to identify risk factors for *Clostridium difficile* Infection (CDI), to assess current management of CDI and to provide local epidemiological data.

Method: Approval from the University Research Ethics Committee (UREC) was obtained. Sixteen publications of *C. difficile* culturing and antibiotic sensitivity testing were reviewed and cost estimates for the materials needed to run the tests were gathered. Available data from 2015 was analysed. Medical records from patients completing a signed written informed consent and having the following inclusion criteria were reviewed: over 18 years of age, inpatients at Mater Dei Hospital (MDH) or Sir Anthony Mamo Oncology Hospital after the implementation of the new "Algorithm for *Clostridium difficile* infection investigation and results interpretation in adults" and faecal specimen positive for Glutamate Dehydrogenase antigen (GDH).

Results: A framework for *C. difficile* culturing and antibiotic sensitivity testing in the clinical setting was proposed with a local cost of €116.30 per sample. In 2015, fifty-six samples tested *C. difficile* toxin positive in Malta. In 2016, 111 samples were toxin positive and 184 reported as *C. difficile* carriers. Out of a population of 241 patients, 130 met the inclusion criteria; of which sixty-seven patient medical records were reviewed: 60% were over 65 years old, 84% had a recent antibiotic exposure, 37% were immunosuppressed patients, 60% were on gastric acid suppression treatment and 34% were on tube feeding or underwent recent gastrointestinal surgery. Lack of protocol adherence was detected in 13 cases.

Conclusions: *C. difficile* culturing and antibiotic sensitivity testing stands a feasible alternative in the management of CDI. Incidence of CDI increased in 2016. Gastric acid suppression and recent antibiotic exposure were the most prevalent modifiable risk factors in the studied population. Local CDI management can be improved by increasing adherence to current protocol, assessing the need for gastric acid suppression therapy, selecting appropriate antibiotic treatment and implementing preventive measures among *C. difficile* carriers.

Safer Anticoagulation Management in the Community: A Pharmacist-Led Approach

Elena M Mifsud

Background: Therapeutic monitoring in patients on warfarin is essential to enhance treatment efficacy with less complications. Medicine use review (MUR) enables individualised patient assessment to check and balance drug-related problems (DRPs).

Purpose: To develop and implement a pharmacist-led MUR for patients on warfarin, assess patient's knowledge and adherence and address identified risks with prescribed treatment.

Method: Patients on warfarin were invited to attend a structured clinical session during which baseline information was collected to assess patient's knowledge and adherence to warfarin. Dedicated consultation and point-of-care INR testing with CoaguChek®XS were undertaken. Medication reconciliation was performed to identify DRPs. For each DRP identified, a clinical intervention was recommended. Patients were re-assessed after 2 months to evaluate the impact of pharmacist intervention and degree of implementation of the clinical pharmacist researcher's recommendations by the physician, pharmacist or patient. The Wilcoxon Signed Rank test and chi-square test were used to compare pre- and post- intervention data.

Results: A total of 100 patients (56 male, 44 female; mean age 70.5 years, range 33-89 years) were assessed. Forty patients had an INR value outside their target range. In the warfarin knowledge test, the mean score improved from 7 to 10 out of 12 post-intervention ($p<0.05$). The number of patients who were not adherent to warfarin decreased from 25 to 11 post-intervention ($p<0.05$). A total of 632 medications were reconciled (mean 6 medications/ patient; range 1-16). A total of 481 DRPs (mean 5 DRPs/ patient; range 0-9) were identified, out of which 40% were related to warfarin. Need for monitoring (30%), lack of compliance (20%) and need for patient education (19%) were the top three DRPs identified. Eighty-four percent of the clinical pharmacist researcher's recommendations were accepted, 20% of which resulted in changes to drug treatment. These modifications included 30 medication discontinuations, 21 dose reductions, 17 medication additions and 12 dose increments.

Conclusion: The improvement in patients' knowledge, adherence to warfarin and high proportion of implemented recommendations, suggests that a pharmacist-led MUR has the potential to improve therapeutic outcomes and patient safety. The findings support the introduction of a pharmacist-led MUR service to enhance the clinical role of local community pharmacists to meet patients' needs.

Patient-Centred Monitoring in Chronic Disease Management in the Community Pharmacy

Martina Muscat

Background: Chronic diseases present a number of challenges on healthcare systems worldwide. Community pharmacists are in a unique position to participate in the chronic care of their patients and greater involvement in patient monitoring can improve patients' health outcomes.

Purpose: The aim is to evaluate the impact of a pharmacist-led chronic disease management service within a community pharmacy setting by assessing the pharmacist's intervention on patients' health outcomes and evaluating pharmaceutical care issues.

Method: During Phase 1 of the study, five data collection tools required for the setting up of the study were compiled. Phase 2 of the study consisted of the implementation of the chronic disease management service in a community pharmacy. Following ethics approval, 50 patients taking at least 1 chronic medication were included in the study. Two medication review sessions were held with the patients; an initial session and a follow-up session after 4 months. During these sessions the data collection tools were completed and a pharmaceutical care plan was developed for each patient. Point-of-care testing for blood pressure, blood glucose and HbA1c monitoring as well as lifestyle advice were provided.

Results: Forty-eight patients completed the study; 22 were male and 26 were female, with a mean age of 69 years and taking an average of 5 chronic medications daily. A total of 207 pharmaceutical care issues were identified with a mean of 4.25 issues per patient. The majority of issues involved under-treatment (18.8%), monitoring (18.4%) and compliance (17.9%). Most of the issues were solved (78.6%) or partially solved (16.5%). Throughout the four-month study period, mean systolic blood pressure decreased from 137.4 mmHg to 126.7 mmHg and mean diastolic blood pressure decreased from 81.3 mmHg to 77.4 mmHg. In patients with diabetes (n=28), mean HbA1c decreased from 7.48% to 6.97%.

Conclusion: The pharmacist-led chronic disease management service was successful in improving the patients' health outcomes by achieving better control of blood pressure and blood glucose and improving compliance towards medication. The majority of pharmaceutical care issues were resolved and patients were satisfied with the service provided.

Detecting Signals of Electrocardiogram *QT prolongation* and *QT shortening* from Pre- and Post-Authorisation data: Regulatory Implications

Amy Tanti

Background: Medicines on the market may have uncharacterized risks on the QT interval within their Product Information (PI). Knowing the risk of QT change is highly relevant as concomitant administration of such products has additive negative effects in patients at risk and can lead to life-threatening cardiac arrhythmias.

Purpose: To detect and characterize the QT change liability of authorised medicinal products by reviewing data from pre and postmarketing settings in the form of preclinical/ animal toxicological studies, Adverse Drug Reaction (ADR) reports, literature review and clinical trial data.

Method: Statistical associations between drugs and QT change were inferred through Proportional Reporting Ratios. For statistically associated drugs, expectedness was checked through review of the PI and a list was created for the frequency of expectedness (study 1). Drugs not expected to cause QT changes were evaluated within the Bradford-Hill criteria for association (study 2).

Results: Four hundred and four medicinal products had signal hits for QT prolongation (QTp) and 13 for QT shortening (QTs). Due to restrictions in data accessibility and time, only centrally authorized products were included in the study (63/404 for QTp and 2/13 for QTs). Of the 63 products with a signal for QTp, 13 were excluded due to withdrawal from EU market or lack of data. Of the remaining 50, 32 were expected to cause QTp. Vandetanib and other antineoplastics had the highest known frequency of occurrence of QTp (study 1). Eighteen products did not have QTp as a listed effect in the PI and were carried forward to study 2. After full assessment, changes to the PI of mirabegron, asenapine and pantoprazole were found to warrant consideration. Signals on QTp were confirmed for mirabegron and asenapine, and sent to the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC). For pantoprazole, an emergent signal of hypokalaemia was identified and may warrant further investigation. For QTs 2 out of 13 drug signals were fully assessed (fingolimod and olanzapine). There were no findings in relation to QTs and no changes to the PI are recommended for fingolimod and olanzapine.

Conclusion: Mirabegron and asenapine carry risks of QTp which may warrant inclusion in their product information. An emergent signal for hypokalemia with pantoprazole should be examined further.

Creating Shared Care Guidelines for Breast and Colon Cancer

Rebecca Theuma

Background: With the development of oral chemotherapy, the contribution of community pharmacists in supporting patients to handle medicines used in the management of cancer conditions became very relevant. These medications may come with novel side effect profiles, narrow therapeutic index together with psychological aspects that may compromise adherence.

Purpose: The aim of this research is to compile shared care guidelines for oral chemotherapy used in the management of breast and colon cancer taking into consideration the role of the community pharmacists who are involved in dispensing these medications and supporting the patient with the use of these drugs.

Method: Five shared care guidelines were created for: capecitabine, everolimus, abiraterone, enzalutamide and ruxolitinib. The developed documents were validated by a panel of experts consisting of: 4 oncologists, a principal and senior pharmacist within the compounding section at Mater Dei Hospital, and a senior pharmacist at Sir Anthony Mamo Oncology Centre. The shared care guidelines were presented to community pharmacists during an educational program about managing chemotherapy side effects. Scored questionnaires were handed out to the pharmacists before and after the program to determine if there was an improvement in responses.

Results: The validation panel reported on the content validity of the shared care guidelines developed**.** An initial educational program was carried out for 11 pharmacists and the mean response rate before the educational program was 5.45 % whilst the mean response rate after the program was 80%.

Conclusion: The shared care guidelines developed within a collaborative framework are intended to further substantiate effective communication between different healthcare professionals at different settings such as the hospital multidisciplinary team and the community pharmacists dispensing oral chemotherapy drugs.

Serum Digoxin Determinations: Clinical Signals

John Vella

Background: Digoxin as a treatment option in cardiology is limited by its narrow therapeutic index. Digoxin use in Malta is not protocol-regulated and may pose efficacy and safety risks to the patient. Current clinical guidelines recommend targeting a serum digoxin concentration (SDC) between 0.5 and 1.0 ng/ml.

Purpose: To analyse SDCs recorded at Mater Dei Hospital (MDH), determine compliance to the clinically recommended SDC target and assess queries concerning digoxin processed by the Drug Information Unit (DIU) at MDH.

Method: All SDCs recorded at the MDH Pathology Laboratory over an eight-year period (January 2008 to February 2016) were analysed. Patient variables selected for inclusion in the analyses were gender, age, reason for testing, origin of request, referring physician and number of tests requested. Incomplete records were excluded. A list of all enquiries processed between April 2002 and September 2014 was obtained from the DIU. Enquiries concerning digoxin were extracted and classified according to the reason for the query. The JASP software package version 0.7.5.6 was used to generate descriptive statistics.

Results: A total of 16,333 valid SDCs from 5,549 patients (60% female, 40% male; mean age 78 years, range 1-111 years) were analysed. Mean number of SDCs per patient was 3 (mode 1, range 1-47). Mean SDC was 1.28 ng/ml (range <0.1-2.0 ng/ml). Variations from the clinically recommended target SDC (0.5-1.0 ng/ml) were: 31% within, 19% below and 50% (15% > 2.0 ng/ml) above. The majority of SDC requests originated from MDH (86%), 44% of which from the Accident and Emergency Department (mean SDC 1.14 ng/ml; range <0.1-11ng/ml). Out of a total of 14,369 reviews processed by the DIU in the thirteen-year period assessed, 91 (0.6%) enquiries concerned digoxin. The top three enquiries were related to administration (26%), interactions (15%) and dosing (15%).

Conclusion: The mean SDC of 1.28 ng/ml is higher than the current clinically recommended target SDC. The number of queries regarding digoxin is low (0.6%) compared to the number of out-of-range SDCs (69%), indicating the need for the DIU to disseminate its services. Further investigation to establish the clinical significance of these signals and their potential impact on patient health outcomes is warranted.

M.Pharm. Students
Dissertation Abstracts

Pharmaceutical Care

Pharmacist Intervention in Improving Compliance in Patients with Heart Failure
Rebecca Bugeja

Improving Monitoring of Rheumatology Patients Across Transitional Care Settings
Jonathan Vella

Development and Evaluation of Shared Paediatric Pharmaceutical Care Plans in Rheumatoid Arthritis
Julian Frederick John Fearne

Development of Rheumatology Shared Care Guidelines: Improving Transitional Care
Daniel Joseph Grixti

Pharmacist Intervention in Improving Compliance in Patients with Heart Failure

Rebecca Bugeja

Background: Factors pertaining to patient-related issues, such as medication non-adherence, are a major cause of exacerbations of heart failure leading to higher rates of hospitalisation worldwide.

Objectives: To assess medication adherence in patients with heart failure at a community pharmacy level.

Design: Heart failure patients who obtained their medications through the Pharmacy-Of-Your-Choice scheme in the selected pharmacies and who accepted to participate were met by the researcher. Following consent, each patient was given the validated eight-item Morisky Medication Adherence Scale (MMAS-8) questionnaire.[1] The MMAS-8 measures the level of adherence of each patient by assigning scores as follows 0 = high adherence, 1 – 2 = medium adherence and 3 -8 = low adherence. The medical history and current treatment of each patient was also reviewed.

Setting: Five community pharmacies in different districts in Malta.

Main Outcome Measures: Adherence to treatment and medication use

Results: A total of 25 patients were recruited from the pharmacies; 13 were female and 12 were male. The mean age was 72 years (range 34-87 years). The mean number of daily medications was 7, ranging from 4 to 12 daily medications. Out of 25 patients, 6 scored low adherence, 10 scored medium adherence and 9 scored high adherence.

Conclusion: It is evident that the majority of heart failure patients taking part in the study are not compliant to their treatment. This highlights the need for more patient education.

Reference:

1. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens 2008; 10(5): 348–354.

Improving Monitoring of Rheumatology Patients Across Transitional Care Settings

Jonathan Vella

Background: Regular and efficient monitoring of patients on methotrexate is essential to ensure patient safety and drug efficacy.

Objectives: To develop a tool which documents effective and safe monitoring of patients as they move across transitional care settings and to assess patient compliance towards monitoring and treatment.

Design: Methotrexate monitoring booklets available internationally were evaluated in order to design a template. The compiled Methotrexate Monitoring Booklet (MMB) was validated by an expert panel. A questionnaire, entitled 'Patient compliance to laboratory blood tests' (PCLBT) was developed to assess patients' compliance towards blood investigations in relation to methotrexate. The same expert panel validated the questionnaire. The medication adherence questionnaire developed and validated in previous studies entitled Medication Compliance (MC)[1] was used to assess compliance to treatment. Both questionnaires were distributed to eligible patients agreeing to participate in the study. The patients were then given the validated MMB.

Setting: Rheumatology clinic at Mater Dei Hospital

Main Outcome Measures: Developed MMB

Results: The first draft of the booklet was amended to focus on monitoring needs and highlight the importance of patient adherence. The design was enhanced so as to make it more patient friendly.

Conclusion: Patients are advised to present the MMB when they need prescriptions from their general practitioner and when collecting their medications from the pharmacy. Through this booklet, the community pharmacist can confirm the dose prescribed and ensure that regular laboratory monitoring is being carried out.

Reference:

1. Zammit L. Compliance Issues in Hypertensive Care [project]. Msida (Malta): University of Malta; 2005.

Development and Evaluation of Shared Paediatric Pharmaceutical Care Plans in Rheumatoid Arthritis

Julian Frederick John Fearne

Background: An individualised pharmaceutical care plan documentation template is currently in use at the Rheumatology Clinic at Mater Dei Hospital. This template limits sharing of pharmaceutical care needs to the hospital setting only.

Objectives: To review the paediatric pharmaceutical care template to improve seamless care between pharmacists across different care settings.

Design: Literature review was carried out to identify the most appropriate template to use. Discussion with an expert panel was held to identify which sections of the current pharmaceutical care plan template required updating to facilitate communication and sharing of identified care needs. For each of the three identified sections, a revision and amendment process was carried out. Format and page structure were also discussed. A validation questionnaire was distributed to the expert panel. Following this primary validation, the finalised care plan was implemented in the monthly paediatric rheumatology outpatient clinic.

Setting: Paediatric Rheumatology Clinic, Mater Dei Hospital

Main Outcome Measures: Likert scale model for the usefulness, practicality and utility of the pharmaceutical care template was applied for both the community and hospital setting.

Results: Following the validation, the first draft of the pharmaceutical care plan was revised to be more patient-friendly. Questionnaire results indicate that all patients recognised the importance and usefulness of the new template to their overall health situation.

Conclusion: Following the initial success with the care plan, patients were advised to keep the new pharmaceutical care plan and present it when collecting their medications from their community pharmacy. The developed care plan can support the community pharmacist to better ensure the dispensing of appropriate medication, including the correct dosage regimen, ensuring seamless care between primary and secondary care settings.

Development of Shared Care Guidelines in Rheumatology: Improving Transitional Care

Daniel Joseph Grixti

Background: Shared care guidelines (SCGs) assist healthcare professionals and patients in clinical decision-making while ensuring safety and continuity of care during transition of patients between primary and secondary care settings.

Objectives: To develop SCGs for rheumatology drugs taking into account the role of the community pharmacist.

Design: SCGs and monitoring guidelines published by various NHS branches and associated hospital Trusts in the UK, Summary of Product Characteristics and the Interface Pharmacist Network Specialist were used to compile the Maltese Rheumatology Shared Care Guideline (MRSCGs) for infliximab, methotrexate, azathioprine and hydroxychloroquine.

Setting: Community Pharmacies and Mater Dei Hospital

Main Outcome Measures: Development and evaluation of MRSCGs in rheumatology.

Results: The MRSCGs consist of 3 sections. Section A outlines pharmacological background, indications, drug administration and dosage regimen. Section B defines (i) the responsibilities of the clinical rheumatology team (consultant, higher specialist trainee, clinical pharmacist, and nurse), general practitioner, community pharmacist, and patient (ii) Shared Care Details sheet to address communication issues between healthcare settings. Section C includes appendices for clinical particulars; monitoring worksheets; Shared Care request form, acceptance letter by physicians to participate in Shared Care, and Pharmaceutical Care Documentation Sheet. All members of the expert panel (n=10) agreed that the community pharmacist dispensing the medications is part of the extended healthcare team with whom communication should be improved.

Conclusion: Patient safety can be compromised when patients move across healthcare settings. The compiled MRSCGs enhance communication between healthcare professionals resulting in improved pharmaceutical care.

Pharmacy Information, Pharmacy Administration and Regulatory Affairs

Development of a Self-evaluation Validation Process for Community Pharmacy
Hannah Flynn

Challenges facing Regulatory Science in Medical Devices
Jasmine Marie Gauci

Strategic Analysis for Sustainable Pharmaceutical Procurement
Caroline Muscat

Student Perception of the Pharmacy Practice Resource Unit
Francesco Cassar

Development of a Self-evaluation Validation Process for Community Pharmacy

Hannah Flynn

Background: Community pharmacists interact with other healthcare professionals in recommending pharmacotherapy and drug therapy. The Validation Method for Community Pharmacy (VMCP) helps to demonstrate the effectiveness of the pharmacist in the community.[1,2]

Objectives: To monitor the standards of services provided by community pharmacists using the VMCP, to measure the impact of the pharmacist on patient care and to measure how effective the pharmacist is in the community.

Design: The internal and external validation tools adopted from Azzopardi[1] and Scicluna[2] were updated. A focus group, consisting of 4 physicians, 4 other health care professionals and 2 lay people revised the updates using the Delphi Method. A self-administered questionnaire was disseminated electronically to 100 community pharmacies selected by random sampling to assess pharmacist feedback regarding the validation tools.

Setting: Community Pharmacies

Main Outcome Measures: Suggestions recommended by the focus group following the updating of the current tools available; pharmacist feedback on the validation process

Results: The members of the focus group believed that the study was constructive. They agreed with the updates carried out and on the strict legislation that is enforced with respect to the dispensing of dangerous drugs since this limits abuse. A response rate of 33% was achieved for the questionnaire. Sixteen of the respondents were in favour of having the validation process completed regularly by community pharmacists as part of the community service.

Conclusion: Through this study, the validation process was reviewed and key sections such as 'Dispensing of Prescriptions' and 'Point of Care Testing' were added. The results indicate the importance of this self-evaluation process, since 45% of the respondents were in favour of this being carried out regularly.

References:

1. Azzopardi LM. Validation Instruments for Community Pharmacy: Pharmaceutical Care for the Third Millenium. Pharmaceutical Products Press: USA; 2000.
2. Scicluna C. Azzopardi LM, Serracino-Inglott A. Validation Instruments for Community Pharmacy: An Update. Lambert: Germany; 2012.

Challenges Facing Regulatory Science in Medical Devices

Jasmine Marie Gauci

Background: Medical devices play a central role in the management of diseases for a wide range of conditions. In recent years, medical device regulations have evolved as a result of the advancement in technology and the increasing awareness for a more consistent and transparent approach to regulatory documentation.

Objectives: To understand the current regulatory system for medical devices in Malta and to determine whether it would be feasible to establish a medical device notified body system locally.

Design: Qualitative research in the form of semi-structured interviews was conducted to study the medical device regulatory system in Malta. Purposive sampling together with chain referral sampling were adopted for this study. The interviews were carried out with the directors and employees of the Malta Competition and Consumer Affairs Authority (MCCAA) and the Central Procurement and Supplies Unit (CPSU).

Setting: Medical Device Stakeholders, CPSU and MCCAA

Main Outcome Measures: Identification of challenging issues faced by stakeholders in the medical device industry

Results: A notified body system has not been established in the local scenario. The process of ensuring safety and performance of medical devices should be clearly understood by all stakeholders. Each stakeholder should contribute to the mutual understanding of pertinent issues and accept the responsibility of being actively involved in on-going discussions and shared education that support best practices. Current policies and regulations should be continuously reviewed and implemented in order to be in line with technology while safeguarding the patient.

Conclusion: Medical devices must meet the primary objectives of safety, quality and efficacy. These characteristics should be achieved in view of enhancing their international and regional trade and competitiveness. A more effective notification and enforcement system will encourage the cost-effective availability of appropriately certified medical devices in Malta.

Strategic Analysis for Sustainable Pharmaceutical Procurement

Caroline Muscat

Background: An effective procurement process ensures the availability of the right drugs in the right quantities, available at the right time, for the right patient at reasonable prices and at recognisable standards of quality.[1]

Objectives: To assess the challenges encountered when purchasing medicine within the Maltese procurement system and to develop and evaluate a practical framework relevant to address the current needs which takes into account sustainability.

Design: This exploratory study follows an inductive approach through case study research of purchasing practices within the Maltese pharmaceutical procurement system. Triangulation is used and qualitative data is collected from focus groups, observational sessions and document analysis.

Setting: Central Procurement and Supplies Unit (CPSU).

Main Outcome Measures: Proposals on solutions to address current limitations encountered at the CPSU.

Results: Sourcing is a prominent issue in the pharmaceutical procurement process at CPSU. The formulary presents challenges such as inflexibility to current requirements and requires rationalisation to promote easy access to cost-effective medicines in demand. The demographic position of Malta and the language are both barriers to effective sourcing and accessibility of pharmaceuticals. Transport of medicines is time-consuming and expensive, while the language incurs re-labelling and re-packaging issues that increase costs. Greater awareness on the use of generic and biosimilar drugs increases competition and controls healthcare costs.

Conclusion: A dynamic and practical framework for the Maltese procurement system is formulated. This adds value to the procurement and supply chain of medicines and promotes sustainability.

Reference:

1. Ombaka E. Current status of medicines procurement. AJHP. 2009; 66(5): Suppl 3: s20-s28.

Student Perception of the Pharmacy Practice Resource Unit

Francesco Cassar

Background: The Pharmacy Practice Resource Unit (PPRU) is a research facility located in the Department of Pharmacy at the University of Malta, consisting of a mock pharmacy and drug research resources.

Objectives: To update the PPRU and evaluate student use and perception of the unit.

Design: An initial questionnaire was sent to all pharmacy students at the start of the study to assess student knowledge and perception of the PPRU. The PPRU was updated by collecting new medicinal products from medical representatives and community pharmacies. The PPRU was opened for students to visit and use the resources available and an evaluation questionnaire was disseminated to those who attended. Statistical analysis was carried out using IBM SPSS version 23. The chi-square test was used to compare variables, whilst the Friedman test was used to compare the mean results given to related statements.

Setting: Pharmacy Practice Resource Unit, Department of Pharmacy, University of Malta

Main Outcome Measure: Update and evaluation of the PPRU

Results: Three hundred and three new products were added to the displays in the PPRU. Seventy students responded to the initial questionnaire, of whom 98.5% knew the exact location of the PPRU. However the main reported use of the unit was for routine pharmacy practice tutorials. Forty-eight students visited the PPRU and completed the evaluation questionnaire, of whom 97.9% agreed that the unit should be opened regularly and 91.7% said that they would visit the PPRU again, mostly because they can view the actual medications in their packaging.

Conclusion: From the study, it transpires that most students are knowledgeable about the PPRU and would like the unit to be continually updated and available for use. The results obtained are very similar to those obtained in a previous study by Azzopardi.[1]

Reference:

1. Azzopardi J. Evaluation of the Pharmacy Practice Resource Unit [project]. Msida (Malta): Department of Pharmacy, University of Malta; 2012.

Medicinal Chemistry I

Compilation, Validation and Evaluation of a 2D/3D Molecular Database as an adjunct to Didactic Teaching Modalities
Gabriella Sultana

Design and Optimisation of Novel Efflux Pump Inhibitors using P-glycoprotein as a Target
Mark Joseph Bondin

Design and Optimisation of RAS Inhibitors using the Polyphenolic Extracts of Green Tea as a Scaffold
Stephanie Cassar

Design and Optimisation of K-Ras protein Inhibitors as Anticancer Agents using Deltarasin as a Case Study
Martina Woods

Design and Optimisation of Novel Antibacterial Compounds using Allicin as a Lead Molecule
Nathaniel Refalo

Drug Design and Optimisation of Adenosine A2A Receptor Modulators using Caffeine and Limonene as Lead Molecules
Danica Micallef

Compilation, Validation and Evaluation of a 2D/3D Molecular Database as an Adjunct to Didactic Teaching Modalities

Gabriella Sultana

Background: Medicinal chemistry is based on abstract concepts requiring considerable effort for undergraduates to comprehend.[1] Studies have shown that students improve their comprehension of the subject by handling computer graphics as adjuncts to traditional lectures.[2]

Objectives: To construct two- and three-dimensional (2D/3D) molecular databases for drugs related to infections, musculoskeletal disorders and endocrine disorders in the British National Formulary (BNF)

Design: Drugs included in the study were selected with reference to the BNF. Datasheets for each relevant chapter were created which included drug name, indications, therapeutic class and physicochemical properties. 2D and 3D models were created. 3D representations of the molecules interacting with their cognate receptors were generated. Accelrys Draw and ACD/3D Viewer were used for 2D/3D models. RCSB PDB sourced graphical information for OCA Browser and VMD.

Setting: Computational tools with use evaluation in the classroom scenario

Main Outcome Measures: 2D/3D molecular databases were prepared and presented on a CD.

Results: The infection chapter datasheet features 135 molecules, the musculoskeletal disorders datasheet includes 38 molecules and the endocrine disorders datasheet features 63 molecules. These all had corresponding 2D and 3D molecular models created. Graphical representations were modelled for 58, 9 and 20 molecules respectively.

Conclusion: All data and visual adjuncts are compiled within a user-friendly CD to be evaluated for utility.

References:

1. Wu C, Foos J. Making chemistry fun to learn. Lit Inf Comput Educ J. 2010;1(1):3-7.
2. Carvalho L, Borges ADL, Bernardes LSC. Medicinal Chemistry and molecular modeling: An integration to teach drug structure-activity relationship and the molecular basis of drug action. J Chem Educ 2005;82(4):588

Design and Optimisation of Novel Efflux Pump Inhibitors using P-glycoprotein as a Target

Mark Joseph Bondin

Background: Literature reports verapamil, an antiarrhythmic drug, to inhibit P-glycoprotein which is overexpressed in tumours, resulting in reduced resistance to chemotherapy.[1]

Objectives: To use verapamil as a lead molecule for further iterative design of novel P-glycoprotein inhibitors in an attempt to enhance binding potential

Design: The Protein Data Bank crystallographic deposition 4M2S, describing the bound coordinates of QZ59 RRR with P-glycoprotein was selected as a template. Structure activity relationships present between QZ59 RRR and P-glycoprotein were analysed from literature. Sybyl X v1.1 was used to generate R and S enantiomers for verapamil and to extract the QZ59 RRR to generate the apo P-glycoprotein. Both P-glycoprotein and verapamil were imported into X Score v1.3 to establish baseline affinity. Five seeds were generated with Sybyl X v1.1, from which *de novo* molecules were generated using LigBuilder v1.2. Molecules were divided into families, each having different pharmacophores. Molecules were filtered with Lipinski rules criteria for further analysis. Virtual screening was conducted on 2 enantiomeric forms of verapamil to elucidate molecules with similar physicochemical properties.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular display, modelling, seed generation, Ligand Binding Energy calculation.

Results: A total of 107 Lipinski Rule compliant molecules were generated.

Conclusion: Some *de novo* molecules display a greater pKd than the baseline value of 5.11. Such molecules are useful candidates for further studies for alternatives of verapamil.

Reference:

1. Aller SG, Yu J, Ward A, Weng Y, Chittaboina S, Zhuo R et al. Structure of P-glycoprotein reveals a molecular basis for poly-specific drug binding. Science. 2009; 323(5922): 1718–22.

Design and Optimisation of RAS Inhibitors using the Polyphenolic Extracts of Green Tea as a Scaffold

Stephanie Cassar

Background: K-Ras proteins are important in the mediation of extracellular signals. Mutation of K-Ras results in the constant induction of proliferation of the cell, which is thought to be responsible for the pathogenesis of tumours. One of the most common oncogenic variants is the K-Ras G12C.[1]

Objectives: To selectively inhibit K-Ras G12C using the green tea extract, epigallocatechin-3-gallate (EGCG), to hinder constant proliferation and prevent tumour growth

Design: An X-Ray crystallographic model of an irreversibly bound SML-8-73-1 was acquired from the Protein Data Bank and separated using SYBYL-X v1.1. Several conformers of EGCG were created and a graph was plotted displaying Ligand Binding Affinity (LBA) against Ligand Binding Energy (LBE). Several seed structures were created based on the optimum conformer identified to be further developed using LigBuilder.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Design and optimisation of novel K-Ras inhibitors

Results: Twenty conformers were generated and conformational analysis was carried out. The LBA was compared to the LBE for each conformer and conformer 1 was selected since it showed highest potential. Eighteen seed structures were generated from conformer 1 for further analysis.

Conclusion: Potential *de novo* structures and molecules identified from virtual screening are segregated. These molecules are selected based on their compliance to Lipinski's Rule of Five[2] inferring oral bioavailability. A second approach is used whereby the similarity suite in SYBYL-X v1.1 will identify structurally-related molecules to the template SML-8-73-1, based on the assumption that structurally related compounds yield a similar affinity.

References:

1. Bos JL. Ras oncogenes in human cancer: A review. Cancer Research 1989;49(17):4682-4689.
2. Keller TH, Pichota A, Yin Z. A practical view of 'druggability'. Curr Opin Chem Biol. 2006;10(4):357–361.

Design and Optimisation of K-Ras protein Inhibitors as Anticancer Agents using Deltarasin as a Case Study

Martina Woods

Background: K-Ras serves as an important component of signalling pathways involved in cell cycle control. Proper functioning of K-Ras is regulated by phosphodiesteraseδ (PDEδ). Deltarasin binds to this prenyl-binding protein thus inhibiting its interaction with K-Ras, hence disrupting Ras signalling.[1]

Objective: To use deltarasin as a template for further iteration of the design of novel drugs with potential clinical use in the management of malignancies.

Design: Deltarasin was constructed using SYBYL-X V1.2, followed by analysis of the critical interactions between deltarasin and the amino acids lining the ligand binding pocket (LBP). Seeds were modelled based on the deltarasin scaffold and virtual screening (VS) was used to identify 'hits' using the same molecule as a template. SYBYL-X, X-SCORE, LigBuilder, Visual Molecular Dynamics (VMD), Accelrys Draw, Accelrys Discovery Studio 3.5, Protein Data Bank and ZINCPharmer were all used to generate results.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display, ligand binding affinity (LBA) and ligand binding energy (LBE) calculations, seed generation, *de novo* design

Results: Based on reviewed Structure Activity Relationship studies, nine seeds were generated using SYBYL-X V1.2. The POCKET and GROW algorithm of LigBuilder V1.2 are used to generate *in silico* molecules for each seed. Surflex-docking in SYBYL-X V1.2 resulted in five molecules with a total docking score of six or greater.

Conclusion: The *de novo* molecules created and optimised present viable leads for high-throughput screening, leading to identification of novel PDEδ inhibitors for use as anti-cancer agents.

Reference:

1. Collins M, Pasca di Magliano M. Kras as a key oncogene and therapeutic target in pancreatic cancer. Front. Physiol. 2014;4:1-8.

Design and Optimisation of Novel Antibacterial Compounds using Allicin as a Lead Molecule

Nathaniel Refalo

Background: Antibacterial resistance is an escalating threat to modern healthcare. Allicin is a garlic constituent with proven antibacterial effects and is therefore suitable as a lead for novel antibacterial development.[1]

Objectives: To develop ligands with a multiple mode of action against the bacterial alcohol dehydrogenase, RNA polymerase and thioredoxin reductase enzymes. These ligands would have two novel modes of action and also hinder development of antibacterial resistance.

Design: Protein data bank (PDB) entries 1LLU, 4KN4 and 2A87 were obtained. The allicin molecule was drawn and docked in each enzyme. The three best allicin conformers in terms of high ligand binding affinity (LBA) and low ligand binding energy (LBE) were derived and submitted for virtual screening (VS). Structure-based design was then used to create seed structures which were used for *de novo* ligand generation. The mean LBA of the resulting ligands for the enzymes was calculated. Another approach used VS to generate a separate ligand library using a consensus pharmacophore derived from the enzymes.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display and modelling, LBA calculation, LBE calculation, ligand generation.

Results: Six hundred Lipinski rule-compliant ligands were generated using LigBuilder and screened for mean LBA to the enzymes (3.21-10.54 pKd). A total of 155 hits were obtained from consensus pharmacophore screening (Mean LBA -0.36-7.48 pKd).

Conclusion: The ligands derived have a significantly high simultaneous affinity to the enzymes and are suitable for molecule dynamics validation and *in vitro* testing.

Reference:

1. Ankri S, Mirelman D. Antimicrobial properties of allicin from garlic. Microbes Infect. 1999;1(2) 125-129.

Drug Design and Optimisation of Adenosine A2A Receptor Modulators using Caffeine and Limonene as Lead Molecules

Danica Micallef

Background: The adenosine A2A receptor has been associated with possible management of various pathophysiological processes. Literature indicates that two naturally occurring compounds, specifically caffeine and limonene, can successfully modulate this receptor. Caffeine is a non-selective antagonist, while limonene was shown to be a selective agonist.[1]

Objectives: To use the caffeine and limonene molecules as scaffolds to rationally design molecules of *in silico* proven affinity for the adenosine A2A ligand binding pocket and *in vivo* bioavailability.

Design: Protein Data Bank crystallographic depositions 2YDO and 3RFM describing the A2A:Adenosine and A2A:Caffeine complex respectively were used as templates. Ligand binding affinity (LBA) was measured for each ligand. Conformational analysis yielded 3 best conformers. The best conformers were used to screen for similar molecules which were used in a docking run to obtain their docking scores. - The optimal conformers were then used to create seeds capable of sustaining molecular growth within the A2A ligand binding pocket.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular visualisation, modelling, LBA calculation, docking run, seed generation

Results: Method 1 - The 4 highest ranking binders for each lead molecule were considered to have superior affinity and were chosen for further investigation. Method 2 – Lipinski-rule compliant molecules generated from the seeds were segregated into families and ranked according to binding affinity. The highest ranking molecules were identified.

Conclusion: The highest ranking molecules with a pKd value greater than the baseline values of the lead molecules were the candidates chosen for further *in silico* drug design.

Reference:

1. Park HM, Lee JH, Yaoyao J, Jun HJ, and, Lee SJ. Limonene, a natural cyclic terpene, is an agonistic ligand for adenosine A2A receptors. Biochemical and Biophysical Research Communications. 2011; 404(1): 345–348.

Medicinal Chemistry II

Design and Optimisation of Novel Structures with Potential Anti-tumorigenic Activity using the Experimental Drug NPI-0052 as a Lead Molecule
Daniel Chetcuti

Evaluation of the affinity of the small Molecule Maltanedienol for Farnesyl Pyrophosphate Synthase and the Design of Novel Structures based on its Scaffold
Andy Vince Falzon

Design and Optimisation of Histone Deacetylase Inhibitors as Anticancer Agents using Diallyl Disulphide as a Case Study
Matthew Zarb

Design and Optimisation of Novel Structures with Potential Anti-tumorigenic Activity using the Experimental Drug NPI-0052 as a Lead Molecule

Daniel Chetcuti

Background: The experimental drug NPI-0052 is a small molecule isolated from the marine organism *Salinispora tropica* which functions as a potent and selective inhibitor of the 20S proteasome. The proteasome complex is composed of a 20S catalytic core and two 19S regulatory subunits. Its function is to regulate the degradation of unwanted proteins.[1]

Objectives: To use NPI-0052 as a scaffold for the design of novel structures capable of inhibiting the β5 subunit of the human 20S proteasome.

Design: The crystallographic depositions 2FAK depicting NPI-0052 bound to the yeast 20S proteasome and 4R67, describing carfilzomib bound to the human 20S proteasome were obtained from the Protein Data Bank. NPI-0052 was extracted and docked into the apo human 20S proteasome. Conformational analysis was performed and the best conformer was chosen based on Ligand Binding Affinity (LBA) and Ligand Binding Energy (LBE). Three seeds were constructed in SYBYL-X using data obtained from 2D topology maps generated by Poseview and Structure Activity Relationship from literature. *De novo* growth was sustained with the aid of LigBuilder v1.2.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular display, molecular modelling, LBA and LBE calculations, seed generation.

Results: A total of 18,168 novel structures were generated from 3 seeds (n=413, n=7544 and n=10,211 respectively). A total of 314 structures were found to be Lipinski rule compliant to be used for further study.
Conclusion: A number of novel structures show potential for further investigation. These structures can be used in future studies and can be compiled into a library for high-throughput screening and further optimisation.

Reference:
1. Chauhan D, Hideshima T, Anderson KC. A novel proteasome inhibitor NPI-0052 as an anticancer therapy. Br J Cancer. 2006; 95(8): 961-965.

Evaluation of the Affinity of the Small Molecule Maltanedienol for Farnesyl Pyrophosphate Synthase and Design of Novel Structures based on its Scaffold

Andy-Vince Falzon

Background: The farnesyl pyrophosphate synthase (FPPS) receptor is the biological target for bisphosphonates, whose ability to stimulate positive bone turnover through calcium deposition is well established.[1] The receptor was consequently chosen as a potential target for maltanedienol.

Objectives: To use *in silico* techniques to understand and compare the critical interactions forged between zoledronic acid and maltanedienol with the FPPS receptor. In the eventuality of a positive outcome, the optimally binding maltanedienol scaffold is used as a lead molecule for the design of novel FPPS modulators.

Design: The X-ray Crystallographic model of zoledronic acid complexed to FPPS was identified from the Protein Data Bank (PDB ID: 2F9K)[2] This was followed by analysis of the ligand-binding pocket and *in silico* design of novel molecules capable of modulating the FPPS receptor. Sybyl-X, X-SCORE, LigBuilder, Accelrys Draw, Discovery Studio, ViCi and ZINC were used to generate results.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display, modelling, Ligand Binding Affinity calculation

Results: The optimal pose of maltanedienol identified was used as a basis to generate a protomol within the FPPS, which could be used to screen molecules from ViCi and ZINCPharmer exhibiting structural similarity to maltanedienol and are Lipinski Rule compliant.

Conclusion: Viable leads identified through virtual screening and molecules generated from the optimal conformer of maltanedienol will be used in subsequent drug-design studies, leading to the identification of novel FPPS receptor modulators for the use in the management of osteoporosis.

References:
1. Okazaki M, Pentecost A, Tanaka Y, Miyata M. A study of calcium carbonate deposition in the genus *Padina* (Phaephyceae, Dictyotales). British Phycological Journal 1986; 21(2):217-224.
2. Rondeau, JM, Bitsch, F, Bourgier E, Geiser M, Hemmig R, Kroemer M, et al. Structural Basis for the Exceptional *in vivo* Efficacy of Bisphosphonate Drugs. ChemMedChem 2006, 1 (2): 267–273.

Design and Optimisation of Histone Deacetylase Inhibitors as Anti-Cancer Agents using Diallyl Disulfide as a Case Study

Matthew Zarb

Background: Diallyl disulfide (DADS), a major lipophilic organic sulphur-compound derived from garlic, can decrease carcinogen-induced cancers in experimental animals and inhibit the proliferation of various types of cancer cells.[1]

Objectives: To generate chemical entities which allow the growth function of additional moieties through the use of software (seeds), by using the proven inhibitory properties of vorinostat on histone deacetylase 8, as a template on which the possible anti-cancer properties of DADS may be improved.

Design: Protein Data Bank file 4QA0 depicted the bound coordinates of histone deacetylase 8 with vorinostat (SAHA). SAHA was extracted and used as a template to generate a series of DADS conformers. A conformational analysis determined the optimum candidate for the generation of seeds based on its favourable low binding energy and high Ligand Binding Affinity (LBA) at the receptor site. The seeds were allowed to grow within the confines of the mapped ligand binding pocket (LBP), which was previously generated. This resulted in a series of novel structures which exhibited improved binding affinities. Software used: Sybyl-X, X-Score, MONA, Poseview, Visual Molecular Dynamics, LigBuilder and Accelrys Draw 4.2.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Drawing of software-generated 2D structures, LBA calculations, LBP elucidation and *de novo* design

Results: The LBA of SAHA was used as a baseline measure against which the DADS conformers were *compared*. The LBAs of these conformers ranged from 3.70 to 4.05. The generation of *de novo* structures from seed molecules planted inside the binding pocket exhibited an improved range of binding affinities.

Conclusion: The generation of *de novo* structures exhibiting improved binding affinities indicates that these candidates may be useful in treating certain cancers whilst simultaneously presenting less toxic side-effects than conventional treatment. This however may not necessarily correlate to results obtained *in vitro*.

Reference:

1. Yi L. Su Q. Molecular mechanisms for the anti-cancer effects of diallyl disulfide. Food Chem Toxicol. 2013;57:362-70.

M.Sc. Pharmacy
Dissertation Descriptions

Synthetic Drugs: The Latest Development in the War against Drugs
Kristina Barbara

Insulin Pump Therapy: A Pharmacoeconomic Analysis
Mariella Mercieca

Analysis of Heavy Metal Content in Conventional and Herbal Toothpaste available at Maltese Pharmacies
Andrew Vella

Consumption of Heavy Metals and Hydroxymethylfurfural (HMF): Analysis of Infant Foods and Formulae
Christian Vella

Risk Management in the Manufacture of Solid Oral Dosage Forms
Mark Sean Zammit

Synthetic Drugs: The Latest Development in the War against Drugs
Kristina Barbara

Synthetic drugs mimicking the narcotic effects of controlled substances of abuse are being marketed under different brand names and indications to avoid importation controls. This research aims to categorise such products according to their narcotic effects so that they can be quickly classified as illegal and stopped before reaching the local market. Local and foreign experiences on the marketing and control of synthetic drugs and legislation are thoroughly reviewed and the view and advice of different stakeholders are sought.

Insulin Pump Therapy: A Pharmacoeconomic Analysis
Mariella Mercieca

Insulin pump therapy is a method of administering short-acting insulin through a catheter placed under the skin. The aim of this study is to assess the cost-effectiveness of insulin pump therapy compared to injectable insulin, either in cartridges or injections. Currently, injectable insulin is the type of insulin therapy offered for type 1 diabetes patients on the National Health Service (NHS). Results obtained will indicate the feasibility of introducing insulin pump therapy on the local NHS.

Analysis of Heavy Metal Content in Conventional and Herbal Toothpaste available at Maltese Pharmacies
Andrew Vella

This study aims to determine heavy metals in conventional and herbal toothpastes available in local pharmacies. The samples are analysed for total polyphenolic content to check for possible correlation between the presence of polyphenols and heavy metals. The analysis for heavy metals includes acid digestion of dried samples, ashing in muffle furnace, followed by analysis using microwave plasma atomic emission spectroscopy. Total polyphenols are analysed using the Folin-Ciocalteu microassay, while other spectrophotometric parameters are determined using a UV-visible spectrophotometer.

Consumption of Heavy Metals and Hydroxymethylfurfural (HMF): Analysis of Infant Foods and Formulae
Christian Vella

The aim of the study is to quantitavely evaluate the concentrations of heavy metals and hydroxymethylfurfural using microwave plasma atomic emission spectroscopy and UV-visible spectrophotometry respectively, in a variety of infant foods and formulae found on the local market. The results will indicate whether the levels of contaminants fall within European Union regulation limits and recommendations by the European Food Safety Authority. These are important for future reference as manufacturing practices and distribution practices can have an effect on the level of these contaminants.

Risk Management in the Manufacture of Solid Oral Dosage Forms
Mark Sean Zammit

This dissertation aims to re-define the quality risk management system currently used by the solid oral dosage form manufacturing industry. This includes how risk is identified, assessed and classified. Gaps not covered by GMP, ICH and ISO guidelines are identified. Data is gathered through focus groups to substantiate the definitions being proposed. A risk classification and assessment tool which can be adapted to any situation, product, or process is developed and validated through focus groups.

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

The Maltese Patient's Perspective regarding Access to Medicine in the National Health System
Stephania Baldacchino

Entry Barriers of Medicines into the Maltese National Formulary
Abigail Bezzina

Herbal Teas: Assessing the Importance of Herbal Tea Products on the Local Market
Maria Calleja

Reporting of Side-Effects
Andrew Cauchi

Analysis of Corrections Following Regulatory Inspections
Andrew Debono

Polyphenolic and Antioxidant Activity of the Local Carob
Luca Galea

Legislation on Child-Resistant Packaging
Anderson Liew

Pharmacist Perception of Access to Medicines in the National Health Service in Malta
Kurt Micallef

The Effects of Brexit on Pharmaceutical Systems
Erika Mifsud

IT Systems and Statistics at the National Pharmaceutical Level in Malta
Alex Psaila

The Consistency of Herbal Teas: How do the Preparation Parameters Affect the Constitution of the Infusion?
Nicholas Rapa

Originators and Generics in the Community Pharmacy
Tiziana Vella

The Maltese Patient's Perspective regarding Access to Medicine in the National Health System
Stephania Baldacchino

Access to medicinal products is a current issue in most developed countries and also in the local National Health System (NHS). In order to evaluate this topic, different factors including patients' perception have to be taken into consideration. This project identifies major obstacles from the patient's perspective with regards to access to medicine in the Maltese NHS. This information is reviewed and recommendations on how to overcome these obstacles are put forward.

Entry Barriers of Medicines into the Maltese National Formulary
Abigail Bezzina

An approach to formulary management enables healthcare professionals to work in harmony by promoting evidence-based pharmaceutical care. Prior to inclusion in the formulary, products are extensively evaluated selecting only the most effective and safest medicines. The project evaluates the challenges encountered for the inclusion of a medicinal product into the national formulary. Shortcomings in the process are identified and the possibility of overcoming obstacles, such as expenditure, is assessed.

Herbal Teas: Assessing the Importance of Herbal Tea Products on the Local Market
Maria Calleja

Herbal teas may be used in combination with, or as an alternative to, conventional pharmaceutical products to prevent and treat common illnesses or health conditions. Two questionnaires are disseminated to gauge pharmacists' and patients' perception on the use of herbal teas. Results are statistically analysed in order to identify a trend.

Reporting of Side-Effects
Andrew Cauchi

The aim is to investigate the current system in Malta with regards to the reporting of side-effects and to suggest alternative procedures which may serve as improvements to the current process. This understanding is captured from the point-of-view of physicians and pharmacists practising in different sectors so as to collate a diverse pool of data.

Analysis of Corrections Following Regulatory Inspections
Andrew Debono

Pharmaceutical inspections verify compliance with principles of good manufacturing practice, good clinical practice, good laboratory practice and good pharmacovigilance practice. This project assesses the results of inspections carried out in local pharmacies and pharmaceutical companies. It aims to analyse this data to compare the results of these inspections. The outcomes of this study address common issues arising from inspections and these can be used for a preventive approach.

Polyphenolic and Antioxidant Activity of the Local Carob
Luca Galea

The polyphenolic and antioxidant activity of a variety of local carob tree pod samples are analysed. The pods are collected from previously assigned carob trees from different localities in Malta during the maturation cycle. Extracts are obtained and the polyphenolic content and antioxidant potency are evaluated using spectrophotochemical methods, such as the Folin-Ciocalteu and radical scavenging methods, respectively. The values are compared by location and maturity of the carob pods.

Legislation on Child-Resistant Packaging
Anderson Liew

Child resistant packaging (CRP) stems from the packaging expertise of prescription and over-the-counter medicines of over half a century. This critical review studies the influence of child-resistant packaging (CRP) legislation on patient behaviour. Following a comprehensive literature review, data analysis is undertaken using a validated questionnaire. This study aims to confirm findings from previous research in literature, substantiating the need for the secure storage of CR-packaged medicines in the prevention of unintentional childhood ingestion of medicines, which may potentially lead to death.

Pharmacist Perception of Access to Medicines in the National Health Service in Malta
Kurt Micallef

Access to medicines is a fundamental patient right and evaluating healthcare professionals' role in this context is crucial. Malta is becoming more demographically diverse, with foreign nationals presenting a prescription issued in the European Union for medicines that may or may not be available locally. Using data collected from community pharmacies in Ireland, England and Malta, various aspects relating to this situation are reviewed and recommendations proposed.

The Effects of Brexit on Pharmaceutical Systems
Erika Mifsud

The referendum of 23rd June 2016, which asked eligible voters whether the United Kingdom (UK) should leave or remain part of the European Union (EU), brought with it much uncertainty for the UK, as well as for the EU and its Member States. This project aims to investigate the potential implications of Brexit on the Maltese pharmaceutical systems, such as accessibility and importation of drugs from the UK, prices of medicines, policy-making and the potential relocation of the European Medicines Agency to Malta. This is established through interviews with various stakeholders.

IT Systems and Statistics at the National Pharmaceutical Level in Malta
Alex Psaila

This project focuses on investigating and evaluating the Pharmacy Of Your Choice IT system. Various stakeholders are interviewed and particular aspects are studied, including the appropriateness of data, patient centricity, accessibility and usage. Recommendations are drawn up to include data identification, resource efficiency and data accessibility.

The Consistency of Herbal Teas: How do the Preparation Parameters Affect the Constitution of the Infusion?
Nicholas Rapa

Herbal teas may exhibit fluctuations in consistency partly due to an inconsistent preparation of the infusion. Two factors influencing tea preparation, namely time and temperature, are investigated to determine their effect on the composition of various commercially-available herbal teas. An investigation to determine whether herbal tea products are consistent in terms of weight composition is also undertaken. The total content of polyphenols is determined using the Folin-Ciocalteu assay and UV analysis is also undertaken.

Originators and Generics in the Community Pharmacy
Tiziana Vella

The aim of this project is to assess the differences between originator and generic drugs in a number of countries including Malta. Questionnaires are distributed to healthcare professionals and patients to study current perception and status in local community pharmacies. Findings of the study look at establishing the ratio of originator to generic drugs use and understanding factors which explain the scenario.

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

Project Descriptions

Pharmaceutical Care Processes used in Psychiatric Institutions
Roberto Briffa

Through observation of current protocols at Mount Carmel Hospital (MCH) Pharmacy, the study addresses the needs of this psychiatric institution and proposes necessary amendments to current protocols focusing mostly on pharmacotherapy management and drug prescribing. Wards chosen for this study are four acute wards. The perspective of all concerned healthcare professionals regarding factors contributing to errors in prescribing and ways to avoid them is sought through the use of a questionnaire.

Identification of Novel Structures capable of Modulating Leishmania Kinases for the Treatment of Leishmaniasis
Yasmin Caruana

Pyruvate kinase (PK) is a druggable target for the treatment of Leishmaniasis, a condition that affects about 12 million persons globally. The suramin antagonist scaffold was used, through conformational analysis, to probe the PK ligand binding pocket with novel molecules being identified through virtual screening and *de novo* design. The two molecular cohorts consequently identified were filtered for Lipinski rule compliance and the highest affinity structures promoted for molecular dynamics simulations.

Medicines Use and Access Intelligence
Stefan Cassar

Access to medicines, a basic social right, is a global issue with millions dying each year due to the limitation of adequate, affordable medicines. The project analyses the intelligent use of medicines and their access. Case studies about barriers to medicine access and factors causing them are recorded and analysed. In 20 cases investigated by the Medicines Intelligence and Access Unit, 14 are resolved, 2 are not and 4 are ongoing. Prices of a number of medicines in Malta are compared to their reference price in the EU market. Lack of access through the National Health Service is also analysed.

Registration of Medicines
Francesca Cilia

All medicines marketed in Europe require a marketing authorisation. This authorisation is meant to ensure the quality, safety and efficacy of medicinal products on the European market. A booklet on registration processes of medicines in Malta is compiled. The booklet consists of information on the regulatory bodies, committees and organisations, the registration processes and the Marketing Authorisation application. The requirements to obtain a marketing authorisation could be complex and bureaucratic in such a manner that accessibility to medicines may be adversely influenced.

***In silico* Design of Polyphenolic Flavonoid Quercetin Analogs as Inhibitors of Histone Deacetylase (HDAC) and Histone Acetyltransferase (HAT) for the Management of Tumour Growth**
Durston Delia

This project targets two enzymes associated with tumour proliferation namely histone acetyltransferase and histone deacetylase. The quercetin scaffold, which inhibits both enzymes, was used after performing conformational analysis as a query for virtual screening and as a basis for the construction of fragments for *de novo* design. The optimal molecules obtained through each approach were identified for molecular dynamics studies and their binding modality at each target receptor compared.

In silico Interaction of Oleuropein and Lisinopril with the MMP-9 Receptor for the Management of Breast Cancer and Alzheimer's Disease

Matthias Karl Farrugia

The MMP-9 receptor is implicated in the mitigation of breast cancer and long-term memory loss associated with Alzheimer's disease. Two scaffolds were used for inhibitor modulation namely oleuropein and lisinopril. These were used in virtual screening for the identification of morphologically and electronically similar molecules. Molecular fragments were constructed from these scaffolds for *de novo* growth. The optimal molecules were identified for molecular dynamics and the utility of each scaffold for further design was assessed.

Use of Medicines in Older Patients in Long-Term Care Facilities

Tiziana Fenech Caruana

The setting for this project is St. Vincent de Paul (SVP) long-term care facility. It involves observational visits and relevant fieldwork at the in-house pharmacy. Questionnaires - validated and tested for reliability - on the drug distribution system at SVP were developed for healthcare professionals. Assessment of the pharmacotherapy administered to residents was based on the established STOPP criteria. Results indicate that 20 out of the 25 patients under study had at least 1 of the 9 significantly practised criteria, highlighting potential need for therapy review.

In silico Design of Phytoalexin Resveratrol (3,5,4'-trihydroxy-trans-stilbene) Polyphenolic Analogs as Inhibitors of Histone Acetyltransferase for the Management of Tumour Growth

Rebecca Hammett

Inhibitors of histone acetyltransferases have the potential to be promising chemotherapeutic agents due to their ability to restrict DNA double strand repair in cancer cells. Amongst such inhibitors is resveratrol, a naturally occurring phytoalexin found in blueberries and peanuts. This study aims to use the optimal binding conformational scaffold of trans-resveratrol as a template for the *in silico* design of novel analogs through the *de novo* and high throughput screening exercises, to identify 'hit' molecules with potential clinical utility for the management of neoplastic disease.

In silico Design of Novel Poly-ADP Ribose Polymerase Inhibitors (PARPIs) using Olaparib as a Lead Molecule

Christopher Muscat

Poly ADP Ribose Polymerase (PARP) inhibition is associated with mitigation of cancer. The inhibitor olaparib, was used to map the PARP ligand binding pocket and to identify the critical interactions between them. Bioactive olaparib was used first as a query in a virtual screening exercise to identify structures with 3D and outer electronic similarity and as a scaffold for the construction of fragments from which molecules could be generated *de novo*. These molecules were filtered for affinity and Lipinski Rule compliance and optimal structures recruited for molecular dynamics simulation.

Pharmacovigilance

Philip Tancred Paris

Pharmacovigilance helps to evaluate adverse risks from medicine use. Templates for reporting drug defects and templates for pharmacovigilance standard operating procedures (SOPs) are compiled. Pharmacovigilance officers are visited in various pharmaceutical scenarios. The pharmacovigilance SOPs available at various stakeholders are listed and evaluated. SOPs including job description, training and processes for pharmacovigilance are developed using templates.

Patient Management with Use of Lithium
Julia Pirotta

Current patient management practices implemented at Mount Carmel Hospital and Psychiatric Out-Patients at Mater Dei Hospital are analysed, focusing on patients receiving lithium therapy. Data collected from patient files reflects trends in demographics, medical background and routine monitoring parameters, through the use of a data collection tool. Identified weaknesses in management practice are used to formulate a prospective care pathway. Interviews with health care professionals are carried out to evaluate the collaborative practice of pharmacists in the provision of optimal lithium therapy.

***In silico* Design of Epigallocatechin-3-Gallate (EGCG) and Genistein Analogs as Inhibitors of Histone Deacetylases (HDACs) for the Management of Tumour Growth**
Luke Xuereb

This study explored the ligand binding pocket of histone deacetylase whose inhibition is known to interfere with tumour growth. Conformational analysis identified the optimally binding poses of epigallocatechin-3-gallate and genistein at this locus. Ligand-based drug design was used to identify query molecule analogs while receptor-based drug design was used for pharmacophore analysis and for seed generation. Molecular growth was allowed and novel structures designed with potential clinical use in neoplastic disease.

Pharmacist Intervention in Ambulatory Care of Older Persons
Rebecca Zammit

Pharmacist intervention is vital in community and in an ageing population the need to focus on patient safety and safer medication use is greater. Individuals require different forms of care and this study identifies patients who require ambulatory care and their specific pharmaceutical needs. The requirements of elderly patients are evaluated with the use of questionnaires. Models for providing pharmacist-led ambulatory care are explored within the local community setting. The perception of community pharmacists on the models is assessed.

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

Project Descriptions

Pharmacist Services in Community Pharmacies
Rand Abdulrahman

Services provided by pharmacists in community pharmacies are reviewed. Areas for development of extended services beyond dispensing and patient counselling, including emergency prescribing, pharmacists on the phone service and a 24-hour pharmacy service are identified. Data is collected through questionnaires and time-and-motion studies carried out in community pharmacies.

Drug Shortages and Economic Impact
Charlene Bartolo

The impact of drug shortages, including the perception of the affected individual, the public and any psychological effects such as on older persons, is evaluated. Negative effects on the image of the health system of the country are analysed. These parameters are evaluated quantitatively by assigning a numerical value such as by adopting a Likert scale. The occurrence of drug shortages in Malta is compared to other countries.

Dosage Forms and Medicine Acceptability
Maria Bartolo

Patient preferences regarding dosage forms is assessed by adapting the 'Medication Delivery Route Preferences Questionnaire' developed by University College, London. The questionnaire was translated to Maltese and validated using a forward-back translation methodology. Following ethics approval, the questionnaire is distributed to the general population.

Rational Design of Structures capable of Modulating Liver X Receptors (LXRs) for the Management of Pancreatic Cancer using the Agonist GW3965 Scaffold as a Lead Molecule
Nicole Bonello

Liver X Receptor (LXR) agonists are useful in managing pancreatic cancer. The GW 3965 experimental molecule and the 4-{3-[3-(methylsulfonyl)phenoxy]phenyl}-8-(trifluoromethyl)quinoline molecule were used to generate a consensus pharmacophore in LigandScout which was then submitted to ZINCPharmer for virtual screening. A total of 5 lead molecules were identified and will be further optimised.

Professional Development Programmes for Pharmacists
Catherine Anne Busuttil

Frameworks for continuing professional development (CPD) for pharmacists in various countries are analysed to develop a prototype for the local setting. The format and structure of the CPD programme are determined through questionnaires distributed to local pharmacists and by analysing trends in other countries.

Formulary for Non-BNF Cited Products
Renita Busuttil

This study aims to evaluate and update the Malta Medicines Handbook (MMH) to its fifth edition. Analysis of whether more frequent and automatic amendments could be undertaken on the electronic version of the MMH in synchronisation with the revision of the Malta Medicines List is determined. The introduction of a new and innovative mobile phone application is assessed for its effectiveness and efficiency.

Forensic Pharmacy: Drugs and Driving
Abigail Calleja

Local studies on how legal drugs impair one's driving ability are limited. A number of road accidents may be due to the use of drugs. Recent local and EU studies are researched and information from the Maltese population is gathered using questionnaires. Regulations implemented in other countries are examined and compared to Malta's regulations.

Health Economic Study of the Use of Warfarin
Grazielle Camilleri

Monitoring of the International Normalised Ratio is performed at the outpatient anticoagulation clinic at Mater Dei Hospital or at one of the eight health centres in Malta. A questionnaire will be distributed to patients from different areas in Malta. A proposal for a seamless care programme for patients on warfarin treatment will be developed.

Design of Novel Protein Kinase Inhibitors using the Naturally Occurring Isojacareubin Scaffold as a Lead in the Management of Solid Tumours
Jeanelle Caruana

Protein Kinase (PK) inhibitors are used in the management of cancer. The lead molecule isojacareubin was drawn in 3D using Sybyl. It was docked into the PK ligand binding pocket, conformational analysis performed and together with bisindolylmaleimide inhibitor used to generate a pharmacophore using LigandScout. Virtual screening will be performed using ZINCPharmer to identify hits for optimisation.

Chronopharmacology in Obesity
Onyinyechi Chesa

A questionnaire to assess the awareness of healthcare professionals and patients on the subject of chronopharmacology is devised and validated through an expert group and a pilot study. The questionnaire is applied for chronopharmacology in relation to the treatment of obesity, for example, in the use of orlistat.

Forensic Pharmacy: Drug Testing
Michaela Cini

The laws related to drugs of abuse in Malta are compared to those of other countries. The facilities available in Malta for testing drugs of abuse, including analysis of drugs in biological fluids, are examined using gap analysis. Experience in drug analysis will be acquired using facilities at the Life Sciences Park and at the University of Malta.

Design of Novel Structures capable of Modulating the Steroid Receptor Co-Activator (SRC) for the Management of Neoplastic Disease
Ruth Fiorentino

Agonism of the steroid receptor co-activator (SRC) mitigates tumours. MCB-613 was used as a lead, constructed in Sybyl and docked into the SRC receptor. The optimal conformer identified through conformational analysis was used with bioactive of AMP-PNP to generate a consensus pharmacophore in LigandScout, uploaded onto ZINCPharmer. Virtual screening identified hits which will be used to probe the SRC ligand binding pocket.

Seamless Pharmaceutical Care in the Management of Rheumatoid Arthritis
Francesca Galea

A collaborative practice referral ticket was developed to be shared with the community pharmacist to help achieve seamless care. The referral ticket is evaluated by healthcare professionals and a system for implementation of this service is proposed to facilitate the process of the transition of information from one healthcare system to another.

3D Printing and Pharmaceutical Dosage Forms
Christopher Johnson

A dosage form, such as a chewable tablet for individual dosing, is designed using inactive parts described in literature. The active substance selected is one needed for paediatric use where no such drug form is available, for example, methyldopa. Autodesk 123D Design and Cura 2.3.1 software are used to design and slice the dosage form 3D model. The Ultimaker 2+ 3D printer is used.

Design of Novel Protein Kinase Inhibitors Using the Naturally Occurring Staurosporine Scaffold as a Lead for the Management of Solid Tumours
Elena Mallia

Protein kinase (PK) inhibitors are important anticancer drugs. Staurosporine was used together with (2S)-3-phenyl-N~1~-[2-(pyridin-4-yl)-5,6,7,8-tetrahydro[1]benzothieno[2,3-d]pyrimidin-4-yl]propane-1,2-diamine in consensus sampling using Ligand Scout. The average pharmacophore was uploaded into ZINCPharmer and a total of 1,282 hit molecules identified. These will be used to further probe the PK enzyme.

Targeting the Kappa Opioid Receptor in the Treatment of Addiction
Maria Mangion

The Kappa Opioid Receptor (KOR) is a target for addiction-controlling drugs. The structure of the agonist Salvinorin A was drawn in 3D in Sybyl. Its optimal conformer was used together with the endogenous JDTic to generate an average pharmacophore in LigandScout, uploaded into ZINCPharmer and the resultant 36,473 hits used for optimisation.

Pharmacist Prescribing and Point-Of-Care Testing
Tricia Micallef

A framework to be followed by pharmacists for repeat prescribing in diabetes mellitus and hypertension was developed according to local and international guidelines. A focus group will be held to assess the feasibility of the framework and a questionnaire on the use of point-of-care testing as biomarkers for these conditions within the developed framework is carried out.

Rational Design of Novel Androgen Receptor Inhibitors using the Experimental Small Androgen Receptor Modulators (S)-11 and (R)-9, and R-bicalutamide Scaffolds as Lead Molecules for the Management of Prostate Cancer
Simona Svetlozarova Neykova

Refractory prostate cancer management is a therapeutic challenge. Novel molecules (S)-11 and (R)-9 were drawn in 3D in Sybyl and conformational analysis was performed on each. The optimal conformers were overlaid in Ligand Scout and used to generate a consensus pharmacophore which was uploaded to ZINCPharmer for hit identification. These will be used to probe the Androgen Receptor Ligand Binding Pocket.

Targeting the BCL-2 Receptor in the Management of Leukaemia and Other Solid Tumours
Yvonne Savona Ventura

The beta cell lymphoma 2 (BCL-2) receptor is a target for pro-apoptotic drugs. Navitoclax and venetoclax were used as probes. Navitoclax was extracted from its receptor and venetoclax was constructed in 3D in Sybyl. The optimal conformation of venetoclax was used together with navitoclax to generate a consensus pharmacophore in LigandScout. This will be used to identify hits through virtual screening.

Point-of-Care in Haemoglobin Measurement
Martina Scicluna

Sensitivity, specificity and reliability testing of two haemoglobin test kits, DiaSpect Tm and Stat-Site M Hgb, is undertaken and compared to standard laboratory testing. Testing is implemented on diabetics, patients with renal failure and healthy adults (control). Feasibility of providing the service of haemoglobin testing in a community setting and patient perception regarding this test is studied.

Rational Design of Partial PPARg Agonists using the Synthetic Analog of Tetrahydrocannabinol (THC), Ajulemic acid (AJA) Scaffold as Lead Molecule for the Management of Diabetes Mellitus and Inflammatory Conditions
Kirby Zammit

The Peroxisome Proliferator Activated Receptor (PPARg) is a target for the design of hypoglycaemic drugs. The ajulemic acid and the indomethacin scaffolds were used in consensus sampling to generate an overlap pharmacophore in LigandScout. This was exported to the online database ZINCPharmer and a total of 37,799 hits were identified. These will be used to further probe the PPARg receptor.

Medicine Reconciliation at Discharge
Thomas Zammit

The project investigates discharge processes at local hospitals. Observational visits to Mater Dei Hospital and Karin Grech Rehabilitation Hospital were carried out. Patient discharge forms will be compared for the two settings and recommendations proposed. Medicine reconciliation will be tackled through ward visits by communication with patients, relatives and carers and analysis of the required patient information.

Pharmacist-Led Management for Insulin Therapy
Jessica Zarb

Through patient blood glucose and HbA1c testing, this study aims to investigate the feasibility of a framework for the implementation of pharmacist-led management of insulin therapy. Care issues are identified and addressed through collaboration with prescribers.

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

Rational Design of Novel Acid Ceramidase Inhibitors for the Management of Melanoma
Gabriel Abela

Bache *et al.,* in their 2015 paper in the Journal of Medicinal Chemistry show acid ceramidase to drive melanoma proliferation and benzoxazolone carbetamide antagonists to be apoptotic. This study uses this scaffold as a lead in the design of novel acid ceramidase antagonists.

Rational Design of Novel Structures based on the PZM21 Scaffold capable of μ-Opioid Receptor (MOR) Modulation for the Management of Pain
Stephanie Attard

This study uses the PZM21 scaffold, a μ-opioid receptor antagonist, described by Manglik *et al*. in Nature in 2012 to model similar receptor subtype specific antagonists capable of producing opioid level analgesia without the typical concomitant side-effects.

Pharmacist-Recommended Medicines for Paediatric Patients
Chiara Baldacchino

There are limitations in the availability of medications for use in paediatric patients. The scientific evidence of safety and efficacy of pharmacist-recommended medications which can be used in these patients is assessed and proposals with regards to updating medicine use are put forward.

Rational Design of Glutathione-S-Transferase Pi1 (GSTP1) Antagonists based on the Novel LAS17 Scaffold for the Management of Triple Negative Breast Cancer
Gabriel Borg

The GSTP1 subtype is recognised as a key metabolic driver in triple negative breast cancer. Molecule LAS17 has been shown to be inhibitory in *in vitro* and animal studies. This study uses LAS17, described in 2016 by Crawford *et al*. as a lead for the design of molecular analogues.

Rational Design of Proto-Oncogene Tyrosine-Protein Kinase SRC Antagonists based on the Novel ECF506 Scaffold for the Management of Breast Cancer
Lara Maria Busuttil

The tyrosine kinase SRC is a target for triple breast and other solid tumour neoplasms as shown by Fraser *et al.* in their 2016 study published in the Journal of Medicinal Chemistry. The described ECF-506 antagonist will be used as a lead for the design of analog structures.

Rational Design of Dual PPARγ and α-**Agonists based on the Novel SR10171 Scaffold for the Management of T2DM and Osteoporosis**
Justin Cassar

A new dual PPARg and a drug candidate capable of treating both diabetes and osteoporosis has been referenced as SR10171. The critical interactions of SR10171 with these receptors are exploited in the context of the design of novel dual agonist molecules.

Use of Antibacterial Drugs in the Intensive Care Unit
Julia Catania

The use of antibacterial drugs in the intensive care unit is reviewed by analysing trends in drug resistance and occurrence of nosocomial infections. Proposals for new guidelines to achieve optimum clinical outcomes within safe parameters and efficient dosage regimens are developed.

Rational Design of Novel Structures based on the Leiodermatolide Scaffolds capable of Inhibiting Tubulin for the Management of Pancreatic Cancer
Graziella Chetcuti

Leiodermatolide isolated from ocean sponges has been shown to reduce pancreatic tumour size through tubulin inhibition to a greater extent than gemcitabine, the gold standard therapy. This study models the leiodermatolide scaffold to identify novel tubulin antagonists.

Rational Design of Novel Molecules based on the AR-42 Scaffold for the Management of Cancer Associated Cachexia
David Gatt

Histone deacetylases (HDACs) are known drivers for tumour growth. Molecule AR-42 has been described by Tseng et al. in 2015 as an HDAC inhibitor which also retards skeletal muscle breakdown or cachexia and will be used in this study as a lead for the design of analog molecules.

Use of the Novel UM-164 Scaffold to Probe the Tyrosine-Protein Kinase SRC receptor for the Rational Design of Antagonist Molecules capable of Mitigating Metastatic Triple Negative Breast Cancer
Thomas Sammut

The SRC receptor has been identified as a mediator of triple negative breast cancer, which may be inhibited *in vitro* by novel molecule UM-164. This molecule will be used as a lead in the design of novel antagonists capable of mitigating this disease.

Rational Design of Novel Structures based on the Fluphenamic Acid and Glibenclamide Scaffolds for the Identification and Design of Novel Structures capable of Inhibiting the AKR1C1 Receptor for the Treatment of Bladder Cancer
Matthew Scicluna

The AKR1C1 receptor is over expressed in bladder tumours. It has been successfully antagonised by fluphenamic acid and glibenclamide in *in vitro* assays. These scaffolds will be repurposed and modelled in this study for the identification of novel antagonist molecules.

Rare Diseases and Orphan Medicines
Sharon Vassallo

The definition of rare diseases and orphan medicines is revisited, validated and disseminated internationally. The development and evidence for efficacy of such drugs are established and documented. A register for rare diseases and the established management protocol for Malta are compiled.

Determination of Orthoesterification Mechanisms in Drug Synthesis
Maria Xiberras

Orthoesterification of steroids is carried out to challenge present documented methods, such as elimination of water from the process, and is monitored using HPLC. The legitimacy of the results is evaluated from a theoretical stand point.

Use of Newer Generation Statins in Cardiovascular Disease
Maia Zarb

Specific risks and benefits of using old generation statins in the management of cardiovascular disease are questioned. This study looks at identifying advantageous clinical outcomes and pharmacoeconomic implications of recommending newer generation statins as first-line treatment.

Doctorate in Pharmacy Dissertation Title Index

M.Pharm. Dissertation Title Index