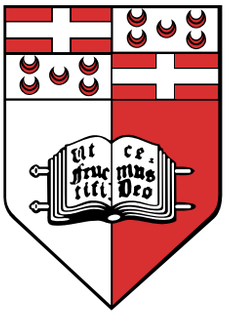

University of Malta

Dissertation Abstracts and Project Descriptions

Department of Pharmacy

Faculty of Medicine and Surgery

University of Malta

2016

Department of Pharmacy

University of Malta, Msida, Malta

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Foreword

The Pharmacy Symposium 2016 tells the story of the academic achievements of the students of the Pharmacy Department of the University of Malta. The research input by all the students be it Master of Pharmacy, Bachelor of Science (Honours) in Pharmaceutical Sciences, Bachelor of Science (Honours) in Pharmaceutical Technology or Master of Science in Pharmacy candidates is a quest leading to a new understanding of pharmaceutical processes and also to understanding what it means to be a pharmacist or a pharmaceutical technologist. All the research projects included in this booklet and presented at the symposium are carried out under the auspices of the Department of Pharmacy.

Projects presented show that pharmacists are on the road to become prescribers, others relate to pharmaceutical sciences, such as green chemistry in the synthesis of steroids and structure activity relationships, clinical pharmacy and pharmaceutical care as well as projects in pharmacoeconomics showing the possible savings of thousands of euros by proper preparation of expensive anti-cancer drugs and the reduction of wastage of biologicals. These are contemporary and futuristic pharmacy visions. Make no mistake, these aspects of pharmacy practice would have seemed to be audacious if not downright preposterous if they had been tackled just a decade ago.

The aim of this symposium is to celebrate and help the audience appreciate the challenges that have been overcome in arriving at the state of excellence in pharmacy – moving from a three year Bachelor to four years and then to five years, culminating in an uphill struggle to reach to the top – a five and a half year Master of Pharmacy with the award of an honours degree a Bachelor of Science in Pharmaceutical Sciences, which gives pharmacists a remarkable state of preparedness for their tasks as healthcare providers. As academics we are concerned not with the intrigues and politics of this great university but with the conquest of knowledge which invariably accompanies developments and which would transfer pharmacy practice in this century. Let there be no misunderstandings – we cannot ignore the development in other fields such as the medical practice and the pharmaceutical industry.

The Department has recently taken up two ambitious undertakings that have been long in gestation. The conception of the Doctor of Pharmacy degree can be traced to 1972 when the words 'Clinical Pharmacy' and later 'Pharmaceutical Care' were being mentioned and the new pharmaceutical sciences such as 'Biopharmaceutics' and 'Pharmacokinetics' started to be taught in our university. A few years later these ideas started to be put in practice. It took a combination of a number of leaders in pharmacy education who exploited the talents available and used synergistic and effective strategy to land the Doctorate of Pharmacy two years ago. Sometime before the launch of the level 8 Doctorate of Pharmacy course, the Department brought forward and cultivated the idea of collaborating with the pharmacy industry, which effort took a deep root, eventually reaching in establishing the Bachelor of Science (Honours) in Pharmaceutical Technology – candidates to this degree are also presenting their learned findings at this symposium.

The list of achievements of the Department of Pharmacy would not be complete without giving merit to the three PhD students who graduated last December. Best wishes are also due to those PhD candidates whose work and thesis presentation is in progress. However, the Department would not have managed on its own and there is a list of clinicians and scientists as well as administrative officers who gave invaluable help in the preparation of all these projects, both in terms of organisation and in scientific and clinical contribution. Thanks go therefore to the Rector, the Pro-rectors, the Dean of the Faculty of Medicine and Surgery, Professors and lecturers in several other Departments and the Faculty and University administration not least the administrative and technical staff at the Department of Pharmacy for all their heroic support overcoming technical and administrative challenges not to mention financial impossibilities.

Our final and great vote of thanks goes to the respective families and friends of the academic, technical and administrative staff but mostly to the beloved wonderful students for their forbearance, understanding, love and help in stressful but also often enjoyable and fruitful circumstances.

Professor Anthony Serracino-Inglott
Pharmacy Practice Projects Co-ordinator

Introduction

The Department of Pharmacy at the University of Malta has a long history of integrating research skills in undergraduate courses and encouraging students to undertake dissemination of research results through different fora. The Annual Pharmacy Symposium is an opportunity for undergraduate and postgraduate students at the Department to present their research activities. Incorporating research skills at the undergraduate level supports the development of critical and analytical thinking and of lifelong learning skills in the students. The experience of participating in a research project during the undergraduate course enables students to handle challenges and situations as they arise. These skills are very useful to the pharmaceutical job setting which is driven by research, innovation and technology where patient safety is the focus of all products, processes and services provided.

Having new pharmacists and pharmaceutical technology graduates with these skills is one factor that contributes to matching skills with what is required by the job market. The Department collaborates with the various pharmaceutical settings so as to ensure that graduates are ready to contribute to these set-ups and can also participate in the dynamic developments that are essential to maintain relevant processes in the pharmaceutical industry and in patient-care settings.

Another academic activity adopted by the Department which improves the matching skills approach are the experiential placements which are built-in during the courses. These placements provide the opportunity to the student to develop links to the 'real-world', to apply knowledge to practice and to develop professionalism. Over 90% of the students participate in an Erasmus mobility and carry out an experiential placement at a partner University in Europe. The Department hosts around 20 students per year from partner Universities. This student exchange promotes the internationalisation of the Department which contributes to dissemination of academic and research activities and to networking with colleagues from other countries.

The Department of Pharmacy provides opportunities for further studies through postgraduate courses. The Master of Science in Pharmacy course is followed by graduates with an interest to focus on pharmaceutical regulatory sciences and pharmacoencomics. The three year Doctorate of Pharmacy programme which is offered in collaboration with the College of Pharmacy of the University of Illinois at Chicago provides the opportunity to pharmacists to read for a Level 8 degree which combines advanced experiential aspects with applied research. This international programme is currently followed by 34 students from 8 countries. Areas of research being undertaken by the second year doctorate students include use of new anticoagulants, safer use of warfarin and digoxin, supporting patients with insulin and glucagon use, stem cell therapy, patient safety and innovative medicines, pharmaceutical regulation and innovative medicines, use of biosimilar drugs, community pharmacist support for cancer patients and patients with chronic disease.

A significant activity in research is dissemination which enables sharing of the work and generation of a research profile which helps to strengthen the extension of international collaborations with colleagues in the field.

Professor Lilian M. Azzopardi
Head, Department of Pharmacy

M.Pharm. Students
Dissertation Abstracts

Pharmaceutical Care

Risk of Drug-Induced Effects and Hospital Admissions
Nicola Farrugia

Risks in Medication Reconciliation During Hospital Admission
Tresha Emelene Formosa

Pharmacist Prescribing in a Hospital Setting
Abigail Aquilina

Pharmacist Intervention in Multidisciplinary Tasking of Cancer Patients
Ann Camilleri

Improving Compliance in Psychiatric Patients
Estelle Borg Falzon

Risk of Drug-Induced Effects and Hospital Admissions

Nicola Farrugia

Background: Drug-induced effects may be due to adverse drug events, drug therapy failures and medication errors which if prevented would improve the clinical outcome of patients.[1]

Objectives: To investigate the occurrence of drug-induced effects, to identify and classify drug-related hospital admissions into different categories according to the effect that occurred and to evaluate the risk associated with these drug-induced effects.

Design: Data collection was carried out on the post-admitting days of six selected consultants from different areas of medicine. A validated data collection form and a questionnaire compiled by the researcher were used to collect essential information from all the patient files seen and to interview the patients admitted due to a drug-induced effect. Data analysis was carried out using SPSS® version 20. A risk matrix was compiled by the researcher to assess the risks associated with drug-induced effects of ten selected cases.

Setting: Mater Dei Hospital

Main Outcome Measures: Incidence and risk of drug-induced effects

Results: From the 538 patient admissions studied, 66 were identified to be due to drug-induced effects. Of these, 15 were caused by more than one drug. Twenty-one cases were due to antihypertensive medications and 15 cases were due to psychiatric drugs.

Conclusion: The study indicates a 12% hospital admission rate due to drug-induced effects. The main types of drug-induced effect cases were identified to be due to toxicity in overdose and side-effects (45 cases).

Reference:

1. Alghamdy MS, Randhawa MA, Al-Wahhas MH, Al-Jumaan MA. Admissions for drug-related problems at the Emergency Department of a University Hospital in the Kingdom of Saudi Arabia. Journal of Family and Community Medicine 2015; 22(1): 44-48.

Risks in Medication Reconciliation During Hospital Admission

Tresha Emelene Formosa

Background: Medication errors are prone to arise during transition of care, particularly on admission. Through medication reconciliation, medication errors are identified and prevented, reducing the risk of patient harm.

Objectives: To carry out medication reconciliation at hospital admission, to assess the potential clinical impact of discrepancies identified and to analyse the role of the pharmacist in medication history-taking.

Design: One hundred patients were chosen by simple random sampling from 5 consultant physicians. Ethics approval was obtained. The best possible medication history (BPMH) was obtained from each patient. Medication reconciliation was carried out and statistical analysis was conducted with SPSS® v20 using the chi-square test. An expert panel consisting of 4 consultant physicians and 5 pharmacists was asked to carry out risk assessment using risk matrices on 15 out of the 100 medication histories obtained to assess likelihood and consequence of the discrepancies between the BPMH and the medication history recorded in the patient file. A questionnaire was distributed to the expert panel to determine their perception on risk assessment.

Setting: Mater Dei Hospital and Gozo General Hospital

Main Outcome Measures: Identification of medication discrepancies in medication history on admission and risk assessment

Results: One hundred patients take a total of 649 medications and 124 discrepancies were found. Of these, 90% were omissions. The pharmacist identified 17% more medications than the non-pharmacist taking the medication history. A significant correlation between the number of medications taken by the patients and the number of discrepancies identified was found ($p=0.043$). Four experts agreed that one discrepancy required immediate attention and 3 experts agreed that two other discrepancies required immediate attention. Eight out of 9 experts agreed that the pharmacist should carry out risk assessment of medication reconciliation.

Conclusion: The pharmacist achieved a more accurate medication history compared to the other healthcare professional.

Pharmacist Prescribing in a Hospital Setting

Abigail Aquilina

Background: Pharmacist prescribing has not yet been authorised locally. In 2014, Vella[1] concluded that clinical pharmacists were most willing to prescribe oral anticoagulants, antihypertensive and antidiabetic medications.

Objectives: To compile and evaluate guidelines for pharmacist prescribing in local hospitals and to study differences between pharmacist and physician prescribing.

Design: Pharmacist prescribing guidelines for oral anticoagulation, hypertension and diabetes management in the hospital setting were developed according to an American model of collaborative drug therapy management. Internationally recognised guidelines which are followed locally were used to develop the guidelines. A case study for each condition identified was designed and disseminated to an expert panel consisting of 5 pharmacists and 4 physicians to determine differences between pharmacist and physician prescribing. A questionnaire was developed and disseminated to the same expert panel together with the guidelines to assess whether the developed guidelines were clear, practical and enable collaborative practice between pharmacists and physicians.

Setting: Local hospitals

Main Outcome Measures: Evaluation of pharmacist prescribing guidelines

Results: From the case studies no differences were noted between pharmacist and physician prescribing for the management of oral anticoagulation and diabetes. For hypertension, differences in drug therapy were attributed to misdiagnosis by 2 pharmacists and 2 physicians. When correct diagnosis was established by the remaining 5 experts similar treatment was prescribed.

Conclusion: The validation panel stated that the guidelines are clear, practical and enable collaborative practice. Seven out of the 9 experts agreed with pharmacist prescribing for the conditions identified. It can be concluded that pharmacist prescribing is safe in all three conditions.

Reference:

1. Vella E. Implementation of pharmacist prescribing in Malta [dissertation]. Msida (Malta): Department of Pharmacy, University of Malta; 2014.

Pharmacist Intervention in Multidisciplinary Tasking of Cancer Patients

Ann Camilleri

Background: A variety of treatment is used to treat cancer requiring input of several health care professionals to develop optimal treatment recommendations. Each professional should be aware of their contribution to treatment and the contribution of other professionals involved.

Objectives: To identify professional tasks perceived by other healthcare professionals as the responsibility of the oncology pharmacist.

Design: A questionnaire was distributed to 165 oncology health care professionals (87 nurses, 12 pharmacists, 31 doctors, 23 radiographers and 12 allied health care professionals) to determine their perception on which profession has the main and supportive responsibility in carrying out tasks within this setting and those professionals who are not involved. Data was analysed with SPSS® using the chi-square test to assess the association between categorical variables.

Setting: Sir Anthony Mamo Oncology Centre, Mater Dei Hospital

Main Outcome Measures: Perception of the role of the oncology pharmacist and how this varied according to the participants' profession and years of experience

Results: Pharmacists were perceived to have a predominant supportive role in identifying and managing drug related problems (37%), patient education and counselling (29%) and authorisation and administration of therapy (26%). When comparing the participants' responses with their profession it was observed that pharmacists classified their profession to be highly involved (60%) whilst radiographers included pharmacists as the professionals with least (10%) of the main responsibility.

Conclusion: Pharmacists believe that current responsibility should be increased since their broad knowledge on cancer and non-cancer medications and any possible drug interactions may enhance therapeutic outcomes for the patient.

Improving Compliance in Psychiatric Patients

Estelle Borg Falzon

Background: Psychiatric outpatients tend to be the most non-compliant patient group in terms of medication administration which may be attributed to several factors.

Objectives: To assess the extent of non-compliance in psychiatric outpatients and investigate the applicability of a compliance aid device within this patient group in terms of practicality, ease of use, cost effectiveness and effect on compliance.

Design: Twenty outpatients were chosen by convenience sampling. The study was divided into 2 phases. During phase 1 patient compliance was assessed by the Medication Adherence Rating Scale (MARS)[1] survey and patients were self-administered Part A of a questionnaire. In phase 2 the chosen patients were given a demonstration on how to use the 7-Day Multi-Dose pill box and the device was given to them to use at home for 1 week. After 1 week the patient completed Part B of the questionnaire and compliance was re-assessed.

Setting: Mount Carmel Hospital Pharmacy

Main Outcome Measures: Medication adherence score before and after use of a compliance aid device

Results: Nine patients were male and 11 were female, mean age was 46 years, and the average number of daily medications was 6. Upon initial scoring using MARS, 5 patients were classified as non-adherent. Only 10 patients accepted to participate in Phase 2 of the study and took the compliance device home. Out of these 10 patients, 4 agreed that the way they administer their medication improved following 1 week of using the compliance aid device. However evaluation using the MARS score before and after use of the device showed no significant difference in patient compliance.

Conclusion: Use of such a compliance aid device in psychiatric patients is challenging due to difficulty in establishing patient communication and maintaining motivation.

Pharmacotherapy

Awareness and Economic Implications of Human Papillomavirus Vaccination
Bettina von Brockdorff

Pharmacist-Led Adherence Clinics for Lymphoma and Congestive Heart Failure Patients
Jessica Vella

Patient Safety in the Use of Non-Steroidal Anti-Inflammatory Drugs
Jessica Nicolette Farrugia

Effect of Treating Sleep Apnoea on Other Comorbidities
Yanica Cassar

A Pilot Study for Methadone Dispensing from a Community Pharmacy
Mark Caruana

Use of Diuretics in Congestive Heart Failure
Katya Xuereb

Awareness and Economic Implications of Human Papillomavirus Vaccination

Bettina von Brockdorff

Background: Human Papillomavirus (HPV) is the main cause of cervical cancer.

Objectives: To investigate the impact of use of HPV vaccines on the local health care system through awareness of HPV and the HPV vaccine amongst gynaecologists, pharmacists and patients, and to assess the economic implications of the administration of HPV vaccines in the health care system.

Design: A self-administered questionnaire aimed at health care professionals (HCPs) was distributed to gynaecologists and managing pharmacists. Another questionnaire was distributed to 100 female patients at Gynaecology Outpatients, Mater Dei Hospital (MDH) and to 140 patients at 14 community pharmacies chosen by stratified random sampling. Data was analysed using SPSS® 20.0. The HPV free entitlement vaccination scheme was assessed in terms of cost, number of patients and doses administered. Using statistical data estimated costs since 2013 (year of implementation) were calculated.

Setting: Gynaecology Department, MDH and community pharmacies

Main Outcome Measures: HCP and patient awareness of HPV

Results: Thirteen gynaecologists, 8 managing pharmacists and 132 patients participated. Five gynaecologists stated that they vaccinated 3 to 5 patients over a one-month period. From 132 patients recruited, 48% were aware of the HPV virus and 53% were aware of the existence of the HPV vaccine ($p<0.05$). The cost for vaccinating 12 year old girls on an average yearly basis since 2013 was approximately €547,000.

Conclusion: Awareness on HPV and HPV vaccines increased from a previously conducted study.[1] Reasons for this are implementation of HPV vaccines in the local healthcare system since 2012 and increased awareness in schools.

Reference:

1. Brincat AM. Human Papillomavirus Awareness [dissertation]. Malta: Department of Pharmacy, University of Malta; 2012.

Pharmacist-Led Adherence Clinics for Lymphoma and Congestive Heart Failure Patients

Jessica Vella

Background: The extent of patient adherence to treatment largely affects outcomes of chronic conditions.

Objectives: To assess pharmacist intervention on medication adherence in patients suffering from heart failure (HF), Hodgkin's Lymphoma (HL) and non-Hodgkin's Lymphoma (NHL).

Design: Following ethics approval, patients who accepted to participate were given a compiled questionnaire which included the Morisky 8-item medication adherence questionnaire (MMAS-8)[1] (t=0). The MMAS-8 gives a score for medication adherence: 0 = high adherence, 1 or 2 = medium adherence and <2 = low adherence. A 'Patient Information Leaflet' (PIL), an individualised treatment chart and verbal advice were provided as part of the pharmacist intervention. After 6 weeks for HL and NHL patients and after 6 months for HF patients (t=1), the same questionnaire was administered to the patients. SPSS® version 23 using the Wilcoxon signed-rank test were used to assess changes in medication adherence between t=0 and t=1.

Setting: Medical Investigations and Treatment Unit and Heart Failure Clinic at Mater Dei Hospital

Main Outcome Measure: Pharmacist intervention on medication adherence

Results: Out of the 41 NHL patients, 3 scored low adherence and 38 medium adherence at t=0 and 41 scored medium adherence (t=1). Out of the 5 HL patients, 2 scored low adherence and 3 medium adherence at t=0 and 5 scored medium adherence at t=1. Out of the 40 HF patients, 17 scored low adherence and 23 medium adherence at t=0 and 40 scored medium adherence at t=1.

Conclusion: Results show that pharmacist intervention helped patients who scored low adherence at t=0. This study shows how pharmacist intervention and extended professional services could be implemented in the clinical setting to impact on the management of chronic conditions.

Reference:

1. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical Care. 1986;24:67-74.

Patient Safety in the Use of Non-Steroidal Anti-Inflammatory Drugs

Jessica Nicolette Farrugia

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are associated with serious adverse reactions which can result in significant morbidity and mortality.

Objectives: To identify risks involved in NSAID administration, including over usage and significant drug-drug interactions, to analyse occurrence of side-effects and to determine trends in NSAID prescribing by physicians and pharmacists.

Design: A sample of 100 patients was recruited from 13 community pharmacies in Malta, one from each electoral district, chosen by stratified sampling. A self-administered questionnaire was disseminated. Trends in NSAID prescribing were determined using another questionnaire directed to 49 pharmacists and physicians which was available online.

Setting: Community pharmacies

Main Outcome Measures: Use of NSAIDs by patients and prescribing trends

Results: Back pain (19), muscular pain (13), headache (12) and arthritic pain (10) accounted for the most frequent use of NSAIDs. Diclofenac was the most commonly administered NSAID taken by 58 patients, of whom 48 use the 50mg dose. Chronic disorders experienced by the patients included hypertension (24), heartburn (22), dyspepsia (21), asthma (4) and a history of *Helicobacter pylori* infection (2). Other disorders suffered by single individuals include epilepsy, Crohn's disease and renal dysfunction. Epigastric pain (65%), stomach ulcers or GI bleeding (31%) and elevated blood pressure (30%) were the most common side-effects encountered by pharmacists and physicians. NSAIDs were frequently found to be co-administered with antihypertensives (68%) and SSRIs (37%) despite risk of interaction with NSAIDs. The majority (76%) of pharmacists and physicians believe that NSAIDs are being overused and 96% state that closer monitoring of NSAID adverse effects is necessary.

Conclusion: The risk involved with NSAID administration due to over usage and drug interactions is identified and healthcare professionals are aware of this risk.

Effect of Treating Sleep Apnoea on Other Comorbidities

Yanica Cassar

Background: Obstructive sleep apnoea (OSA) involves multiple episodes of upper airway collapse during sleep. Hypertension, type II diabetes mellitus and insomnia are the main comorbidities associated with presence of OSA.[1,2]

Objectives: To identify a relationship between the use of different pharmacological therapies in uncontrolled and controlled OSA and to determine the effects of commonly used medications on continuous positive airway pressure therapy (CPAP).

Design: A total of 183 medical records of patients who underwent the sleep study between 2009 and 2013 were reviewed. Data collected includes body mass index, gender, age, Epworth Sleepiness Score (ESS), drug history and Apnoea Hypopnoea Index (AHI). Likelihood ratio, chi-square test, paired sample t-test and multinomial logistic regression were the statistical tools used for data analysis.

Setting: Sleep Laboratory, Mater Dei Hospital

Main Outcome Measures: Assessment of drug history in response to OSA control using ESS and AHI scores

Results: Angiotensin II receptor antagonists (ARBs) ($p=0.022$), sulphonylureas ($p=0.051$), insulin therapy ($p=0.040$) and non-benzodiazepine hypnotics ($p=0.040$) were found to be associated with the presence of OSA. Reduction in CPAP therapy benefit was observed with use of histamine (H1) antagonists, β-adrenergic blocking agents and antiplatelets. Reduction in the use of ARBs and angiotensin converting enzyme inhibitors was identified in patients with controlled OSA.

Conclusion: OSA screening is beneficial for treating OSA and could provide a better outcome in the treatment of other comorbidities such as hypertension.

References:

1. Park PJ, Rammar P, Olson EJ. Updates on Definition, Consequences and Management of Obstructive Sleep Apnoea. Mayo Clin Proc. 2011; 86(6): 549-555.

2. Zhang XJ, Li QY, Wang Y, Xu HJ, Lin NY. The effect of non-benzodiazepine hypnotics on sleep quality and severity in patients with OSA: A meta-analysis. Sleep Breath. 2014; 18(4):781-789.

A Pilot Study for Methadone Dispensing from a Community Pharmacy

Mark Caruana

Background: Methadone is the most frequently prescribed opioid used in substitution therapy of drug dependence Methadone treatment was introduced in Malta in 1987 and is provided by SEDQA through the Substance Misuse Outpatient Unit (SMOPU). In 2012, 1013 patients were taking methadone.[1] Prescribing and dispensing of methadone is regulated by subsidiary legislation 101.06 entitled Methadone Rules.[2]

Objectives: To determine whether community pharmacists in Malta would be willing to dispense and supervise the consumption of methadone and to investigate the involvement of community pharmacies in development of a regionalised methadone dispensing service.

Design: A questionnaire, consisting of 19 questions, was distributed via electronic mail to the managing pharmacist of each of the 218 community pharmacies in Malta. Statistical analysis was carried out with SPSS® using the chi-square test, Friedman's test and binary and multinomial logistic regression models.

Setting: Community pharmacies

Main Outcome Measures: Pharmacist perception on methadone dispensing from community pharmacies

Results: A total of 63 community pharmacists completed the online questionnaire. Twenty-three pharmacists were willing to dispense methadone. Twenty-eight pharmacists were willing to dispense methadone if they were provided with the appropriate training. Nineteen pharmacists were willing to supervise the consumption of methadone. Seventeen pharmacists agreed that community pharmacists should play a role in the dispensing of methadone as part of methadone maintenance treatment programs.

Conclusion: The results indicate that when provided with appropriate training community pharmacists are in favour of having a role in methadone dispensing from community pharmacies.

References:

1. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). Drug treatment overview for Malta [Online]. Malta: EMCDDA; 2015 [cited 2016 Jan 24]. Available from: URL: www.emcdda.europa.eu/data/treatment-overviews/Malta

2. Ministry for Justice, Culture and Local Government. Subsidiary Legislation 101.06 Methadone Rules [Online]. Malta: The Ministry; 2005 [cited 2016 Jan 24]. Available from: URL:www.justiceservices.gov.mt/DownloadDocument.aspx?app=lom&itemid=9264&l=1

Use of Diuretics in Congestive Heart Failure

Katya Xuereb

Background: Diuretic therapy is routinely used in the management of congestive heart failure (CHF) and a dose of bumetanide 1mg daily or less is recommended.[1]

Objectives: To investigate management of patients suffering from CHF in a hospital scenario and to assess the effect of pharmacist intervention on compliance to diuretic treatment.

Design: Subjects were chosen according to established inclusion criteria, 37 from the hospital setting and 38 from the community. Descriptive statistics were used to interpret changes in diuretic dose of patients and compliance.

Setting: Rehabilitation Hospital Karin Grech (RHKG) and community pharmacies

Main Outcome Measure: Change in compliance to diuretic therapy in relation to pharmacist intervention

Results: Bumetanide dose on patient discharge was recorded. Four patients were discharged with a dose of 0.5mg, 11 patients on a dose of 1mg, and 22 patients on a dose greater than 1mg. Twenty-four patients had the following parameters out of range: creatinine, glomerular filtration rate, urea and sodium. Out of these patients, 3 had the bumetanide dose reduced to less than 1mg daily and 4 patients had a dose reduced but which was still greater than 1mg daily. In 8 patients the dose was reduced but had to be increased again, while in 9 patients the dose was kept the same. Highly compliant patients at RHKG and in the community increased by 15 and 2 patients respectively following intervention.

Conclusion: When the pharmacist intervened to reduce diuretic dose and dose was reduced, it had to be increased again due to presenting symptoms of oedema in 8 patients. A pharmacist intervention resulted in an increased compliance in both hospitalised and community subjects.

Reference:

1. MacFadyen R, Gorski C, Brater C, Struthers A. Furosemide responsiveness, non-adherence and resistance during the chronic treatment of heart failure: a longitudinal study. Br J Clin Pharmacol. 2004; 57(5):622-631.

Pharmacy Information

Update and Evaluation of the Maltese Medicines Handbook
Timothy Scicluna

Herbal Medicines: Development and Evaluation of an Interactive Website
Justine Borg

Comparative Study of Research on Medicinal Plants carried out in Malta
Katrina Saliba

Dissemination of Care Protocols for Community Pharmacy
Kyle Marston

Update and Evaluation of the Maltese Medicines Handbook

Timothy Scicluna

Background: Maltese healthcare professionals use the British National Formulary (BNF) as the main source of reference for medicinal products. A number of products which are available on the local market are not listed in the BNF. The Maltese Medicines Handbook (MMH) was designed to include these medicinal products.

Objectives: To update the MMH to its fourth edition (2015 version)

Design: The products authorised in Malta which are not listed in the BNF were identified by comparing the list published yearly by the Medicines Authority (MA) to the BNF. A draft version of the MMH was published. Evaluation of the MMH was conducted through questionnaires distributed to 30 healthcare professionals from randomly selected pharmacies.

Setting: Community pharmacies in Malta and Gozo

Main Outcome Measures: Evaluation of the updated MMH

Results: The July 2014 MA list consisting of 4438 entries was used for this study. When compared to the BNF, it was observed that 2888 preparations are found in the BNF while 1550 have their trade name, active ingredient or both not available in the BNF. From these 1550 entries, 1321 products have their active ingredient present but the trade name is not the same, while 229 medicinal products have neither their active ingredient nor trade name in the BNF. Eight out of 16 pharmacists who completed the questionnaire stated that they intend to use the MMH frequently.

Conclusion: The number of products included in the fourth edition of the MMH has increased from 510[1] to 1550 since the 2012 edition.

Reference:

1. Corso D. Evaluation of a formulary for non-BNF cited items [dissertation]. Malta: Department of Pharmacy, University of Malta; 2013.

Herbal Medicines: Development and Evaluation of an Interactive Website

Justine Borg

Background: Use of herbal medicines requires knowledge related to side-effects that may occur and compatibility with comorbidities.

Objectives: To assess pharmacists' and patients' knowledge regarding available herbal medicines and to develop a website providing information on the use of herbal medicines.

Design: A self-administered questionnaire was distributed to 45 pharmacists and 156 patients from 22 community pharmacies to determine their knowledge on herbal medicines. Responses were analysed and knowledge gaps, which served as a guide to develop the website, were identified.

Setting: Community pharmacies

Main Outcome Measures: Perception of pharmacists and patients on the use of herbal medicines

Results: A total of 38 pharmacists completed the questionnaire. Of these, 23 stated that the general public has a misplaced faith in herbal medicines, 21 stated that they are poorly informed regarding herbal medicines and 31 stated that they have less knowledge on herbal medicines than on synthetic medicines. A total of 125 patients completed the questionnaire. Lemon (18.4), cranberry (14.4%), tea tree (13.6%) and aloe vera (10.4%) were identified as the most frequently used herbal medicines. The majority (74%) of patients believed that herbal medicines have a beneficial effect, 58% stated that herbal medicines are free from side-effects and 46% were aware of the interactions with synthetic medicines. The website is divided into information for healthcare professions, information for patients, use of herbal medicines in pregnancy, glossary and contact for possible questions.

Conclusion: Both pharmacists and patients showed lack of knowledge regarding herbal medicines. Evaluation of the website will be carried out.

Comparative Study of Research on Medicinal Plants carried out in Malta

Katrina Saliba

Background: For centuries plants have been used as herbal medicine due to their therapeutic properties.[1]

Objectives: Research about herbal products conducted by pharmacy students at the University of Malta was compared to related scientific studies conducted by biology students at Argotti Gardens.

Design: A list of research project titles was obtained from the Pharmacy Department and from Argotti Gardens. A step-by-step content analysis was conducted for each research project. The methods, results, discussion and conclusion of the studies were reviewed and summarised. Similarities and discrepancies between the projects were analysed.

Setting: Department of Pharmacy, University of Malta and Argotti Gardens

Main Outcome Measures: Main features of past research projects of pharmacy and biology students

Results: The first step common to all projects was the extraction of essential oils. This step was followed by analysis of the essential oil using either gas chromatography, infrared spectroscopy or thin layer chromatography. Antimicrobial activity of the essential oils was examined in twelve out of the seventeen studies analysed. Experiments carried out by biology students only were germination inhibition tests and cytotoxicity tests. Seed germination control by the essential oil was determined through *in vitro* methods. Cytotoxicity tests involved determining bioactivity of the essential oils on cancer cell lines.

Conclusion: Evaluation of the studies offers a clearer insight of possible therapeutic benefits of the herbal plants selected. The different perspective of the studies presents a more comprehensive insight about the properties of the plants.

Reference:

1. Benzie IFF, Wachtel-Galor S. Herbal medicine: Biomolecular and clinical aspects. Florida: CRC Press; 2011. p. 5-8.

Dissemination of Care Protocols for Community Pharmacy

Kyle Marston

Background: Community pharmacy services have been present since early 2000BC. Protocols used by pharmacists should be frequently reviewed and updated to help in the delivery of high standard of care to the community.

Objectives: To compile and evaluate a handbook consisting of protocols for community pharmacy practice.

Design: Four previously-published protocols were identified namely; dental conditions[1], paediatric care[2], eye conditions[3] and gastro-intestinal disorders.[4] These protocols were evaluated by an expert panel of 4 pharmacists and streamlined into a handbook.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Evaluation of presentation and content of the developed protocol handbook

Results: The developed handbook consists of 52 pages. Five different sections were incorporated namely; introduction, dental conditions protocol, paediatric care protocol, eye conditions protocol and gastro-intestinal disorders protocol. Protocol review resulted in a reduction in protocol steps by 40.5% and of 58.4% in page content.

Conclusion: All four pharmacists agreed that the book should be available in soft copy. This is mainly due to accessibility, reduction of costs and scientific updates.

References:

1. Attard D. Compliance with protocols in dental conditions [dissertation]. Malta: Department of Pharmacy, University of Malta; 2012.

2. Muscat M. Implementation of protocols for paediatric care [dissertation]. Malta: Department of Pharmacy, University of Malta; 2012.

3. Stivala B. Compliance with protocols in eye conditions [dissertation]. Malta: Department of Pharmacy, University of Malta; 2012.

4. Carbonaro M. Dissemination of treatment protocols in gastro-intestinal disorders [dissertation]. Malta: Department of Pharmacy, University of Malta; 2012.

Pharmacy Administration

Practical Implication in Shelf-Life Extension of Cytotoxic Admixtures
Dylan Said

Proposals for Improving Medication Administration Systems at Mount Carmel Hospital
Nicola Xuereb

Proposals for Improving Pharmacist and Patient Satisfaction within the Pharmacy Of Your Choice
Hannah Bonnici

Risk Matrix for Assessing a Temperature Control System in a Pharmaceutical Warehouse
Matthew Chircop

Time-Motion Study of Community Pharmacy Practice
Andrew Joseph Busuttil

Proposals for Improving Pharmacists' Satisfaction
Petra Abdilla

Practical Implication in Shelf-Life Extension of Cytotoxic Admixtures

Dylan Said

Background: Locally, a stringent 24-hour shelf-life for compounded anticancer admixtures has hindered the introduction of novel approaches in the preparation of doses. Hospital pharmacies must ensure maximal drug utilisation without compromising patient safety.

Objectives: To quantitatively capture cytotoxic waste, perform cost analyses using recorded and retrospective data and suggest proposals to improve compounding processes.

Design: A cross-sectional study was conducted between August and September 2014 and 22,796 doses were retrospectively evaluated for 2014 using the hospital pharmacy logbook databases. Items not included in the national formulary list were excluded from the analyses. Volumetric and dosage values were translated to costs based on 2014 public procurement prices.

Setting: Mater Dei Hospital and Sir Paul Boffa Hospital cytotoxic compounding units

Main Outcome Measures: Volume and cost of wasted anticancer medicines; risks and benefits implicated in shelf-life extension of admixtures

Results: Vial wastage samples observed at the haematology (n=320) and oncology (n=743) units amounted to €10,380 with an annual estimate of €220,000. Waste costs (€301,138) represented approximately 7.2% of the combined yearly expenditure (€4.2M). Thirty six agents were prescribed comprising cytotoxic and biological therapies. Bortezomib and trastuzumab were the agents which contributed predominantly to this waste.

Conclusion: Significant cytotoxic waste is being generated in the settings studied. Advanced grouped preparation of antineoplastics offers cost savings amongst other benefits. Physicochemical integrity is demonstrated for 35 days and 180 days for diluted bortezomib and trastuzumab respectively, supporting shelf-life extension.[1]

Reference:

1. Vigneron J, Astier A, Trittler R, Hecq JD, Daouphars M, Larsson I, *et al*. SFPO and ESOP recommendations for the practical stability of anticancer drugs: An update. Ann Pharm Fr. 2013;71(6):376-389.

Proposals for Improving Medication Administration Systems at Mount Carmel Hospital

Nicola Xuereb

Background: Psychiatric settings present obstacles to smooth medication administration, particularly due to the increased vulnerability of patients.[1]

Objectives: To propose improvements aimed at strengthening and increasing efficiency of the medication administration systems currently practiced at Mount Carmel Hospital (MCH).

Design: Three wards were selected for the direct observational study and three observations were conducted per ward at each time of preparation and administration. A total of 385 preparations and 350 administrations were observed. Questionnaires were disseminated to nurses [N=42] on the three wards to establish the effect of being observed and their opinions regarding medication administration. A focus group meeting was held to evaluate the results and available literature to propose improvements to the current system.

Setting: Mount Carmel Hospital

Main Outcome Measures: Identification of strengths, weaknesses and opinions of the current system of medication administration at MCH to enable proposal of methods to strengthen the system.

Results: Out of 385 observed preparations, 77% of treatment charts were legible. Out of 379 observed administrations, 37% of patients were identified by both name and surname and in 15% of the observations a nurse checked that treatment was taken. The questionnaire indicated that the three factors which nurses consider as contributing most to hindering the administration process are interruptions [n=20], understaffing [n=19] and stress [n=18].

Conclusion: The culture at MCH is a major obstacle to improvement and a patient-centred multidisciplinary approach is needed. Reproducible standard operating procedures need to be adhered to by all staff at MCH with staff taking ownership of their tasks.

Reference:

1. Haw CM, Dickens G, Stubbs J. A review of medication administration errors reported in a large psychiatric hospital in the United Kingdom. Psychiatric Services 2005; 56 (12): 1610-3.

Proposals for Improving Pharmacist and Patient Satisfaction within the Pharmacy Of Your Choice

Hannah Bonnici

Background: The Pharmacy Of Your Choice (POYC) scheme involves collection of free medications for chronic conditions by patients from their chosen pharmacy. It aims to facilitate medicine distribution, expand the pharmacists' role and enhance communication between patients and pharmacists to reduce medication errors.[1]

Objectives: To assess the POYC scheme from a patient and pharmacist perspective and to suggest proposals for improvement.

Design: Two focus groups consisting of both patients and pharmacists were conducted. The total number of participants was 11 for the first focus group and 9 participants for the second focus group. Discussion was led by the investigator prompted by set questions, recorded and transcribed. Questionnaires were administered to 60 patients and 12 pharmacists from 12 community pharmacies. Data was analysed using SPSS® v.23

Setting: Department of Pharmacy, University of Malta and community pharmacies

Main Outcome Measures: Evaluation of patient and pharmacist perception of the POYC scheme and proposals for improvement

Results: Fifty-four patients and 7 pharmacists agreed that the POYC scheme improved the patient-pharmacist relationship. Forty-four patients and all pharmacists were affected by issues related to out-of-stock (OOS) medicines. Thirty-one of these 44 patients and all pharmacists claimed that 2015 was the best year since the introduction of the scheme. Forty-six patients had their medication checked by the pharmacist prior to dispensing. Fifty patients and all pharmacists agreed that electronic prescriptions should replace current prescriptions.

Conclusion: Although the number of OOS medications has been reduced, wastage is still occurring due to hoarding. Suggestions for improvement include educating patients further regarding the running of the scheme and introduction of a small fee for patients for products collected. Pharmacists should be encouraged to inform their patients of changes in medication packaging, doses and indications. Paper prescriptions are causing numerous problems due to illegibility and replacing them with electronic prescriptions reduces risks to patient safety.

Reference:

1. Briffa Rizzo G. Distribution of free medicine in Malta [project]. Msida (Malta): Department of Pharmacy, University of Malta; 2010.

Risk Matrix for Assessing a Temperature Control System in a Pharmaceutical Warehouse

Matthew Chircop

Background: Risk refers to the probability that an action or lack of action will result in an unfavourable situation or an undesired, non-beneficial loss. In the pharmaceutical industry, there is a volatile relationship between the risk a company has to take and its success, since any positive or negative events that might impact on the company will have a significant outcome on the influence of stakeholders.[1]

Objectives: To identify and assess risk factors leading to temperature fluctuations in pharmaceutical warehouses and to propose actions to mitigate these risks.

Design: A temperature logging exercise over a 7-day period was undertaken. A Fault Tree Analysis (FTA) outlining all subsystems involved in temperature control was developed and validated. Further amendments were made following discussion with different stakeholders. Risks obtained from the fault tree were developed into a risk matrix and severity of outcome and probability were assessed. Data obtained from the temperature logging exercise was analysed using the Kruskal-Wallis test to compare mean probe scores.

Setting: Central Procurement and Supplies Unit

Main Outcome Measures: Development of FTA and risk matrix

Results: Fourteen temperature probes were reviewed; 8 probes indicated significant fluctuations in temperature ($p<0.05$) while 6 probes indicated minimal fluctuations ($p>0.05$).

Conclusion: Most probes indicated significant fluctuations in temperature. This might be influenced by the location of the probe. The FTA developed presents faults which can be mitigated for optimum temperature control.

Reference:

1. World Health Organisation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Geneva, Switzerland: WHO Press; 2013.

Time-Motion Study of Community Pharmacy Practice

Andrew Joseph Busuttil

Background: Factors affecting the amount of time dedicated to patients in community pharmacies include employment of additional pharmacy personnel, longer opening hours and workload of the pharmacist.[1]

Objectives: To determine the time spent by pharmacists on community pharmacy activities

Design: Twenty-two community pharmacies were randomly selected and approval to carry out the study was obtained from each pharmacy. The investigator visited each pharmacy, observed and timed the pharmacist's activities, in seconds, using a stopwatch. Observation was carried out without interfering with the pharmacist's work activities.

Setting: Community pharmacies

Main Outcome Measures: Time spent by community pharmacists on different activities

Results: Most time (65076 seconds) was taken up by waiting and personal time, the highest value being in a pharmacy with a pharmacy technician and the lowest value in a pharmacy where there is no pharmacy technician (p=0.054). The second most time-consuming activity is POYC (42650 seconds).

Conclusion: Waiting and personal time consisted of a large proportion of time during the observed hours.

Reference:

1. Lanzon A. Time Management in Pharmacy [project]. Msida (Malta): Department of Pharmacy, University of Malta; 2002.

Proposals for Improving Pharmacists' Satisfaction

Petra Abdilla

Background: In the 2012 International Pharmaceutical Federation 'Global Pharmacy Workforce Report', Malta was reported to have the highest density of pharmacists among the 90 countries considered.[1] Compared to other countries all Maltese pharmacy graduates are in employment despite the high pharmacist to population ratio.

Objectives: To identify the current area of practice of Maltese pharmacists and to assess their job satisfaction.

Design: A questionnaire was compiled and tested for face and content validity by a panel of 10 pharmacists practicing in different areas of the profession. The validated questionnaire was circulated via electronic mail to all 935 registered pharmacists.

Setting: Pharmacists registered with the Pharmacy Council

Main Outcome Measure: Assessment of pharmacists' job satisfaction

Results: Two hundred pharmacists completed the questionnaire of whom 127 were female and year of graduation ranged between 1968 and 2014. Seventy-eight pharmacists work in a community setting. The majority (n=114) of pharmacists earning a yearly gross wage less than €36,000 stated that they are satisfied with their profession. Eight pharmacists earning more than €36,000 per year stated that they are very satisfied. Respondents who are not satisfied were 12 community pharmacists, 2 hospital pharmacists, 2 pharmacists working in wholesale and distribution and 5 pharmacists who did not specify their current employment.

Conclusion: Community pharmacists who were not satisfied stated that they have been working for 11 to 30 years with minimal increments in their yearly salary. Moreover these pharmacists stated that they are underpaid for the advice and service which they offer compared to other healthcare professionals.

Reference:

1. International Pharmaceutical Federation (FIP). 2012 FIP Global Pharmacy Workforce Report. The Hague, Netherlands; FIP; 2012 [cited 2016 Jan 15]. Available from: URL: http://www.fip.org/files/members/library/FIP_workforce_Report_2012.pdf

Industrial Pharmacy, Regulatory Affairs and Clinical Analysis

Evaluation of the Current Partial Manufacturing Process Within the Pharmacy Of Your Choice Scheme
Matthew Gatt

Development of a Greener Selective Acylation Method for Steroids
Darren Cioffi

Steroid Orthoesterification
Christopher Davis Mallia

Feasibility of Solvent Waste Management
Shirley Tabone

Impact of the Identifier System on Pharmaceutical Services
Luca Giudice

Extraction and Analysis of Antibiotics from Biological Fluids
Maria Vella

Evaluation of the Current Partial Manufacturing Process Within the Pharmacy Of Your Choice Scheme

Matthew Gatt

Background: Medicinal products dispensed through the Pharmacy Of Your Choice (POYC) scheme are procured from different suppliers and may vary in their packaging and labelling. Partial Manufacturing (PM) is the process of re-packaging and re-labelling of medicinal products.[1] PM may be adopted to a higher degree by the POYC Unit to overcome issues faced by both patients and pharmacists in a community scenario.

Objectives: To identify issues with packaging and labelling of medicinal products dispensed through the POYC scheme and to evaluate improvements through PM.

Design: Patient and pharmacist perceptions on the packaging and labelling of medicinal products dispensed through the POYC scheme were assessed through structured interviews. Twenty-six pharmacists and 520 patients were selected randomly. Data analysis was carried out using SPSS® v.23. The process of PM within the POYC scheme was analysed using a template for in-depth process analysis and compilation of possible improvements.

Setting: Community pharmacies and POYC unit

Main Outcome Measures: Identification of packaging and labelling issues of medicinal products dispensed through the POYC scheme and evaluation of PM

Results: Twenty-two of the 26 pharmacists stated that introduction of a new labelling system is essential. Most (93%) patients believe that having a simple label indicating the specific use of the drug would increase medication compliance. Most (85%) patients with primary level education believe that medicinal product labels are illegible. Twenty-three of the 26 pharmacists and 81% of patients believe that contrasting colours would make medicines easier to distinguish.

Conclusion: Improved packaging and labelling using PM for medicinal products dispensed through the POYC scheme is imperative to increase patient compliance.

Reference:

1. So T,Wertheimer A. Unit-of-Use Versus Traditional Bulk Packaging [dissertation]. Philadelphia: Temple University School of Pharmacy; 2012.

Development of a Greener Selective Acylation Method for Steroids

Darren Cioffi

Background: The 11,21-dihydroxy steroid has a primary hydroxyl (OH) group at C21 and a secondary OH group at C11. An attempt was made to selectively acylate the primary OH group.

Objective: To identify and use an alternative solvent to dichloromethane (DCM) for the selective acylation of the steroid.

Design: The method by Procopiou et al[1,2] which used DCM as a solvent was adopted. The steroid was dissolved in DCM using equimolar starting material and acetic anhydride at 0 to 5°C. Trimethylsilyl trifluoromethanesulfonate was used as catalyst. The reaction was repeated first using ethyl acetate instead of DCM then using ethyl acetate in excess reagent. Thin layer chromatography and high performance liquid chromatography (HPLC) were used to monitor the reaction.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measure: Percentage yield of the product against retention time obtained from HPLC chromatograms

Results: The highest product yield obtained in DCM was approximately 66%, which started to decrease as the reaction progressed. An estimated product yield of 73% was obtained in ethyl acetate which remained unchanged during the reaction, while limited amount of impurities were observed. In excess reagent, an estimated highest product yield of 50% was obtained within 5 minutes, at which the impurity yield was 30%.

Conclusion: When ethyl acetate was used as solvent with equimolar starting material and reagent, a higher product yield with minimal impurities was observed compared to the other two reactions. This method resulted in a greener selective acylation for the 11,21-dihydroxy steroid molecule.

References:

1. Procopiou PA, Baugh SPD, Flack SS, Inglis GGA. An extremely fast and efficient acylation reaction of alcohols with acid anhydrides in the presence of trimethylsilyl trifluoromethanesulfonate as catalyst. Chemical Communications 1996; 23, 2625-6.

2. Procopiou PA, Baugh SPD, Flack SS, Inglis GGA. An extremely powerful acylation reaction of alcohols with acid anhydrides catalysed by trimethylsilyl trifluoromethanesulfonate. J Org Chem 1998; 63(7): 2342-7.

Steroid Orthoesterification

Christopher Davis Mallia

Background: Product yield can be affected by various factors such as temperature, reagents used and their concentrations. Variation in these factors may lead to yield optimisation.

Objective: To improve the yield of a 17α,21-steroid orthoester which is synthetically produced.

Design: Optimisation of the synthesis of a 17α,21-steroid orthoester was attempted through reaction of a 17α,21-dihydroxy steroid with the corresponding orthoester using the acid catalysts, p-toluenesulfonic acid (PTSA) or pyridinium p-toluenesulfonate (PPSA). Various conditions were tried to observe which conditions gave the best yield. The catalysts were first added at room temperature followed by reflux. An attempt was made by increasing the temperature at which the catalyst was added, followed by reflux. The method which gave the best yield was further modified by increasing reagent excess to determine whether yield could be further improved. HPLC and TLC were used to monitor the reaction. Purification was conducted using a rotary evaporator and vacuum filtration.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Yield in the synthesis of steroid orthoesters

Results: The desired product was not obtained when the catalyst was added at room temperature. When the catalyst was added to reagents at a temperature of 45°C followed by reflux, an estimated yield of up to 73% was achieved when using PTSA as catalyst and 90% yield when using PPSA. When the concentration of the orthoester was increased using PPSA as a catalyst, an estimated yield of 92% was achieved.

Conclusion: When the catalyst was added at a higher temperature followed by reflux, the desired product was obtained. Reactions catalysed using PPSA resulted in better yields. Increasing the amount of reagent in excess did not lead to any significant improvement in the yield obtained when PPSA was used.

Feasibility of Solvent Waste Management

Shirley Tabone

Background: There are presently no facilities for recovery and disposal of pharmaceutical waste such as solvent waste in Malta. Solvents are not managed in non-hazardous public landfills but are sent abroad where they are incinerated or recovered into the pure state.[1]

Objectives: To determine the current local situation with respect to pharmaceutical waste processes, which options are available to dispose of or recycle solvents and whether it is feasible to set up a solvent recovery plant locally.

Design: Structured and unstructured interviews were conducted with two pharmaceutical companies and two waste brokers to evaluate the local scenario. A cost-benefit analysis was carried out by identifying the cost of equipment, electricity, labour and premises incurred to implement a local waste recovery system.

Setting: Pharmaceutical companies and waste brokers

Main Outcome Measure: Cost of disposal of solvent waste in Malta compared to cost of exporting waste for disposal

Results: Methods used for processing solvent waste abroad include waste solvent incineration and solvent distillation such as vacuum distillation.[2] Since different types and amount of solvent waste is generated in Malta, vacuum distillation would be the most appropriate method for recovery of solvents. The cost to build a solvent plant in Malta is about €205,765, while the cost to export solvent waste for disposal is approximately €639,601 per year.

Conclusion: Cost-benefit analysis demonstrated that it is not feasible to build a solvent recovery plant in Malta. It is more cost-effective to upgrade the local incinerator for disposal of solvent waste.

References:

1. National Statistics Office (NSO). Solid waste management in Malta: 2004-2011 [Online]. Malta: NSO; 2013 [cited 2016 Feb 6]. Available from: URL: http://nso.gov.mt/en/News_Releases/Archived_News_Releases/Documents/2013/News2013_002.pdf

2. Capello C, Fischer U, Hungerbühler K. Environmental assessment of waste-solvent treatment options. Journal of Industrial Ecology 2007;11(4):26–38.

Impact of the Identifier System on Pharmaceutical Services

Luca Giudice

Background: An update of the European Union guidelines on 'Good Distribution Practice (GDP) of medicinal products for human use' (2013/C33/01) was published in 2013. This provided the necessary groundwork for future implementation of a unique identifier system.

Objectives: To investigate the recent revisions to the guidelines and examine the impact of the unique identifier on pharmaceutical services.

Design: Literature review regarding the regulation and distribution of medicinal products worldwide was carried out. Comparison between the previous (1994) and current revised (2013) GDP guidelines was undertaken. Assessment of the effect of the revised guidelines on different stakeholders was carried out via semi-structured interviews with 5 inspectors at the Malta Medicines Authority. A progressive focusing technique was used to highlight points of interest. Data from the stakeholders' responses regarding the unique identifier was compiled.

Setting: Malta Medicines Authority

Main Outcome Measures: Comparison of previous and revised GDP guidelines and impact of revised guidelines on stakeholders

Results: The current guidelines cover all areas of the pharmaceutical supply chain whereas the previous guidelines focused only on parts of the supply chain. All interviewees agreed that an update in GDP guidelines was needed since the industry has become more complex. Three of the 5 inspectors thought that more extensive training for Responsible Persons should be available. Some stakeholders are encountering problems as regards supplier verification when the supply chain is complex.

Conclusion: The recent revision in GDP guidelines has provided wholesalers with clear and detailed requirements necessary for the distribution of medicinal products. The pharmaceutical industry has become increasingly complex over the past two decades, increasing the risk of falsified medicines entering the legal supply chain, hence greater control is required.

Extraction and Analysis of Antibiotics from Biological Fluids

Maria Vella

Background: Diabetic patients have impaired wound healing due to abnormal inflammatory pathways, neuropathy and peripheral arterial disease (PAD). This can lead to foot ulceration, infection and gangrene which often require lower limb amputation.[1]

Objectives: To observe characteristics of patients admitted for amputation or debridement procedures.

Design: Ethics approval was obtained. A patient information form was developed. This form included patient characteristics and patient medical history. Patients who met the inclusion criteria and who were about to undergo an amputation or a debridement procedure were selected following informed written consent. Patient information forms were completed from patient hospital files. Data was analysed using SPSS® version 20.

Setting: Mater Dei Hospital (June 2014 to March 2015)

Main Outcome Measures: Patient demographic data, smoking habits, past medical history, antibiotic administration and wound characteristics of patients admitted for amputation or debridement procedures

Results: Fifty patients (33 male, 17 female; age 28-92 years) participated in the study. Six patients were admitted for a debridement and 44 patients for amputation procedures. Forty-nine patients were diabetic (35 Type 2, 14 Type 1), 44 patients suffered from neuropathy and 47 patients suffered from PAD (35 severe, 12 mild to moderate). Almost all patients who were suffering from PAD (n=47) were suffering from diabetes. A positive correlation was observed between the severity of PAD and diabetes (p-value=0.020).

Conclusion: The presence of diabetes can have several complications such as PAD, which increases the need for amputation and debridement procedures and impacts on the amount of antibacterial reaching the peripheries.

Reference:

1. Gibbons GW, Habershaw G. Special considerations for the diabetic foot. In: Coffman JD, Eberhardt RT, editors. Peripheral arterial disease: Diagnosis and treatment. New Jersey: Humana Press; 2003. p 265-79

Medicinal Chemistry I

Optimisation of *in silico* Designed Fatty Acid Synthase Modulators Derived from the Lead Molecule Orlistat
Ramon Sciberras

Evaluation of the Utility of the Aminopiperazinone, Aminoimidazole and Aminoquinazoline Scaffolds as Leads in β-secretase Modulation for the Management of Alzheimer's Disease
Luke Borg

Evaluation and Optimisation of *in silico* Designed A2A Adenosine Receptor Antagonists for the Treatment of Parkinson's Disease
Yana Vella

Evaluation and Optimisation of *in silico* Designed PDE4 Receptor Modulators
Daniel Attard

Evaluation and Optimisation of *in silico* Designed b-Secretase Modulators for the Treatment of Alzheimer's Disease
Keith Xuereb

Evaluation and Optimisation of *in silico* Designed Sphingosine-1-Phosphate (S1P) Receptor Modulators for the Management of Multiple Sclerosis
Daphne Gusman

Optimisation of *in silico* Designed Fatty Acid Synthase Modulators Derived from the Lead Molecule Orlistat

Ramon Sciberras

Background: *In silico* studies have established a mechanism for the inhibition of the thioesterase domain in human fatty acid synthase, an enzyme overexpressed in tumours. As a result of this action, disease prognosis is improved.[1]

Objectives: To propose a series of molecules with potential utility through a database for high throughput screening using information extrapolated from crystallographic data, bioactive conformation analysis, structure activity relationship and *in silico* estimations on affinity of small molecules to fatty acid synthase.

Design: The X-ray crystallographic deposition 2PX6 describing orlistat bound to the thioesterase domain in the human fatty acid synthase were used. Bioactive conformations of orlistat were generated, calculating the ligand binding energy and the ligand binding affinity (LBA) for each conformer. Using these two parameters the optimal binding pose was established. *de novo* design based on the three-dimensional volume which was occupied by orlistat were carried out. LigBuilder®, Sybyl®, VMD and Chimera and XSCORE were used for LBP elucidation and *de novo* design, modelling, molecule visualisation and animation, and LBA calculation respectively.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: LBP elucidation and *de novo* design; modelling; molecule visualisation and animation; LBA calculation

Results: The 3 modelled seeds generated 403 new entities. These newly generated molecules were checked against Lipinski's rule of 5, out of which 173 molecules were compliant.

Conclusion: Rational structure based design can be seen as the stepping stone for further research in the use of orlistat as a possible target as a drug to be used effectively as a biomarker and a chemotherapeutic agent.

Reference:

1. Richardson RD, Smith JW. Novel antagonists of the thioesterase domain of human fatty acid synthase. Mol Cancer Ther. 2007;6(7):2120–6.

Evaluation of the Utility of the Aminopiperazinone, Aminoimidazole and Aminoquinazoline Scaffolds as Leads in β-secretase Modulation for the Management of Alzheimer's Disease

Luke Borg

Background: Alzheimer's disease is a neurodegenerative disorder associated with dementia. Formation of amyloid-beta plaques, which is mediated by β-secretase, are characteristic hallmarks associated with disease pathogenesis. This enzyme is consequently cited in literature as a potential disease modifying target for this condition.

Objectives: To utilise the aminopiperazinone, aminoimidazole and aminoquinazoline scaffold for the *in silico* design of novel structures capable of inhibition of the β-secretase enzyme.

Design: Three Protein Data Bank (PDB) crystallographic depositions describing the bound coordinates of the holo- β-secretase bound to an aminopiperazinone, aminoimidazole and aminoquinazoline molecule (PDB ID 3u6a, 3igb and 2q11 respectively) were identified and their affinity measured using X-Score® to create a comparative baseline. 2D topology maps were generated in Poseview® and used together with SAR data from literature to create 2 seed structures from each representative molecular class which were planted into their cognate ligand binding pockets such that novel moieties could be introduced at the pre-designated growing sites using the GROW module of LigBuilder® v1.2.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular visualisation, molecular modelling and seed generation

Results: Two hundred novel structures were generated from each seed segregated into families according to structural similarity and ranked by affinity and physicochemical parameters. The affinity of the optimal generated molecules exceeded baseline (pKd = 8.87 and 6.8, 9.95 and 8.35, 9.99 and 10.00 versus 6.38, 5.98 and 6.76) for both seeds of the aminopiperazinones, aminoimidazoles and aminoquinazolines respectively. Assessment for compliance with Lipinski's rules yielded 176, 58 and 15 molecules from the aminoimidazole, aminopiperazinone and aminoquinazoline seeds respectively.

Conclusion: *In silico* calculated high affinity and predisposition for cerebral penetration makes a case for synthesis of the optimal generated molecules and further *in vitro* validation.

Evaluation and Optimisation of *in silico* Designed A2A Adenosine Receptor Antagonists for the Treatment of Parkinson's Disease

Yana Vella

Background: Parkinson's disease (PD) is a neurodegenerative condition which arises from progressive damage of intra-cerebral dopaminergic neurons resulting in decreased dopamine concentration and generalised muscle contractions. Management of PD includes restoring dopamine levels to compensate for the loss of dopamine input. Research on the design of non-dopaminergic agents specifically acting at the A2A adenosine receptors found abundantly in the basal ganglia co-localised with the D2 receptor is relevant. A2A adenosine receptor inhibition enhances D2 receptor signalling, increasing dopamine levels and causing motor symptoms to subside.[1]

Objectives: To design and optimise *in silico* novel molecules capable of antagonising the A2A adenosine receptor using the investigational antagonist SCH412348 as a lead molecule through a *de novo* approach for management of PD.

Design: PDB crystallographic deposition 3EML describing the bound co-ordinates of human A2A receptor bound to the experimental drug ZM241385 was used as a template for this study. The affinity of the complex was established; SCH412348 docked into the A2A receptor ligand binding pocket and conformational analysis performed such that two SCH412348 conformers with optimal stability and affinity were identified each being used to generate seeds capable of sustaining molecular growth.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display, modelling, seed generation and ligand binding affinity (LBA) calculation

Results: This process yielded 1621 structures which led to identification of 17 Lipinski Rule compliant molecules with a LBA (pKd) ranging from 6.45 to 9.92.

Conclusion: The 17 novel molecules are robust for further optimisation and molecular dynamics validation. The optimal structures will be recommended for synthesis and *in vitro* studies.

Reference:

1. Cieślak M, Komoszyński M, Wojtczak A. Adenosine A2A receptors in Parkinson's disease treatment. Purinergic Signalling 2008; 4 (4):305–12.

Evaluation and Optimisation of *in silico* Designed PDE4 Receptor Modulators

Daniel Attard

Background: Cyclic nucleotide phosphodiesterase 4B (PDE4B) isozymes catalyse the hydrolysis of cyclic AMP (cAMP) to 5' AMP.[1] Inhibition of the receptor preserves intracellular cAMP resulting in the suppression of tumour necrosis factor alpha (TNF-α) and other pro-inflammatory cytokines whilst promoting the expression of anti-inflammatory mediators.

Objectives: *De novo in silico* design of novel structures capable of PDE4B inhibition with potential for clinical use in therapeutic management of autoimmune, anti-inflammatory disorders.

Design: Protein databank crystallographic deposition 4MYQ describing the holo-PDE4B: antagonist A-33 complex was used as a template. The small molecule was separated from the complex and baseline binding affinity was determined. An analogue series of xanthine derivatives obtained from Jagiellonian University in Poland were used. Each xanthine analogue was successively docked into the PDE4B ligand binding pocket, conformational analysis was performed and the optimal scaffold for each was determined. The two overall best scaffolds were selected for construction of a seed structure and seed modelling was based on 2D topology maps generated in Poseview®. *De novo* growth was subsequently sustained using LigBuilder® v1.2 and the generated structures were evaluated for Lipinski Rule compliance.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular display, modelling and seed generation

Results: Six families giving a total of 1012 novel structures were generated. Of these, 240 molecules were found to be Lipinski Rule compliant and affinities (pKd) ranged between 5.27 and 9.73 versus 7.55 for A-33.

Conclusion: The xanthine scaffold is suitable for the design of PDE4B modulators. The designed molecules were computationally locked into an antagonist conformation. The optimal structures require further computational validation, synthesis and *in vitro* testing.

Reference:

1. Cai A, Hoffman CS. Determining the amino acids involved in inhibition of PDE4B by structurally-diverse compounds. Research Science Institute; July 2011.

Evaluation and Optimisation of *in silico* Designed β-Secretase Modulators for the Treatment of Alzheimer's Disease

Keith Xuereb

Background: The β-Secretase enzyme is an aspartic acid protease important for the formation of myelin sheaths in the peripheral nerves of the brain.[1] It has been implicated in the formation of the β amyloid plaques that characterise Alzheimer's disease (AD).

Objectives: This study utilises the AZD3839, GRL-8234 and an indoleacylguanidine experimental drug scaffolds for the *de novo in silico* design of novel structures capable of modulating the β–Secretase enzyme with potential for clinical use in the therapeutic management of AD.

Design: Protein Data Bank crystallographic depositions describing the bound co-ordinates of the three lead structures complexed with β-Secretase were identified (PDB ID- 2VKM, 4B05, 4IVS respectively). The affinity of each small molecule for its cognate receptor was calculated in X-Score® v1.3 for baseline affinity establishment. 2D topology maps explaining the important interactions between resident ligand and receptor were generated in each case using Poseview®. Seed structures (n=3, 2, 3 respectively) were created, onto which novel moieties were computationally introduced using the GROW module of LigBuilder®. The resulting structures were then selected according to Lipinski's Rules.

Setting: Department of Pharmacy, University of Malta

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

Results: Four hundred thirty six de novo molecules were generated; 4 molecules were found to be Lipinski Rule compliant, hence will be further used in the study for pharmacophoric evaluation.

Conclusion: This study was of utility in the identification of novel high affinity, Lipinski Rule compliant molecules which could be further optimised to yield clinically useful agents in the management of AD.

Reference:

1. Shimizu H, Tosaki A, Kaneko K, Hisano T, Sakurai T, Nukina N. Crystal Structure of an Active Form of BACE1, an Enzyme Responsible for Amyloidβ Protein Production. Mol Cell Biol. 2008; 28(11): 3663–3671.

Evaluation and Optimisation of *in silico* Designed Sphingosine-1-Phosphate (S1P) Receptor Modulators for the Management of Multiple Sclerosis

Daphne Gusman

Background: Multiple Sclerosis (MS) is a chronic autoimmune disorder affecting the central nervous system by inflammation, demyelination and neurodegeneration. Sphingosine-1-phosphate receptor (S1PR1) modulators have been approved for the management of MS. Phosphorylated fingolimod mimics endogenous sphingosine-1-phosphate (S1P), a bioactive lipid that regulates remyelination.[1]

Objectives: To use fingolimod as a lead molecule for further iterative design of novel S1PR1 modulators that are not associated with first-dose bradycardia.

Design: The X-ray crystallographic deposition 3V2Y describing the holo-selective antagonist mimic, ML5, bound to S1PR1 was selected as a template. Molecular modelling was carried out in Sybyl-X®. The apo S1PR1 Ligand Binding Pocket delineated the 3D-space within which novel molecular growth could be sustained on four seed structures. Novel moieties could be computationally introduced at loci considered non-critical for binding onto the fingolimod conformer identified as optimal through conformational analysis and topology maps.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display, ligand binding affinity (LBA) calculation, seed generation

Results: A total of 630 molecules (n=30, 200, 200 and 200 for seeds 1 to 4 respectively) were generated and classified according to physicochemical parameters, structural similarity and binding affinity. Assessment for Lipinski rule compliance further reduced the cohort size to 125 over 4 seeds (seed number=3, 9, 2 and 111).

Conclusion: The optimal structures from each pharmacophoric class are suggested for optimisation, synthesis and *in vitro* validation to assess potential clinical efficacy.

Reference:

1. Brinkmann V, Billich A, Baumruker T, Heining P, Schmouder R, Francis G, *et al.* Fingolimod (FTY720): Discovery and development of an oral drug to treat multiple sclerosis. Nat Rev Drug Discov. 2010;9(11):883-97.

Medicinal Chemistry II

Evaluation of the Utility of the Abiraterone Scaffold as Lead in CYP17A1 Receptor Modulation for the Management of Prostate Cancer
Kurt Degabriele

Evaluation and Optimisation of *in silico* Designed CYP17A1 Receptor Modulators for the Management of Prostate Cancer
Michael Grima

Evaluation and Optimisation of *in silico* Designed Non-Steroidal Oestrogen Related Receptor (ERR) α Modulators for the Management of Breast Cancer
Keith Muscat

Evaluation and Optimisation of *in silico* Designed HIV Reverse Transcriptase Modulators
Marie Mifsud

Evaluation and Optimisation of *in silico* Designed Oestrogen Receptor Modulators for the Management of Breast Cancer
Sharon Zammit

Evaluation of the Utility of the Rubiatriol Scaffold as Lead in Angiotensin Converting Enzyme Modulation for the Management of Hypertension
Althea Marie Xuereb

Evaluation of the Utility of the Abiraterone Scaffold as Lead in CYP17A1 Receptor Modulation for the Management of Prostate Cancer

Kurt Degabriele

Background: Abiraterone is a selective, irreversible inhibitor of the CYP17A1 enzyme resulting in inhibition of oestrogen and androgen biosynthesis helping to lower the rate at which prostate cancer develops.[1]

Objectives: To use abiraterone as a lead molecule for further iterative design of novel anti-prostate cancer drugs which modulate the CYP17A1 receptor; optimisation of this ligand could yield better CYP17A1 enzyme inhibitors with anti-prostate cancer properties.

Design: The PDB crystallographic deposition describing the bound co-ordinates of abiraterone and the CYP17A1 enzyme was selected as a template. Abiraterone and the CYP17A1 were examined from a structure activity relationship point of view using available literature. Sybyl®-X v1.1 was used to generate the apo-receptor of CYP17A1 and abiraterone extract. Both abiraterone extract and the apo-receptor were later imported into X-SCORE® v1.3 to establish baseline affinity. A total of three seeds were created using Sybyl®-X v1.1, from which *de novo* molecules were generated using LigBuilder® v1.2. Novel structures divided into various families were acquired having different pharmacophores. All molecules were selected according to Lipinski rule of five for further study analysis.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular display, modelling, seed generation, LBE calculation

Results: A total of 727 *de novo* molecules were generated of which 465 *de novo* molecules were found to be Lipinski rule compliant to be used further in the study for pharmacophoric evaluation.

Conclusion: Some *de novo* molecules exhibit a pKd higher than baseline value of 7.04 for abiraterone molecule. These are useful candidates for further studies researching alternatives to abiraterone.

Reference:

1. Attard G, Reid AH, Yap TA, Raynaud F, Dowsett M, Settatree S et al. Phase I clinical trial of a selective inhibitor of CYP17, abiraterone acetate, confirms that castration-resistant prostate cancer commonly remains hormone driven. J Clin Oncol 2008; 26: 4563–71.

Evaluation and Optimisation of *in silico* Designed CYP17A1 Receptor Modulators for the Management of Prostate Cancer

Michael Grima

Background: Ketoconazole is a broad spectrum imidazole antifungal with weak and non-specific CYP17A1 inhibitory properties. Orteronel is a novel hormonal therapy which inhibits the 17,20 lyase activity of the enzyme CYP17A1 essential for androgen synthesis. Pre-clinical studies have demonstrated that these drugs decrease androgen levels and cause reduction of the prostate gland.[1]

Objectives: To use ketoconazole and orteronel as lead molecules for further iterative design of *de novo* anti-prostate cancer drugs resulting in improved CYP17A1 receptor modulation.

Design: The PDB deposition 3RUK describing the bound co-ordinates of abiraterone with the CYP17A1 enzyme was used as a template. The structure activity relationships of abiraterone and the CYP17A1 receptor were analysed from literature and separated resulting in the apo receptor and abiraterone extract. Ketoconazole was obtained from PDB complex 1JIN and further examined, while orteronel was modelled in Sybyl®-X v1.1 and evaluated. Both apo receptor and extracts were later introduced into X-SCORE® v1.3 to establish baseline affinity. A total of five seeds were created using Sybyl®-X v1.1, 3 for orteronel and 2 for ketoconazole. From these seeds a large number of *de novo* molecules were generated where each novel molecule was grouped into different families exhibiting a different pharmacophoric structure.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular display, modelling, seed generation, LBE calculation

Results: A total of 1000 *de novo* molecules were generated, of which 65 novel molecules were filtered based on Lipinski rule of 5 and narrowed down to 6 molecules for ketoconazole and 59 molecules for orteronel.

Conclusion: All novel molecules which exhibited a pkd value greater than the baseline value of abiraterone were the candidates chosen for further *in silico* drug design.

Reference:

1. Watson PA, Arora VK, Sawyers CL. Emerging mechanisms of resistance to androgen receptor inhibitors in prostate cancer. Nature Reviews Cancer 2015; 15: 701-711.

Evaluation and Optimisation of *in silico* Designed Non-Steroidal Oestrogen Related Receptor (ERR) α Modulators for the Management of Breast Cancer

Keith Muscat

Background: Oestrogen related receptor alpha (ERRα) maintains growth of breast cancer cells by simulating oestrogen receptor function and vital cancer cell metabolism. This makes ERRα a viable drug target for ER-negative breast cancer management. The experimental molecule SR16388 is an inverse ERRα agonist and was used as a template for the *in silico* design of novel ERRα modulators.

Objectives: To use the scaffold of SR16388 to design structures capable of inhibiting the ERRα whilst reducing steroidal adverse effects.

Design: The Protein Data Bank was used to find an X-ray crystallographic deposition (2PJL) describing the bound co-ordinates of an inverse agonist: ERRα complex.[1] This was modelled and the components separated. SR16388 was docked into the ERRα Ligand Binding Pocket and conformational analysis was performed. The optimal scaffold was identified for further modelling. Structure activity relationship studies guided the formation of seed structures onto which moieties were attached to create novel structures. Modelling and conformational analysis were done using SYBYL-X®v1.1. The GROW module of LigBuilder® v.1.2 was used to create novel structures.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule modelling, seed generation, creation of novel non-steroidal molecules with a high ligand binding affinity to the ERRα

Results: A total of 310 molecules were generated (n=67, 84 and 159 from seeds 1, 2 and 3 respectively). These were segregated into families according to their pharmacophores and ranked in relation to their physicochemical properties and Lipinski Rule compliance.

Conclusion: Non-steroidal ERRα high affinity structures that were Lipinski Rule compliant were designed. These were identified for optimisation and *in vitro* validation to propose lower side-effect profile molecules suitable for long-term use.

Reference:

1. Kallen J, Lattman R, Beerli R, Blechschmidt A, Blommer MJ, Geiser M, *et al*. Crystal structure of human oestrogen-related receptor α in complex with a synthetic inverse agonist reveals its novel molecular mechanism. Journal of Biological Chemistry. 2007;282(32):23231-23239.

Evaluation and Optimisation of *in silico* Designed HIV Reverse Transcriptase Modulators

Marie Mifsud

Background: Reverse transcriptase (RT) is a key enzyme which regulates human immunodeficiency virus (HIV) replication. Through knowledge of the 3D structure of this enzyme, molecular chemists were able to design drugs capable of affecting enzyme function thus interfering with the HIV-1 lifecycle.

Objectives: To design novel non-nucleoside reverse transcriptase inhibitors (NNRTIs) which are able to bind at an alternative locus to the catalytic site of RT causing a conformational change that inhibits conversion of viral RNA to DNA.

Design: Five protein crystallographic depositions each describing the NNRTIs, nevirapine (3HVT), rilpivirine (2ZD1), doravirine (4NCG), MK-4965 (3DRP) and GW695634 (3DOL), bound to RT were selected as templates for this study. Structure activity relationship data guided the creation of a seed structure for each lead NNRTI. The seeds were planted into the RT ligand binding pocket and novel molecular growth sustained at non-critical binding sites in each case. The ligand binding affinity (pKd) of the generated molecular cohort was compared to that of the lead molecules and categorised for each lead according to pharmacophoric similarity, physicochemical parameters and pKd.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Design of novel NNRTIs with increased binding affinity and adequate bioavailability capable of modulating RT enzyme

Results: A total of 1266 novel structures were generated from 7 seed structures. Lipinski rules of compliance reduced this cohort to 824 molecules.[1] The optimal structures derived from each pharmacophoric family were proposed for optimisation of critical chemical moieties, synthesis and *in vitro* validation.

Conclusion: *de novo* molecules designed will be compiled into a library for high throughput screening processes and future optimisation.

Reference:

1. Lipinski CA. Lead and drug like compounds: The rule-of-five revolution. Drug Discovery Today: Technologies 2004;1(4):337–341.

Evaluation and Optimisation of *in silico* Designed Oestrogen Receptor Modulators for the Management of Breast Cancer

Sharon Zammit

Background: The experimental drug GW 5638 has been reported to be of use in the management of breast cancer by antagonising the oestrogen receptor (ER) through a novel binding modality. In comparison to tamoxifen, the dimethylaminoethyoxy group is replaced by an acrylate side chain which gives the molecule beneficial oestrogenic properties making it a more potent antagonist than tamoxifen with no uterotrophic behaviour.[1]

Objectives: To use this molecule as a template for further iterative design of novel drugs with potential clinical use in the management of tamoxifen-resistant breast cancer.

Design: X-Ray crystallographic deposition 1R5K describing ERα bound to GW 5638 was used as a template. This was followed by analysis of the ligand-binding pocket and *in silico* design of novel molecules capable of modulating this proposed structure. SYBYL-X®, X-SCORE®, LigBuilder®, Visual Molecular Dynamics (VMD), Accelrys Draw®, Accelrys Discovery Studio® 3.5 and Protein Data Bank were used to generate the results.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: To discover and optimise *in silico* high binding affinity ERα antagonistic drug molecules

Results: Analyses of the ligand binding pocket resulted in 5 Lipinski-rule-compliant molecules. These generated a total of 1000 molecules, each classified into different chemical families, 482 of which conformed to Lipinski's Rules. Highest and lowest-ranked molecules in each chemical family were structurally-analysed, which yielded chemical moieties responsible for optimal chemical binding.

Conclusion: *de novo* molecules created and optimised present viable leads for high-throughput screening, leading to identification of novel ERα antagonists for the use in the management of breast cancer.

Reference:

1. Wu YL, Yang X, Ren Z, McDonnell DP, Norris JD, Willson TM *et al*. Structural basis for an unexpected mode of SERM-mediated ER antagonism. Molecular Cell. 2005; 18(4): 413-424.

Evaluation of the Utility of the Rubiatriol Scaffold as Lead in Angiotensin Converting Enzyme Modulation for the Management of Hypertension

Althea Marie Xuereb

Background: Angiotensin Converting Enzyme (ACE), a key enzyme in the renin angiotensin system for production of angiotensin II is a target for cardiovascular disease management. Arisawa*et al*[1] claim that the naturally occurring triterpene rubiatriol has ACE-inhibitory activity.

Objectives: To validate the hypothesis made by Arisawa *et al*. using *in silico* techniques and to design novel high affinity structures for the ACE using *de novo* methods.

Design: Protein Databank crystallographic deposition 2C6N[2] describing the ACE:lisinopril complex was selected as a template. Rubiatriol was docked into the ACE_ Ligand Binding Pocket (LBP) and conformational analysis performed. Structure activity relationship data and 2D topology maps highlighting the interactions of the optimal conformer with the LBP amino acids, guided the creation of five seed structures onto which novel growth was sustained within the ACE LBP. The generated molecular cohort was assessed for Lipinski Rule compliance.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule modelling, seed generation, *de novo* design of novel structures

Results: The Lipinski rule compliant molecular cohort was segregated into families and ranked according to binding affinity and physicochemical parameters for each seed. The highest ranking molecules were identified for optimisation and *in vitro* validation.

Conclusion: This study is valuable for validation of the hypothesis of Arisawa *et al*. using *in silico* methods and for suggesting that the rubiatriol scaffold was a suitable lead for the generation of ACE modulating molecules.

References:

1. Arisawa M, Ueno H, Nimura M, Hayashi T, Morita N. Rubiatriol, a new triterpenoid from the Chinese drug, 'qiáncáogén', Rubiacordifolia. Journal of Natural Products. 1986; 49 (6):1114-1116.

2. Corradi HR, Schwager SL, Nchinda AT, Sturrock ED, Acharya KR. Crystal structure of the N Domain of human somatic Angiotensin I-converting enzyme provides a structural basis for domain-specific inhibitor design. J Mol Biol. 2006; 357 (3): 964-74.

M.Sc. Pharmacy
Dissertation Descriptions

Cleaning Validation of a Glassware Washer
Charlene Apap

The Fair Pricing of Medicines
Kurt Anthony Borg

Practical Pre-Requisites for Pharmaceutical Technology
Daniel DeGaetano

Accessibility to Medicines: The Perception of the Pharmaceutical Industry
Kirsten Mangion

Cleaning Validation of a Glassware Washer
Charlene Apap

Laboratory glassware used for analysis is not product-specific. The glassware unit must be free of contaminants since it is essential that laboratory testing is conducted without interference from residues from previous analyses. The aim is to establish and assure, with documented evidence, that residue from product and detergent does not exceed established acceptance criteria.

The Fair Pricing of Medicines
Kurt Anthony Borg

A formula to determine fairness of medicine pricing is devised. Core factors affecting price are identified, a numerical value is assigned to each factor and an index indicative of price fairness is calculated. This index is applied to assess fairness in current prices for medicines with comparable indications.

Practical Pre-Requisites for Pharmaceutical Technology
Daniel DeGaetano

Gap analysis to evaluate practical skills that should be attained by pharmaceutical technology graduates and skills which are actually attained in practice is undertaken by focus groups and interviews involving students, graduates, academia and the pharmaceutical industry. Following this gap analysis, recommendations on how to improve skills according to the industry's expectations of the pharmaceutical technology course offered by the Department of Pharmacy are proposed.

Accessibility to Medicines: The Perception of the Pharmaceutical Industry
Kirsten Mangion

Perception of the pharmaceutical industry towards accessibility to medicines within the European Union, particularly the Maltese scenario, is discussed. The study examines the impact of the legislative framework on the industry, assesses opportunities and issues encountered by Maltese companies and proposes suggestions to facilitate local accessibility to medicines. Literature review, questionnaires and interviews are used to capture data. Barriers to accessibility and proposals to overcome these issues are determined taking into consideration the perspective of the stakeholder.

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

Access to Medicines in Small Countries
Yana Chircop

Pharmacoeconomics, Human Resources and Turnover
Luke Farrugia

Qualification of a Water System
Noeleene Mangion

Risk and Temperature Control in Community Pharmacies
Cristina Miceli

Cost and Access to Medicines in the Health System
Mandy Muscat

Anti-Counterfeiting and Safety Packaging in Tablets
Celine Psaila

Access to Medicines in the National Formulary
Chiara Scerri Herrera

Information Technology in the Pharmaceutical Field
Steven Schiavone

Child-Resistant and Senior Friendly Packaging
Lara Sciberras

Medicine Management Processes on Hospital Wards
Stephanie Wonnacott

Access to Medicines in Small Countries
Yana Chircop

Limitations of access to medicines in small countries, which may adversely affect patients, can be due to various factors influencing a small pharmaceutical market. This project explores the difficulties and the obstacles associated with a small pharmaceutical market due to a small patient population. Research is done within the limits specified through the definition of a small pharmaceutical market. Literature search and interviews with relevant personnel are conducted, focusing on the Maltese scenario and comparing with other pharmaceutical markets.

Pharmacoeconomics, Human Resources and Turnover
Luke Farrugia

This project will analyse and examine the relationship between the number of employees working in pharmaceutical companies in Malta, including manufacturing and wholesale businesses, and the annual turnover of these companies. This study will also evaluate the various job classifications in the local pharmaceutical market and compare them with the actual turnover of the companies responding to the questionnaire.

Qualification of a Water System
Noeleene Mangion

The purpose of this project is to validate the water system at a local pharmaceutical company. Tests on water from the different sampling points were carried out according to Ph. EUR Version 8.0. Appropriate measures were taken based on the results of these tests. After a four week period of testing during the Operational Qualification and Performance Qualification, the water system was qualified and validated for pharmaceutical use.

Risk and Temperature Control in Community Pharmacies
Cristina Miceli

The quality of medicines is dependent on a multitude of factors, not least of which is their storage. A major influence on the quality of the storage and therefore the ongoing quality of the product is the temperature of the surrounding environment. Taking into account the facts presented by stakeholders when it comes to risks of temperature deviations, this study highlights the local temperature scenario. A validated questionnaire dealing with the upkeep of pharmacy temperatures and product storage is developed and administered to community pharmacies, samples from logbooks are also collected and analysed.

Cost and Access to Medicines in the Health System
Mandy Muscat

Cost is one of the main barriers to access, when it comes to pharmaceuticals. In this study the policies involved in the determination of costs and budget allocation within this context will be studied. Data relating to access to medicinal products in Malta and Italy will be collated and compared. The expenditure on pharmaceuticals both as a percentage of healthcare expenditure, as well as a percentage of the gross domestic product will also be evaluated.

Anti-Counterfeiting and Safety Packaging in Tablets
Celine Psaila

Patient safety is the main goal of anti-counterfeiting measures. The aims of this project are to identify, evaluate and understand the knowledge and awareness regarding anti-counterfeiting, both locally and internationally. Technologies used in anti-tampering devices as part of safety packaging in tablets are researched. The faults in the system are recognised in order to highlight the stages possible for counterfeiters to infiltrate the legal supply chain.

Access to Medicines in the National Formulary
Chiara Scerri Herrera

This study will investigate the impact of national formularies on access to medicines. Particular issues addressed will include European directives and national legislation, as well as the limitations of certain medicinal products included in the national formulary. The influence pharmacists and other healthcare professionals have on the system in Malta will also be evaluated. Interviews will be conducted with stakeholders involved in the decision making process.

Information Technology in the Pharmaceutical Field
Steven Schiavone

The project is based on the study of data tracking and different information technology systems found within the pharmaceutical industry, while considering advantages and disadvantages of these systems, types of data tracked, how data is processed, levels of accessibility to historic database and storage as well as the objectives and use for collecting data within pharmaceutical industry.

Child-Resistant and Senior Friendly Packaging
Lara Sciberras

Nowadays many medicinal products come with a child resistant package in order to prevent drug intoxication of children. However many elderly experience difficulties in opening such a package. This study focuses on evaluating the relationship between a pharmaceutical package being child resistant and at the same time, elderly friendly. It also sets out to establish the pharmacists' awareness of this type of packaging and their experience in dealing with any problems arising from suck packaging.

Medicine Management Processes on Hospital Wards
Stephanie Wonnacott

Two wards at Mater Dei Hospital were chosen and an assessment of the medicine management processes employed in these wards was performed at baseline using a specifically-designed evaluation sheet. Corrective actions and improvement in the system are implemented over a four week period. A questionnaire directed to all nursing staff in these wards is implemented at baseline and the end of the four week period.

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

Design of Novel Efflux Pump Inhibitors using P-Glycoprotein as a Target

Mark Joseph Bondin

P-glycoprotein is an efflux transporter which regulates entry of molecules into cells. Literature shows that verapamil, an antiarrhythmic drug, shows P-glycoprotein inhibitory effects. The Protein Data Bank crystallographic deposition 4M2S was used to delineate the ligand binding pocket into which verapamil was docked. It was used as a scaffold from which seed structures were generated and novel growth could be sustained. The molecular cohort obtained was then analysed with respect to affinity and Lipinski Rule compliance such that the optimal structures will be proposed for *in vitro* validation.

Monitoring of Patients with Heart Failure

Rebecca Bugeja

Non-compliance is associated with poor treatment outcomes and clinical repercussions. Heart failure patients recruited from five pharmacies are divided into a control and a study group. Pharmacist intervention is carried out in the study group through distribution and explanation of personalised medication charts with the aim of improving their understanding of prescribed medications. Patient compliance to medications is measured. A questionnaire is completed to assess usefulness of the developed medication chart. The impact of the intervention is established through an adherence questionnaire.

Development and Evaluation of the Pharmacy Practice Resource Unit

Francesco Cassar

The Pharmacy Practice Resource Unit (PPRU) is being updated to reflect contemporary pharmacotherapy and student research requirements throughout the pharmacy course. A questionnaire was distributed to 135 pharmacy students and 70 completed the questionnaire. Results show that 69 students know the location of the PPRU and 68 students have entered the PPRU. The majority of students (69) used the PPRU for pharmacy practice tutorials whilst 1 student used the PPRU for research purposes. Requests for sponsorship have been sent to medical representatives and 179 new medicinal products were collected.

Design of RAS inhibitors using Polyphenolic Extracts from Green Tea as a Scaffold

Stephanie Cassar

K-Ras proteins are involved in the epidermal growth factor receptor signalling network which controls proliferation and apoptosis. Aberrant K-Ras plays a role in 30% of all human cancers including colon and lung cancer. The aim of this project is to create an inhibitor using the green tea extract, epigallocatechin-3-gallate, as a scaffold. Twenty-one conformers have been generated *in silico*, the one with the greatest difference between ligand binding affinity and ligand binding energy has been chosen to be further developed to produce K-Ras inhibitors for use in cancer prevention.

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

Daniel Chetcuti

NPI-0052 is a β-lactone-y-lactam compound isolated from the marine organism *Salinispora tropica*. NPI-0052 inhibits all catalytic sites of the proteasome, resulting in a build-up of misfolded and aged proteins which triggers apoptosis. The binding modality of NPI-0052 with the yeast proteasome and carfilzomib with the human proteasome was studied. Different conformers were generated from this dual scaffold using Sybyl®. The best conformer was selected with emphasis on affinity and energy and will be used to design novel structures which are capable of inhibiting the proteasome complex.

Evaluation of the Affinity of the Small Molecule Maltanedienol for Farenesyl Pyrophosphate Synthase

Andy-Vince Falzon

This study evaluates whether maltanedienol, a molecule with proven *in vitro/vivo* calcium fixation abilities does this through modulation of the bisphosphonate target farnesyl pyrophosphate synthase. *in silico* evaluation results show that maltanedienol binds with high affinity to the farenesyl pyrophosphate synthase (FPPS) enzyme. The binding modality of maltanedienol to the FPPS enzyme will be evaluated and novel analogs proposed.

Interdisciplinary Management of Arthritis in Children

Julian Fearne

An individualised pharmaceutical care plan documentation template is currently in use for paediatric rheumatology patients. This template limits sharing of pharmaceutical care needs to the hospital setting only, creating a gap in seamless care which impacts the quality of service and level of patient care. A pharmaceutical care plan was compiled and submitted for review and validation. The care plan is divided into three sections: Patient details, past and current drug history, as well as pharmaceutical care issues together with pharmacist actions and plans.

Validation Instruments for Community Pharmacy: An Update

Hannah Flynn

Studies show that community pharmacy has spread immensely and a large number of pharmacists work in the community. 'Validation Instruments for Community Pharmacy' is a quality care system that helps to establish the effectiveness of the pharmacist in the community. The aim of this study is to review this system and analyse pharmacist perception within the profession, including aspects of self-implementation. Weaknesses and areas for improvement are identified and documented.

Implications of Regulation for Medical Devices

Jasmine Marie Gauci

Medical device regulation aims at safeguarding public health and ensuring that high-quality and effective technologies reach patients. Research was conducted to study the variation in regulation between the United States of America and the European Union with special references to the regulatory system in Malta. Differences in the device approval mechanisms were reviewed since governing states can interpret the essential requirements for quality assurance and adverse event reporting in various ways.

Adverse Drug Reactions Database

Rachel Gauci

A database including side-effects of drugs used in cardiovascular, gastrointestinal and respiratory conditions was set up. Subscription to the MedDRA was obtained and the MedDRA Lowest Level Terminology and Preferred Terminology is being applied in the database accordingly. The most common side-effects presented with each of the pharmacological classes has been established from the compiled database.

Shared Care Guidelines in Rheumatology

Daniel Joseph Grixti

Rheumatology Shared Care Guidelines (MRSCGs) for infliximab, methotrexate, azathioprine and hydroxychloroquine were compiled through evaluation of SCGs established for international National Health Service systems, Summary of Product Characteristics and the Mater Dei Hospital Patient Management Care Protocols. The MRSCGs consist of 3 main sections: Section A outlines pharmacological background of the drug, Section B defines the associated responsibilities of the healthcare professionals involved, and Section C consists of appendices including Shared Care request form, referral checklists and a general practitioner confirmation letter.

Drug design at the Human Glucocorticoid Receptor

Sean Meachen

Glucocorticoids are involved in a variety of drug functions. Their chronic use is associated with a plethora of side-effects which greatly limits their use. The aim of this project is to identify novel structures capable of superior modulation of the aforementioned protein target. This will be done using specialised software such as VMD and LigBuilder.

Drug Design at the Adenosine A2 Receptor using Caffeine and Limonene as Lead Molecules

Danica Micallef

Evidence from literature indicates that caffeine and limonene are high affinity binders for the A2A receptor, a mediator of neurodegenerative and inflammatory disease. This study identified optimal template scaffolds of these molecules through conformational analysis. These will be used for the *de novo* design of Lipinski Rule compliant and bioavailable molecules with predicted *in silico* high affinity for this receptor.

Procurement of Medicinal Products and Medical Devices

Caroline Muscat

Performance-based monitoring of the Maltese procurement system is carried out to develop a retrospective and prospective evaluation of the system which is constantly undergoing challenges and modifications. Data from the initial focus group showed several positive and negative factors. Fast track procurement within the Central Procurement and Supplies Unit purchases low stock medicines to avoid out of stock situations ensuring that patient needs are met. Negative factors include a long evaluation process in the procurement of medical devices and a limited unflexible formulary list.

Design of Novel Antibacterial Compounds using Allicin as a Lead Molecule

Nathaniel Refalo

Literature relates the antibacterial activity of allicin to the inhibition of the bacterial enzymes RNA polymerase, thioredoxin reductase and alcohol dehydrogenase. Crystallographic depositions of these enzymes complexed with ligands have been obtained. Conformational analysis has been carried out on the ligands and allicin was inserted into different enzymes. The best conformers in terms of ligand binding energy and ligand binding affinity were derived. These will be subjected to a structure activity relationship study and used for the generation of novel enzyme inhibitors.

Compilation and Evaluation of a Two/Three-Dimensional Molecular Database as an Adjunct to Didactic Teaching Modalities

Gabriella Sultana

Visualisation of molecules in their two and three dimensional forms is considered to be an essential facet to comprehend medicinal chemistry principles such as ligand-protein interactions. Models of molecules featured in the 'Infection' and 'Musculoskeletal system' chapters of the British National Formulary, and where possible their receptors, are used to investigate this premise. Searchable databases of these molecules are being constructed. Two-dimensional molecules and their physicochemical properties were constructed using Symyx while three-dimensional models were generated using VMD and Sybyl®.

Patient monitoring of out-patients at the Rheumatology Clinic

Jonathan Vella

The aim of this study is to enhance methotrexate patient safety by reviewing monitoring guideline algorithms, analysing patient compliance to attending for laboratory blood tests for monitoring, and developing a quick method to alert healthcare professions regarding abnormal test results. Following distribution of a methotrexate monitoring booklet with the aim to improve documentation and patient compliance to blood tests and treatment plans, a questionnaire to assess compliance to blood tests is disseminated to patients. A focus group will also take place amongst healthcare professions.

Design of K-Ras Protein Inhibitors as Anticancer Agents using Deltarasin as a Case Study

Martina Woods

The K-Ras gene is mutated in one-third of tumours. This protein only becomes fully functional once it is anchored in the cell membrane. It is the prenyl-binding protein PDEδ which facilitates the diffusion of this K-Ras protein through the cytoplasm. The aim of this project is to use the deltarasin scaffold to design novel therapeutic agents capable of inhibiting prenyl-binding protein to be used in the treatment of malignant disease.

Design of Histone Deacetylase Inhibitors as Anticancer Agents using Diallyl Disulfide as a Case Study

Matthew Zarb

A crystal structure was identified (ID = 4QA0) from the Protein Data Bank. It described the bound co-ordinates of the histone deacetylase 8 enzyme receptor complexed with the vorinostat ligand. The molecular modelling computer programme Sybyl® was used to model this holo structure, such that only the chemical moieties essential to describe ligand binding were retained. Sybyl® was then used to extract the ligand from the ligand binding pocket.

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

Pharmaceutical Care Processes in Psychiatric Institutions

Roberto Briffa

Through observation of current protocols at Mount Carmel Hospital pharmacy, the study addresses needs of this psychiatric institution and proposes any necessary changes in current pharmacy protocols. The observations undertaken will involve the concerned healthcare professionals' perspective on protocols regarding pharmacotherapy management, drug administration, risk management and polypharmacy.

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

Yasmin Caruana

Leishmaniasis affects approximately 12 million people globally. Leishmania kinases have been identified as critical in the life cycle of this protozoan. The suramin scaffold will be used to probe the leishmania pyruvate kinase ligand binding pocket to rationally design *in silico* novel modulators of this enzyme.

Medicine Use and Access Intelligence

Stefan Cassar

Access to medicines is a basic social right and a global issue with millions of people dying each year due to the limitation of adequate and affordable medicines. This project will analyse the intelligent use of medicines and their access. Case studies about barriers to medicine access and factors causing them are recorded and analysed. Ways to overcome these barriers in a cost-effective manner are proposed.

Registration of Medicines

Francesca Cilia

All medicines marketed in Europe require a marketing authorisation. The process involved is specific to the type of medicine. Each process is analysed and documented in a booklet. A critical review is undertaken highlighting the bureaucracy in the registration of medicines related to small countries such as Malta. Alternatives will be proposed with the aim of simplifying the registration process.

***in silico* design of Polyphenolic Flavonoid Quercetin Analogs as Inhibitors of Histone Deacetylase and Histone Acetyltransferase for the Management of Tumour Growth**

Durston Delia

This project targets two enzymes, histone deacetylase (HDAC) and histone acetyl transferase (HAT), which are both associated with tumour proliferation. Literature indicates that quercetin is capable of inhibiting both enzymes and it will consequently be used as a lead in the *in silico* identification of novel inhibiting molecules.

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

Matthias Karl Farrugia

This study targets the MMP-9 receptor implicated in breast cancer proliferation and long-term memory loss in Alzheimer's disease. Oleuropein, a molecule derived from the olive tree, was used as an experimental scaffold and docked into the MMP-9 ligand binding pocket. The optimally binding conformation was used as a template for *de novo* drug design. A parallel study using lisinopril as a lead is undertaken.

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

Tiziana Fenech Caruana

Models of best practice for appropriate drug administration and prescribing in long-term care facilities are proposed. An evaluation of the process adopted at St. Vincent de Paul Residence is carried out through observational visits and questionnaires to relevant healthcare professionals. A tool to improve chronic disease management is developed and reviewed by a panel of experts.

in silico Design of Phytoalexin Resveratrol Polyphenolic Analogs as Inhibitors of Histone Acetyltransferase for the Management of Tumour Growth

Rebecca Hammett

The co-ordinates of Acetonyl-CoA bound to the p300 HAT was used as a template for this study. Resveratrol (3,5,4-trihydroxy-trans-stilbene) was computationally docked into the HAT_LBP and conformational analysis performed. The optimal resveratrol conformational scaffold was used as a template for the *in silico* design of novel analogs with potential clinical utility for the management of cancer.

in silico Design of Novel Poly (ADP-ribose) Polymerase Inhibitors using Olaparib as Lead Molecule

Christopher Muscat

Tankyrase inhibition is associated with mitigation of neoplastic disease. This study utilises the olaparib scaffold for the *in silico* design of novel poly-ADP ribose polymerase inhibitors.

Pharmacovigilance

Philip Paris

The aim of this project is to investigate how pharmacovigilance helps to evaluate adverse risks from medicine use. Templates for reporting drug defects by different stakeholders are developed and evaluated. Pharmacovigilance officers are interviewed in various pharmaceutical scenarios. Standard Operating Procedures (SOPs) including job description, training and processes are developed and evaluated. Templates for the SOPs are to be provided.

Patient Management with Use of Lithium

Julia Pirotta

This project aims to observe and analyse the current patient management system implemented within local psychiatric institutions, with a particular focus on pharmacist intervention. Through collaboration with the clinical team, the strengths and weaknesses are outlined and a model guiding health care professionals towards a more patient-tailored management scheme is developed.

in silico Design using the Polyphenolic Molecules Epigallocatechin-3-Gallate and Genistein as Inhibitors of Histone Deacetylases for the Management of Tumour Growth

Luke Xuereb

This study explored the Ligand Binding Pocket of histone deacetylase and established the optimally binding conformers of epigallocatechin-3-gallate and genistein at this locus through conformational analysis. Their scaffolds will be used to design novel structures with potential clinical use for neoplastic disease.

Pharmacist Intervention in Ambulatory Care of Older Persons

Rebecca Zammit

The understanding of patients needing ambulatory care and the type of care required is investigated. This study examines how the elderly's quality of life can be improved through pharmacist intervention. Models for providing pharmacist-led ambulatory care are explored within a local setting.

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

Pharmacist Services in Community Pharmacies
Rand Abdulrahman
Current services provided by pharmacists in community pharmacies are reviewed and areas for development of extended services beyond dispensing and patient counselling are identified. Legal frameworks for these new services are proposed.

Drug Shortages and Economic Impact
Charlene Bartolo
The situations when, how and why medicines are found to be out-of-stock in Malta is investigated and compared to other European countries including the economical impact. The history, current situation and prediction of future out-of-stock situations is analysed.

Dosage Forms and Medicine Acceptability
Maria Bartolo
Medicines can be formulated into different dosage forms such as tablets and capsules. The aim of the study is to find a link between dosage forms and medicine acceptability and to assess patient preferences in dosage forms and their presentation.

Rational Design of Structures Capable of Modulating Liver X Receptors for the Management of Pancreatic Cancer
Nicole Bonello
The liver X receptor (LXR) is a nuclear receptor whose agonism is useful in the management of pancreatic cancer. The GW3965 experimental scaffold will be used as a template for *in silico* design of similar LXR agonists.

Professional Development Programmes for Pharmacists
Catherine Anne Busuttil
Programmes and frameworks for pharmacists in different countries which serve as refreshers to ensure that professionals are up-to-date are reviewed. Proposed frameworks which could be applied locally are developed.

Formulary for Non-BNF Cited Products
Renita Busuttil
The aim of this study is to evaluate and update the Maltese Medicines Handbook (MMH) to its fifth edition. The present system of online accessibility of the MMH is analysed and updated. The introduction of a new and innovative MMH electronic phone application is assessed.

Forensic Pharmacy: Drugs and Driving
Abigail Calleja
Drug driving is today regulated in a number of countries. Regulations on drug driving in Malta will be proposed taking into consideration the various drug classes, interactions such as with alcohol, and the opinion of stakeholders.

Health Economic Study of the Use of Warfarin
Grazielle Camilleri
To follow up case studies of patients on warfarin, investigate outcomes and assess the pharmacist's role in the treatment process. The present system will be analysed in comparison with other countries and proposals to be implemented are discussed.

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 represent an important class of anticancer drugs. Isojacareubin isolated from *Hypericum japonicum* has recognised PK inhibitory ability and is used as a template for the design of high affinity inhibitors.

Chronopharmacology in Obesity

Onyinyechi Chesa

Chronopharmacology of drugs used to manage obesity is studied by identifying patients on drug therapy for obesity and instructing them to take it at different times for a stipulated period. The results are statistically analysed taking into account patient compliance.

Forensic Pharmacy: Drug Testing

Michaela Cini

The identification and origin of illegal drugs and their source is carried out using techniques such as studying the presence of impurities. Instrumentation used in analysis includes gas chromatography, mass spectrometry and high performance liquid chromatography.

Design of Novel Structures Capable of Modulating the Steroid Receptor Co-Activator for the Management of Neoplastic Disease

Ruth Fiorentino

Literature indicates that super agonism of the steroid receptor co-activator (SRC) mitigates tumour growth. The MCB-613 scaffold will be used as a template to probe the SRC ligand binding pocket and design novel high affinity super agonists.

Seamless Pharmaceutical Care in the Management of Rheumatoid Arthritis

Francesca Galea

Opportunities to enhance seamless care for rheumatoid arthritis patients are studied. Procedures to support patients and medication assessment processes shared between hospital and community pharmacy settings are developed.

3D Printing and Pharmaceutical Dosage Forms

Christopher Johnson

The aims are to assess how drug delivery systems can be made more convenient and personalised with 3D printing and to determine the least expensive and optimal method to carry out 3D printing. The risks, pros and cons related to the innovative dosage forms achieved through 3D printing are analysed.

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 represent an important class of anticancer drugs. The alkaloid staurosporine isolated from *Streptomyces staurosporeus* has recognised PK inhibitory ability and is used as a template for the design of high affinity inhibitors.

Targeting the Kappa Opioid Receptor in the Treatment of Addiction

Maria Mangion

The kappa opioid receptor (KOR) is a natural addiction control mechanism. Salvinorin A from *Salvia divinorum* is the first non-alkaloid molecule to have agonist activity at the KOR. Its scaffold will be used as a template in the *in silico* design of novel agonist molecules.

Pharmacist Prescribing and Point-of-Care Testing
Tricia Micallef
Point-of-care testing services offered in community pharmacies are identified. Opportunities to develop frameworks for patient monitoring and pharmacist prescribing for optimisation of treatment are studied with respect to feasibility including time, privacy and human resources.

Rational Design of Novel Androgen Receptor Inhibitors using the Naturally Occurring Lycopene Scaffold as a Lead Molecule for the Management of Prostate Cancer
Simona Neykova
The polyisoprenoid lycopene has been shown through *in vitro* studies to inhibit the androgen receptor (AR). Its structure will be modelled and used as a template to probe the AR ligand binding pocket and to design novel structures capable of its inhibition.

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 regulates apoptosis and is a target in the design of tumour mitigating drugs. The navitoclax and venetoclax antagonist scaffolds will be used as templates for the *in silico* design of similar high affinity antagonists.

Point-of-Care in Haemoglobin Measurement
Martina Scicluna
Sensitivity, specificity and reliability of haemoglobin test results taken by point-of-care (POC) test kits are compared to laboratory test results. Feasibility of providing a POC haemoglobin testing service in a community setting and patient perception regarding this service are studied.

Rational Design of Partial PPARg Agonists using the Synthetic Analog of Tetrahydrocannabinol Ajulemic Acid Scaffold as Lead Molecule for the Management of Diabetes Mellitus and Other Inflammatory Conditions
Kirby Zammit
The Peroxisome Proliferator Activated Receptor (PPARg) is a target for the design of hypoglycaemic drugs. Ajulemic acid binds selectively to PPARg. Its novel scaffold will be used as a template for the *in silico* design of similar novel high affinity agonists.

Medicine Reconciliation at Discharge
Thomas Zammit
Medicine reconciliation is an evaluation of patients' previous medication regimen on admission and medication at discharge. Patient and carer awareness and education on the medication at discharge is assessed since it promotes optimal patient adherence and prevents errors.

Pharmacist-Led Management of Insulin Therapy
Jessica Zarb
The practicality and feasibility of a pharmacist-led intervention programme intended for diabetic patients receiving insulin is studied. Patient monitoring and identification of care issues including insulin dose adjustments are the outcomes to be assessed.

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