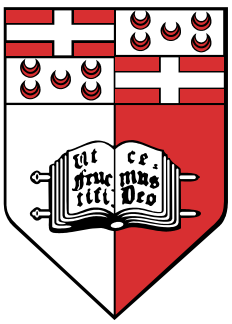

University of Malta

Dissertation Abstracts and Project Descriptions

Department of Pharmacy

Faculty of Medicine and Surgery

University of Malta

2015

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Foreword

Evolution of Pharmacy Practice and Research

Pharmacists are important members of the healthcare team. In addition to traditional roles of medicines distribution and dispensing many consider a number of other professional activities to be the responsibility of the pharmaceutical profession whether one is working in the community, industry, hospital, marketing, regulatory or administration. Students following courses at the Department of Pharmacy are stimulated to contribute significantly to these areas through the knowledge acquired throughout the direction given in the versatile course structures which involve acquiring knowledge and practice in pharmaceutical care, clinical pharmacy, pharmoeconomics, administration, quality control, manufacturing and marketing.

Students following the B.Sc course in Pharmaceutical Sciences and the entry grade to the pharmacy profession through the Masters in Pharmacy degree achieve excellence in their direct response to patient needs. The pharmacists' advice on rational effective and safe use of medicines as a traditional role is now joined to the duty of the pharmacist to deal with the more recent concepts of advice in a range of services which include healthy lifestyles. Those following the new course of Doctorate in Pharmacy aim to contribute to advance practice in the clinical role of the pharmacist not least by their supporting public health through their pharmacy practice environments becoming areas where to promote, regulate and support healthy living and health literacy. These practitioners offer patients and the public the choice of healthy lifestyle, self-care, treatment of minor ailments and a pharmaceutical care plan of patients with long-term conditions. In addition, they contribute to the continuous access of safe and effective medicines through processes such as rigorous pharmacovigilance. Through the introduction of the course leading to the Bachelor of Pharmaceutical Technology, the Department is responding to the needs of the pharmaceutical industry. Through the evolvement of the course content of the Master of Science in Pharmacy post-graduate degree, through the introduction this year of the new study options, which include areas such as pharmacovigilance, regulatory affairs and upgrade courses to assist those aspiring to become qualified persons, the Department continued to satisfy the aspirations of students and stakeholders.

The introduction of students to fundamentals of research and to induce their appetite to investigate areas of their own interest with the elements that are basic to scientific publications, students are encouraged to insert themselves in the process of carrying out a project or thesis. This process very often leads to the publication in peer-reviewed journals or a presentation in international scientific conferences. Students learn to conduct research in an ethical and responsible manner, to present their results clearly and honestly in an appropriate manner, to support their findings with data, to present a good and organised methodology, to ensure that the work is not plagiarised and that they are responsible researchers. These abstracts are presented in this symposium booklet while the original work is available for consultation at the Department of Pharmacy.

Professor Anthony Serracino-Inglott
Pharmacy Practice Projects Co-ordinator

Introduction

The Department of Pharmacy at the University of Malta has played a very pivotal role in the development of pharmacy services in Malta. As an academic institution, it has supported the development of the pharmacy workforce. This has been achieved not only in numbers (Malta has one of the highest pharmacist: population ratio in the world) but also in quality. The balance presented between the pharmaceutical sciences and pharmaceutical practice and the adoption of experiential learning models have been emulated by colleges of pharmacy in other countries during restructuring of curricula.

The Department has responded to the emerging needs in different pharmaceutical settings to prepare pharmaceutical technologists, as graduates, who specialise in the development and maintenance of pharmaceutical processes, which guarantee safe and good quality medicines. The first group of students from the three year Bachelor degree in Pharmaceutical Technology course graduated last November. A large number of opportunities exist in this area and it is encouraging to note the increasing number of students joining this course.

The Department looks beyond the professional entry level degrees and has been active in modelling post-graduate opportunities. The evolvement of the Master of Science in Pharmacy Degree to provide an opportunity for pharmaceutical technologists and pharmacists to take up a Masters degree with the possibility of focusing on pharmaceutical regulatory affairs has been positively received.

The launch of the Doctorate in Pharmacy degree is an innovative approach to postgraduate pharmacy education. Last October, eighteen pharmacists hailing from Malta, Germany, Libya and Spain joined the doctorate of pharmacy programme which leads to a Level 8 doctorate degree. The programme is offered in collaboration with the College of Pharmacy of the University of Illinois (UIC) at Chicago. The course includes sessions run live with faculty from UIC, rotations and applied research. Within this programme pharmacists develop advanced professional skills in direct patient care services and in the development of pharmaceutical processes that ensure safety, quality, equity and access to pharmaceutical services. Students following the Doctorate of Pharmacy course undertake a dissertation in a practical aspect of pharmacy.

A number of research projects carried out by the Department were published in peer-reviewed journals and the results of these studies have been adopted in academia, industry and professional practice settings. For example the quality care research study which included developing quality systems for clinical pharmacy hospital services has led to the implementation of such a system at Karin Grech Hospital Pharmacy, the publication of a number of scholarly contributions and reference to this work in connection with the updating of the American Standards of Practice for Clinical Pharmacists.

Professor Lilian M. Azzopardi
Head, Department of Pharmacy

M.Pharm. Students
Dissertation Abstracts

Pharmaceutical Care

Dietary Practices in Cardiac Patients
Francesca Attard Baldacchino

Comparison of Patient Knowledge regarding Diabetes between Health Centre Patients and the Central Diabetic Clinic at Mater Dei Hospital
Leanne Bason

Difference in Antidepressant Prescribing Trends between General Practitioners and Psychiatric Specialists
Deborah Camilleri

Development and Patient Evaluation of a Medicines Use Review Framework
Matthew Camilleri

Dietary Practices in Cardiac Patients

Francesca Attard Baldacchino

Background: Diet plays an important role in cardiovascular disease (CVD). A diet consisting of fruit and vegetables and low intake of saturated fats is linked to a 73% decreased risk of new major CVD events when compared with typical diets in the developed world.[1]

Objectives: To identify the dietary practices of cardiac patients and determine if these are optimal for their condition.

Design: A food frequency questionnaire was developed, validated and distributed to 66 outpatients whose conditions included arrhythmias, post-myocardial infarction, hypertension and ischaemia. The resulting scenario of weekly food consumption was then compared with current dietary recommendations.

Setting: Cardiac Lab and Cardiac Rehabilitation Centre, Mater Dei Hospital

Main Outcome Measures: Type and frequency of food consumption

Results: Patients' dietary practices were identified. Patients' choices included moderate consumption of fruit, vegetables and fish. Poultry, rabbit and ham were the most frequent meat choices. High fat cheeses are chosen more often than low fat cheeses, while skimmed milk is preferred. Consumption of sugary beverages is higher than that of mineral water. On average, alcoholic drinks are consumed weekly. Low fat oils and frying were the most common choices for use in cooking. Cereals, pasta and nuts are moderately consumed, while sweet pastries and biscuits are consumed daily.

Conclusion: The study shows that cardiac patients have mixed dietary habits. This indicates that raising awareness on such a modifiable risk factor would further aid patients to make healthy and practical choices to optimise their cardiac health.

Reference:

1. World Heart Federation. Diet [Online].2015 [cited 2015 Jan 03]. Available from: URL: http://www.world-heart-federation.org/cardiovascular-health/cardiovascular-disease-risk-factors/diet

Comparison of Patient Knowledge regarding Diabetes between Health Centre Patients and the Central Diabetic Clinic at Mater Dei Hospital

Leanne Bason

Background: Malta has 40,000 registered diabetic patients. The rate of diabetes and its complications have been on the increase taking a huge toll on the patient, the patient's families as well as the healthcare system.[1]

Objectives: To recognise the motivation, drug treatment and current patient knowledge of type 2 diabetic patients and to compare parameters of patients visiting the Diabetes and Endocrine Clinic at Mater Dei Hospital (MDH) and health centre diabetic clinics.

Design: One hundred type 2 diabetic patients were recruited by convenience sampling from each of the two health care settings. Fasting blood glucose level, high-density lipoprotein cholesterol (HDL-c), HbA1c and triglycerides (TG) were recorded from computerised records. Each patient was presented with a questionnaire to obtain the required patient details, drug treatment, current knowledge and motivation.

Setting: Diabetes and Endocrine Clinic, MDH and 3 Health Centre Diabetic Clinics

Main Outcome Measures: Comparing two health care settings for the care of type 2 diabetic patients

Results: A total of 193 patients completed this study with a mean age of 65 years. Smokers amounted to 21.4% visiting MDH and 8.4% visiting health centres. Patients visiting health centres include physical activity (67.4%) in their daily regimen while only 32.7% of the patients visiting MDH exercise regularly. Only 29.3% of patients from both health care settings always follow a nutritionist's diet plan. The mean values of HbA1c for patients visiting MDH and health centres were 8% and 7% (p-value <0.001) and the mean values of fasting glucose were 9.3 mmol/l and 8.2 mmol/l (p-value=0.040) respectively.

Conclusion: Type 2 diabetic patients have the knowledge regarding the condition and the importance of lifestyle modifications however they lack the motivation to adhere to lifestyle changes in order to improve their quality of life.

Reference:

1. Formosa C, Savona-Ventura C, Mandy A. Cultural contributors to the development of diabetes mellitus in Malta. Int J Diabetes and Metab 2012;20:25-9.

Difference in Antidepressant Prescribing Trends between General Practitioners and Psychiatric Specialists

Deborah Camilleri

Background: Pharmacist interventions in patients with mental illness have been evaluated and demonstrate that a collaborative care approach involving pharmacists may be correlated with multiple beneficial outcomes.[1]

Objectives: To carry out an extensive analysis on current prescribing practices among psychiatrists and general practitioners in the treatment of major depression and to investigate the perception of the role of the pharmacist in this field.

Design: The method included the design and validation of a healthcare professional questionnaire aimed to collect quantitative and qualitative data. The questionnaire was self-administered or sent via electronic mail to a sample of 50 GPs and 28 psychiatrists. A comparison was then compiled.

Setting: Mount Carmel Hospital and Doctors' Clinics

Main Outcome Measures: Comparative analysis and physician perception on local antidepressant use

Results: Forty-three general practitioners and 13 psychiatrists completed the questionnaire. Twenty-five GPs (n=43) and 9 psychiatrists (n=13) stated they prescribe SSRIs as first line therapy "very often", indicating that this group is presently the gold standard of treatment. Paroxetine was found to be prescribed "very often" among 17 GPs and 8 psychiatrists. Regarding the factor that influences the choice of antidepressant the most, 12 psychiatrists strongly agreed to "previous response to treatment" while 27 GPs strongly agreed to "drug-drug interactions". Eleven out of 12 psychiatrists practicing within a hospital setting would find the availability of a clinical pharmacist in this field "very useful".

Conclusion: A more collaborative approach within the healthcare team can lead to improved outcomes. While analysis of results indicates that current prescribing practices are in line with guidelines, the input of the pharmacist remains invaluable.

Reference:

1. Finley PR, Crismon ML, Rush AJ. Evaluating the impact of pharmacists in mental health: A systematic review. Pharmacotherapy 2003; 23(12): 1634-44.

Development and Patient Evaluation of a Medicines Use Review Framework

Matthew Camilleri

Background: Medicines Use Reviews (MURs) have been implemented in a number of countries with the aim to improve patients' overall medication knowledge and identify drug-related problems.

Objectives: To propose a framework for a concordance and compliance review within local community pharmacies, to identify drug-related problems and the evaluation of the impact of the service.

Design: Five validated and reliability tested tools were developed for the scope of the study. Inclusion criteria were developed to include patients who are more at risk of developing drug-related problems. Ethics approval was obtained from the University Research Ethics Committee. Patients were contacted via convenience sampling and if consent was granted, the MUR was undertaken. A yearly follow-up was conducted to assess impact of the service. Ten community pharmacies around Malta were selected via stratified random sampling. Pharmacies required a private area where the review could take place as an inclusion criterion.

Setting: Community pharmacies

Main Outcome Measures: Assessment of patient compliance and patient knowledge, identification of medication issues, comparison of results from the first MUR interview and the follow-up

Results: One hundred and twenty patients (61 male, 59 female) participated in the study during the first MUR. Of these, 81% were older than 51 years. The average number of medicines was 5 medicines per patient ranging from 1 to 12. During the first interview, 662 interventions were made averaging 5.5 interventions per patient and 317 interventions were made in the 95 patients who participated in the follow-up.

Conclusion: With the number of interventions undertaken, the usefulness of such a service in a Maltese setting is identified. The most common intervention during the first interview and the follow-up was providing first time information regarding side-effects.

Pharmacotherapy

Chronopharmacology of Prednisolone in Rheumatoid Arthritis
Christine Attard

Management of Chemotherapy Side-effects in Breast Cancer Patients
Danika Caruana

Chronopharmacology of Valsartan and Amlodipine
Sephorah Falzon

Patient-Controlled Analgesia in Post-Caeserean Section
Deborah Mangion

The Status of Buprenorphine Use in Malta Compared to Methadone
Maria Pace

Once Daily Gentamicin Dosing in the Intensive Therapy Unit
Annalisa Thake

Chronopharmacology of Prednisolone in Rheumatoid Arthritis

Christine Attard

Background: Prednisolone is broadly used in the management of rheumatoid arthritis (RA), a condition that exhibits a circadian rhythmic variation in the levels of pain felt throughout the day.[1]

Objectives: To study the effect of prednisolone chronotherapy in patients with RA in relation to the diurnal variation of pain and to evaluate prescribers' perception of the chronopharmacology of prednisolone.

Design: From the 186 rheumatology patient files assessed, 11 patients were on prednisolone due to RA, of which 6 were not eligible due to mental impairment and 1 dropped out. The pain scores of RA patients (n=4) on prednisolone morning doses were compared to scores of the same patients on evening doses. Expert panel validation (N=4) of a questionnaire given to physicians was carried out. Data was analysed using SPSS® version 22.

Setting: Rheumatology Outpatient Clinic, Mater Dei Hospital

Main Outcome Measures: Patient responses to an adapted version of the McGill Short-Form Pain Questionnaire[2] obtained from a longitudinal study, physician's perspective of prednisolone chronopharmacology in RA

Results: The visual analogues scales (pain scores) completed by the patients were analysed using the paired samples t-test obtaining a p-value of 0.08. Out of 20 physicians, 17 prescribed prednisolone in the morning. Fifteen stated that the duration of prednisolone treatment in the majority of cases lasted between 2 months and 1 year, whilst 5 stated that it lasted less than 2 months. All physicians agreed that they would change the timing of prednisolone administration should an evidence-based study reveal it to be more beneficial.

Conclusion: No statistically significant difference was found in the amount of pain felt by patients between the morning and evening administration of prednisolone.

References:

1. Klerman EB. Clinical aspects of human circadian rhythms. J Biol Rhythms 2005;20(4):375-86.
2. Melzack R. The short-form McGill pain questionnaire. Pain 1987;30(2):191-7.

Management of Chemotherapy Side-effects in Breast Cancer Patients

Danika Caruana

Background: Despite its distressing side effects, chemotherapy is an important cancer treatment modality.

Objectives: To assess the incidence and management of FEC (a combination regimen of 5-fluorouracil, epirubicin and cyclophosphamide)–induced nausea and vomiting (CINV), diarrhoea and oral mucositis and to evaluate patients' quality-of-life (QoL).

Design: Thirty-nine newly diagnosed or relapsed breast cancer patients, initiating FEC or FEC-T (usually 3 cycles FEC followed by 3 cycles of docetaxel) were recruited. QoL was assessed before Cycle 1 and after Cycle 3 whilst side effect occurrence was evaluated after Cycle 1 and Cycle 3. Psychometric evaluation of the developed tools was carried out.

Setting: Oncology Day Ward, Sir Paul Boffa Hospital.

Main Outcome Measures: Morrow Assessment of Nausea and Emesis[1] for CINV evaluation, developed tools for oral mucositis and diarrhoea assessment, EORTC-QLQ-C30 v.3[2] for QoL assessment

Results: Thirty-seven female patients completed the study (mean age= 54.32 years). Breakthrough nausea was greatly experienced in both cycles (Cycle 1= 26 patients; Cycle 3= 27 patients) while only a few patients reported vomiting. Following Cycle 1 and Cycle 3, 9 and 6 patients respectively reported oral mucositis. No episodes of diarrhoea were recorded. QoL assessment over the first 3 cycles indicated a statistically significant decrease in QoL (p-value= 0.000).

Conclusion: The high occurrence of breakthrough nausea sustains the vital need for healthcare providers to follow recent clinical practice guidelines as well as evidence-based information.

References:

1. Morrow GR. A patient report measure for the quantification of chemotherapy induced nausea and emesis: psychometric properties of the Morrow assessment of nausea and emesis. Br. J. Cancer. 1992;66(19):S72-S74.
2. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ et al. The European Organisation for Research and Treatment of Cancer QLQ-C30: A QoL instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993;85:365-376.

Chronopharmacology of Valsartan and Amlodipine

Sephorah Falzon

Background: Chronotherapy can be used to identify the ideal dosing time of antihypertensive drugs to optimise 24h blood pressure (BP) control.[1]

Objectives: To test the effect on 24h BP profile of valsartan and amlodipine and to compare the effects of morning versus evening dosing on circadian BP.

Design: Sixty one patients aged 40-75 years had their 24h BP measured using an ambulatory BP monitor (ABPM). Patients suffering from essential hypertension who were prescribed valsartan (n=20) or amlodipine (n=8) as monotherapy were monitored twice, 7 days apart. They were asked to change the time of dosing of their medication for a week for the second measurement. Patients suffering from hypertension but taking no medication (n=14) and normotensive patients (n=19) were recruited as controls. Data was analysed using SPSS® version 22. The Mann-Whitney and Kruskal Wallis tests were carried out.

Setting: Community pharmacies; Cardiac Lab and Medical Outpatients, Mater Dei Hospital.

Main Outcome Measures: Using ABPM to obtain 24h BP profile results

Results: Compared to morning dosing, evening valsartan dosing resulted in an insignificantly lower systolic BP (SBP) during whole day, early morning, day time and night time periods (p=0.715, 0.791, 0.854 and 0.318 respectively). Evening dosing resulted in lower diastolic BP (DBP) during 24h and night time periods (p=0.494, 0.213 respectively). Compared with evening dosing, morning amlodipine dosing resulted in lower BP during whole day, day time and night time periods (p=0.658, 0.483 and 0.091 respectively for SBP and p=0.980, 0.961 and 0.065 respectively for DBP).

Conclusion: Morning and evening administered valsartan or amlodipine are equally effective for BP control. Evening valsartan and morning amlodipine produce a more controlled BP profile throughout the 24h period.

References:

1. Hermida RC, Ayala DE, Portaluppi F. Circadian variation of blood pressure: The basis for the chronotherapy of hypertension. Advanced Drug Delivery Reviews 2007; 59: 904-22.

Patient-Controlled Analgesia in Post-Caeserean Section

Deborah Mangion

Background: Pain and discomfort in patients post-caesarean section (C-section) can be managed via self-administration of intravenous opioids using patient controlled analgesia (PCA).

Objectives: To assess pain management in post C-section focusing on PCA assessing efficacy, safety and cost-effectiveness and to compare the use of traditional PCA with disposable PCA.

Design: A patient interview sheet and audit form were prepared. Psychometric evaluation of these forms was carried out. The developed and validated tools were used for data collection from 28 patients who were interviewed within the first 24 hours after having a C-section. The audit form was completed using data from patient files. Data was used to assess nurse compliance and to assess concordance between results obtained from interview with results from audit.

Setting: Obstetrics wards 1 and 3, Mater Dei Hospital

Main Outcome Measures: Patient outcomes and satisfaction with the post-operative pain management received; nurse compliance and concordance of results between audit and patient interview

Results: The study proved to be reliable, practical and valid. Seven out of 28 patients received a disposable PCA. All patients were satisfied with pain management received. No patients experienced significant problems post-surgery. Seven out of 28 patients received a PCA information leaflet. The average morphine consumption recorded was 9mg. Six out of 28 patients did not use PCA. In 26 cases discrepancies were found between pain scores recorded in patient files and those reported by the patient.

Conclusion: Patients are satisfied with pain management received for post C-section pain. Patients are misinformed about PCA. This may be having an impact on the consumption of morphine. Pain scores are not always recorded as indicated. There is a need for support to aid nurse compliance to ensure that the appropriate protocol is followed.

The Status of Buprenorphine Use in Malta Compared to Methadone

Maria Pace

Background: According to a 2010 estimate, Malta has 6.1 opioid users per 1000 capita, the third highest rate in Europe.[1] Current opioid substitution treatment (OST) available locally includes methadone (MST), buprenorphine, buprenorphine/naloxone (BST) and naltrexone. Of all individuals seeking OST at the Substance Misuse Outpatient Unit (SMOPU), 95% are on MST. Untreated opioid dependence harms the individual, with heroin users having a 20 times higher mortality risk than the general population and an increased risk of blood borne infections such as Hepatitis C and HIV.[2] To-date, no local health technology assessments are available for these drugs.

Objectives: To establish the possible advantages and disadvantages of introducing BST on the Government Formulary List

Design: A study with 92 participants was carried out. Participants were enrolled using non-probability convenience sampling since the group of individuals was difficult to identify. Recruited participants were older than 18 years, opioid dependent and attendees of SMOPU. Results were analysed using IBM SPSS® version 22.

Setting: SMOPU, Gwardamangia

Main Outcome Measures: Evaluation of patient data and opinions; evaluation of costings of MST and BST

Results: The mean age of opioid dependent patients at the SMOPU is 34.14 years, of whom 66.3% are unemployed. The type of OST significantly affects the success rates (p=0.018) of MST and BST, with 100% of BST and 54.1% of MST patients being opioid-free.

Conclusion: The average age of opioid dependent patients indicates that the majority of these individuals are young and therefore there is potential for these individuals to become opioid-free and improve their quality of life.

References:

1. Gellel M, Olivari D'Emanuele C, Muscat R (Reitox National Focal Point, Malta). 2008 – 2010 National Report on the Drug Situation in Malta. Malta; 2011. 70p.
2. UNODC. World Drug Report 2010. Vienna: United Nations Publication; 2010. 307p.

Once Daily Gentamicin Dosing in the Intensive Therapy Unit

Annalisa Thake

Background: Gentamicin used to treat serious infections in the Intensive Therapy Unit (ITU) is given as a once daily 7mg/kg dose in 100ml 5% dextrose or 0.9% sodium chloride solution administered over 30-60 minutes by IV infusion.[1]

Objectives: To assess dosing and drug blood levels of gentamicin and to propose guidelines for once daily dosing of gentamicin for the local scenario.

Design: Following ethics approval, a data collection form was developed and validated by 8 health care professionals. A total of 42 critically-ill adult patients were recruited by convenience sampling. A scenario analysis of gentamicin dosing in ITU was carried out. Patient medical records and drug treatment charts were reviewed for data related to gentamicin therapy. Drug blood levels of gentamicin, serum creatinine levels and sensitivity results were reviewed. Data was analysed using SPSS® version 20. Guidelines were proposed and validated by 8 health care professionals.

Setting: ITU, Mater Dei Hospital

Main Outcome Measures: Clinical outcomes assessed when underdosing, correct dosing and overdosing; validation of guidelines

Results: A total of 42 critically-ill adult patients (32 male, 10 female) with a mean age of 54 years were eligible for once daily gentamicin treatment and all had a baseline creatinine clearance of >20ml/min. The treatment doses resulted in 36% underdosing, 59% correct dosing and 6% overdosing (n=198). Six patients had treatment stopped due to high gentamicin levels and renal issues. Validation of guidelines indicated that they were user-friendly, comprehensive, practical, scientific and beneficial.

Conclusion: Underdosing or overdosing is still occurring and this highlights the relevance of the developed guidelines.

Reference:

1. Calderdale and Huddersfield NHS Foundation Trust. Antibiotic guidelines: Parenteral gentamicin protocols [Online]. UK:Calderdale and Huddersfield NHS Foundation Trust; October 2007 [cited 2015 Jan 20]. Available from: URL: www.formulary.cht.nhs.uk/pdf,_doc_files_etc/MMC/066_Antibiotic%20Guidelines%20-%20Dr%20Booklet/Gentamicin.pdf

Pharmacy Protocols

Pharmacist Prescribing Frameworks for Ophthalmic and Skin Conditions
Gianella Casha

Developing and Auditing Standard Operating Procedures for Community Pharmacies
Michelle Marie Cassar

Evaluation of Prophylactic Practice for Venous Thromboembolism
Jeanine Grech

Pharmacist Prescribing Frameworks for Ophthalmic and Skin Conditions

Gianella Casha

Background: Locally, the perception of pharmacist prescribing has been improving and this is shown by various local studies. Tabone et al.[1] concluded that pharmacists are willing to prescribe in minor infections, skin and painful conditions by collaborating with a general practitioner in supplementary prescribing.

Objective: To create a framework for pharmacists to be used in the prescribing scenario. This is achieved by designing a set of guidelines for 3 common eye and skin conditions encountered in community practice which includes bacterial conjunctivitis, chalazion, hordeolum, insect bites and stings, acne and psoriasis.

Design: An intensive literature review was carried out to obtain knowledge on the causes and management of these conditions. A set of guidelines was set up consisting of protocol algorithms and corresponding treatment charts together with a prescription template and a referral form as part of the documentation scheme. For psoriasis, a repeat prescription was formulated. The guidelines were validated by a panel of experts.

Setting: Community pharmacies

Main Outcome Measure: Validation of the guidelines developed

Results: The protocol algorithms were designed to include the signs and symptoms for each condition for the pharmacist to establish the diagnosis after following the algorithm through a yes or no answer which leads to the corresponding section of the treatment chart. The latter includes non-pharmacological measures and patient advice as well as details on the drug prescribed. It also includes when patients should be reviewed and when they should be referred.

Conclusion: The validation panel concluded that the guidelines designed were easy to follow and informative, however could be too time consuming to follow during practice. The practical implementation is studied through the feedback from medical practitioners and pharmacists.

Reference:

1. Tabone F, Azzopardi LM, Serracino-Inglott A. Perception of the community pharmacist: Impact of pharmacy services and development of pharmacist prescribing. Germany: LAP Lambert Academic Publishing; 2013.

Developing and Auditing Standard Operating Procedures for Community Pharmacies

Michelle Marie Cassar

Background: Pharmacy is a regulated profession. Locally the use of Standard Operating Procedures (SOPs) in community pharmacy is not legally required and it is not common practice for a community pharmacy to have SOPs.

Objectives: To develop, implement and audit SOPs in a community pharmacy setting.

Design: Common processes were identified and procedures were developed accordingly. The SOPs were written in the format adopted from Grima.[1] These procedures were validated by feedback from pharmacists and implemented in nineteen pharmacies around Malta and Gozo. Audits were done to assess the system after six and twelve months from implementation. Reports were drawn up to identify trends and propose improvements.

Setting: Nineteen community pharmacies in Malta and Gozo.

Main Outcome Measures: Developing, implementing and auditing SOPs in community pharmacies

Results: Seven procedures were developed and implemented- 'Recruitment, training and monitoring of staff', 'Cleaning and waste control', 'Documentation and record control', 'Dispensing of medicines', 'Storage of medicines', 'Non-medicinal and clinical services', 'Ordering of new stock'. All pharmacies audited would recommend the use of these SOPs as guidelines, however they showed reluctance for implementation due to a high work load. An average of 3 non-conformances arose during audits as the required documents were not available.

Conclusion: Seven SOPs for community pharmacy were developed and implemented in nineteen pharmacies. They were accepted by pharmacists as tools to help in providing a better service to the patient whilst abiding by the legal framework, and to standardise procedures followed by locum pharmacists.

Reference:

1. Grima C. Cost analysis of standard operating procedures in community pharmacies [MSc dissertation]. Msida (Malta): Department of Pharmacy, University of Malta; 2012.

Evaluation of Prophylactic Practice for Venous Thromboembolism

Jeanine Grech

Background: Venous thromboembolism (VTE) is an unprecedented condition which is responsible for 10% of hospital mortality[1]. VTE is easily preventable by implementation of evidence-based prophylactic protocols.

Objectives: To analyse risk factors for VTE in hospitalised patients and to evaluate the extent of prophylaxis administered.

Design: The National Institute for Health and Clinical Excellence risk assessment chart[2] for VTE was used to review patient files and to collect data regarding risk factors, the type, dose and duration of any prescribed prophylaxis. Relational statistical tests were performed using SPSS® v20. A focus group discussion was undertaken, mainly addressing the importance of VTE prevention and recommendations for local practice.

Setting: Medical and Surgical wards, Mater Dei Hospital

Main Outcome Measure: Management of VTE prophylaxis

Results: Out of 80 patients, 31 were male and 49 were female and all patients were older than 45 years. VTE prophylaxis was prescribed to 25 surgical and 27 medical patients. The p-value (p=0.747) generated by the Chi-square test indicates that there is no statistically significant difference between the two groups. The prophylactic agent used for the majority of patients (42 out of 52 cases) was enoxaparin.

Conclusion: The results provide evidence that prophylactic measures are being undertaken locally. There is the need for formalisation, standardisation and better documentation systems for these practices which would unify all the local clinical institutions.

References:

1. Moores L. Meeting patient safety goals in VTE prevention. Chest. 2012;141(3):578-80.
2. National Institute for Health and Clinical Excellence (NICE). Venous thromboembolism: Reducing the risk of VTE in patients admitted to hospital. NICE Clinical Guideline 92. London,UK: NICE;2010.

Pharmacy Information

Evaluation of the Journal of EuroMed Pharmacy
Joseph Christian Abela

Veterinary Medicine: A Guidebook for Pharmacists and Pet Owners
Annalise Attard

Attitudes and Knowledge of Parents on Vaccinations
Maria Galea

Evaluating Requests for Advice from Community Pharmacists
Lisa Warrington

Evaluation of the Journal of EuroMed Pharmacy

Joseph Christian Abela

Background: The Journal of EuroMed Pharmacy (JEMP) is an annual publication by the Department of Pharmacy at the University of Malta and sponsored by Actavis.[1]

Objectives: To evaluate previous editions of the journal and to establish views of editors of healthcare-related journals.

Design: A questionnaire and semi-structured interviews were devised. Questionnaires were distributed amongst all registered pharmacists (N=916) and pharmacy students (N=154) to analyse previous issues. The same questionnaire is currently being distributed to analyse the 2014 issue. Editors of 4 local scientific journals were interviewed.[2]

Setting: Department of Pharmacy, University of Malta

Main Outcome Measure: Evaluation of JEMP editions

Results: Questionnaires indicate that 45% of respondents are not willing to pay for the JEMP, 94% agree that the overall presentation is good. Results obtained are similar to a previous study conducted by Gauci Borda in 2002.[1] Eighty five percent of respondents agree that the journal is aiding their continuous professional development or area of study. The interviewed editors gave positive reviews.

Conclusion: Both the questionnaires and the interviews indicate the journal is of a high standard and is reaching its aim to disseminate information and should continue to be published.

References:

Gauci Borda R. The Journal of EuroMed Pharmacy [project]. Msida (Malta): Department of Pharmacy, University of Malta; 2002.

Veterinary Medicine: A Guidebook for Pharmacists and Pet Owners

Annalise Attard

Background: The practice of veterinary pharmacy is a relatively new concept in Malta. At some point in their career, pharmacists practising in a community setting have been presented with veterinary prescriptions so the need for pharmacists to gain knowledge in this area is important.

Objectives: To develop a guidebook for pharmacists and pet owners which incorporate information about the treatment of common ailments in pets.

Design: Five questions were compiled to obtain both quantitative and qualitative results. These were aimed at gathering information about common ailments, ailments requiring referral and medicines dispensed. Interviews were carried out in a structured manner with pharmacists in each veterinary pharmacy (N=6). The booklet is divided into different sections and includes an introduction on its structure and use. Research about diseases which animals commonly present with was conducted. For each disease details are given under the respective sections: Description, Recognition, Signs and Symptoms, Similar Conditions, Treatment and Advice.

Setting: Veterinary Pharmacies, Veterinary Clinics

Main Outcome Measures: Publication of the first veterinary guidebook for pharmacists and pet owners in Malta

Results: From the information collected during the interviews, it was found that the most frequent cases involved pigeons. This does not necessarily reflect the fact that pigeons are the most common pets in Malta, but it may be the result of the treatment offered by the owners towards these animals. The booklet compiled includes over 50 common ailments and is sectioned in a structured manner to render it more user-friendly.

Conclusion: The booklet can be used to support pharmacists during dispensing and advising on the use of medicines in animals.

Attitudes and Knowledge of Parents on Vaccinations

Maria Galea

Background: Despite vaccinations being a breakthrough in preventive care which have reduced disease burden, parents' decisions on vaccination programmes may be difficult. Studies have described vaccines as 'victims of their own success' since their effectiveness led to generations of parents who are unfamiliar with the preventable illnesses giving the perception that vaccination is futile and more attention being given to the perceived risks of vaccines rather than of the diseases they prevent.[1] As a result vaccination rates against certain illnesses are decreasing and previously controlled illnesses are re-emerging.

Objectives: To assess knowledge and perception of parents on vaccines and vaccine-preventable illnesses and to identify misconceptions and lack of knowledge.

Design: A structured questionnaire to assess knowledge, attitude and perception of parents on vaccines, preventable illnesses, information available and cost was designed and psychometrically evaluated.

Setting: Pharmacies, clinics and other public places with a high parent attendance

Main Outcome Measures: Knowledge, attitude and perception of parents

Results: Two hundred and sixty one parents completed the questionnaire. When asked why they did not give their child a particular vaccine, the commonest reason chosen was lack of awareness of the vaccine's existence. Ninety one percent of participating parents agreed or strongly agreed that they are willing to consult their trusted healthcare professional and pay for the recommended vaccines. Six percent stated that they will wait until the vaccine is free.

Conclusion: The study confirmed that lack of information by the parents is a major reason for not giving certain vaccines to their children. Providing a reliable information resource can prevent a significant proportion of decisions against vaccination which are made due to lack of adequate information.

Reference:

1.Larson HJ, Cooper LZ, Eskola J, Katz SL, Ratzan S. Addressing the vaccine confidence gap. The Lancet. 2011;378:526-35.

Evaluating Requests for Advice from Community Pharmacists

Lisa Warrington

Background: Community pharmacists are easily accessible health care professionals[1] and are highly sought for advice on the treatment of common complaints and symptom relief.[2]

Objectives: To evaluate requests for advice from community pharmacists and patients' satisfaction with the advice provided.

Design: Observation studies were carried out in 4 community pharmacies selected by stratified random sampling. A questionnaire was distributed to 18 patients randomly selected from each of 15 community pharmacies (N=270). The questionnaires were statistically analysed with the Friedman and Kruskal Wallis tests and mean rating scores were calculated.

Setting: Community pharmacies

Main Outcome Measures: Determination of the most popular requests for advice and patient satisfaction

Results: Observation studies showed that 56% (n=57) of patients seek pharmacist's advice for treatment of their symptoms. Seventy percent of the questionnaire respondents were female and 30% were male. The statement 'I often seek my pharmacist's advice on how to take my medications' received the highest mean rating score (3.76), implying high agreement (5 highest). The statement 'I often seek advice about quitting smoking from my pharmacist' received the lowest mean rating score (1.65). A higher mean rating score (4.24) was obtained for satisfaction from advice given by pharmacists before dispensing a medicine, and for instructions for self-administering the medicine. A mean rating score of 4.11 was obtained for questions asked by pharmacists before dispensing over-the-counter (OTC) medicines.

Conclusion: The highest requests for advice concerned medication administration. Patients were most satisfied with advice provided by the pharmacist; they were less satisfied with questions asked by the pharmacist before dispensing OTC products.

References:

1. Beardsley RS, Kimberlin CL, Tindall WN. Communication Skills in Pharmacy Practice. 5th ed. Baltimore: Williams & Wilkins; 2008.
2. Stone P, Curtis SJ. Pharmacy Practice. 2nd ed. London: Farrand Press; 1999.

Pharmacy Administration

Evidence-Based Standards for Clinical Pharmacy Practice
Jessica Attard

Comparison Between Oncology Medicinal Products in the Government Formulary in Malta and Other European Countries
Alexandra Cachia

A Glossary of Risk Management Terminology for Use in a Pharmaceutical Setting
Matthew Manfre

Medication Compliance in Paediatric and Elderly Patients
Clarissa Rizzo

Evaluating Use of Technology to Support Shared Care
Analise Said

Evaluating Knowledge Available to the Public on Women's Health
Nicola Warrington

Evidence-Based Standards for Clinical Pharmacy Practice

Jessica Attard

Background: Evidence-based medicine is the practice of incorporating current information to clinical decisions, while keeping the patient's welfare central. It comprises the clinician's ability and experience, together with the best clinical evidence obtained from research and studies.[1] The clinical pharmacist has the potential of implementing evidence-based medicine into practice which will ensure that the most appropriate treatment is given to the patient.

Objectives: To identify clinical pharmacy services in hospital settings worldwide and analyse the effects of clinical pharmacists in different specialisation areas and to propose clinical pharmacy recommendations for the local setting.

Design: Clinical pharmacy activities offered worldwide were identified and outcomes consequent to clinical pharmacists' intervention in 10 medical specialisation areas were evaluated from published studies. Proposed recommendations were reviewed by a focus group consisting of 4 clinical pharmacists, 1 hospital pharmacist, 2 community pharmacists and 1 physician.

Setting: Hospital pharmacy

Main Outcome Measure: Effects of clinical pharmacy services

Results: Medication profile review, identification or change in drug administration (routes, dose or frequency) and participation of the clinical pharmacist in medical rounds are the most common services. Rational use of medication, identification and decrease in medication risks, provision of recommendations to healthcare staff and economic benefit are the most prevailing outcomes of clinical pharmacy services. The proposed recommendations were all positively received by the focus group.

Conclusion: Implementing clinical pharmacy services has been demonstrated to be beneficial to the patient and to healthcare systems.

Reference:

1. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: What it is and what it isn't. BMJ 1996;312(7023):71-2.

Comparison Between Oncology Medicinal Products in the Government Formulary in Malta and Other European Countries

Alexandra Cachia

Background: The Government Formulary List (GFL) is a list of medicines covered by the national health plan. Most European (EU) countries have a positive list of medicines used to make reimbursement decisions. The availability of oncology medicines in Malta is compared to those of other EU member states.

Objective: To compare medicines available in Malta for oncology with those in other EU Member States.

Design: Positive lists were obtained for EU member states when available. Oncology products were determined based on their ATC codes. Products having ATC codes L01 and L02 were identified and compared to those available on the GFL. In the case of the UK where a positive list is not used to make reimbursement decisions, the British National Formulary was used.

Setting: National and international pharmacy information

Main Outcome Measures: Positive lists from different EU member states; collection, compilation and comparison of local and foreign pharmaceutical reimbursement policies

Results: Every EU member state uses a positive list for reimbursement decisions except the UK and Germany. France does not have an official list of reimbursable products while the Croatian, Hungarian, Lithuanian, Portuguese, Romanian, Slovak and Spanish formularies are not available to the public. Malta has 59 different antineoplastic active ingredients available. Ireland has the lowest amount of antineoplastic active ingredients with 15, while the UK has the highest amount with 113. Neither of these countries reimburses amsacrine which is available on the local GFL. The UK has 18 protein kinase inhibitors available that are not on the GFL.

Conclusion: Statistics collected show that Malta has an above average amount of oncology medicines available. Medicines listed on the GFL are free whereas medicines listed on positive formularies in other EU Member States are reimbursed. The amount of oncology medicines available for reimbursement in a country is related to the country's economic situation and cancer incidence.

A Glossary of Risk Management Terminology in Pharmacy

Matthew Manfre

Background: Risk management provides the right tools for balancing the conflicts inherent in exploring opportunities whilst avoiding losses, accidents and disasters.[1] A glossary has been set up to standardise risk management terminology used in pharmaceutical settings. No such glossary has been developed to-date. The glossary is aimed at aiding the development of practice standards to ensure that pharmacy remains dedicated to improving patient outcomes whilst decreasing patient risks.

Objectives: To compile, validate and disseminate a glossary of risk management terminology

Design: Following an extensive literature review on the subject of risk management in different scenarios, risk management terms were attained from different sources. A template for the glossary was created and the terms defined. Literature sources used were peer reviewed journals and books. The majority of searches were performed using online databases. An expert panel made up of four pharmacists, two physicians, a linguist, a layperson and two risk management experts, was recruited in order to validate the glossary.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Publication of a 'Glossary of Risk Management Terminology for Use in a Pharmaceutical Setting'

Results: A total of 145 terms related to risk management have been defined. A validation questionnaire for the expert panel was created.

Conclusion: The terms found in the 'Glossary of Risk Management Terminology for use in a Pharmaceutical Setting' which is currently being developed will be validated by an expert panel prior to dissemination.

Reference:

1. Aven T. On the new ISO guide on risk management terminology: Reliability engineering and system safety. 2011. 96 (7): 719 - 26.

Medication Compliance in Paediatric and Elderly Patients

Clarissa Rizzo

Background: The paediatric and geriatric population can be regarded as being the most vulnerable age groups within society.[1] Due to physiological changes and the communication barrier, patient compliance still remains an obstacle yet to be overcome.[2]

Objectives: Identifying the current and local shortcomings in medicine management and how it affects patient compliance.

Design: Recruitment of 200 participants was undertaken, 100 elderly and 100 parents of paediatric patients. Each of these participants were asked to complete a questionnaire in the form of an interview.

Setting: Community pharmacies (elderly patients), Paediatric Outpatients Department, Mater Dei Hospital (parents of pediatric patients)

Main Outcome Measure: Measurement of the extent of compliance in both age groups

Results: The results obtained highlighted many areas of medicine management which should be targeted for further improvement. According to the questionnaire results, 80% of elderly patients did not know anything regarding their condition or medication being taken, 70% complained that they have too many medications in similar boxes, especially those provided by the Pharmacy Of Your Choice Scheme. From the paediatric population, 95% of parents complained about the taste of most medications, mostly antibiotics, which make it more difficult to comply to the proposed dosage regimen.

Conclusion: The results indicate the importance of improving the packaging design of each medication to make it more easily distinguishable and recognised for its use. With regards to the paediatric population, healthcare professionals must look further into possible ways of improving taste and means of administration to improve compliance in these patients.

References:

1. Patel VP, Desai TR, Chavda BG, Katira RM. Extemporaneous dosage form for oral liquids. Pharmacophore 2001; 2 (2): 86-103.

2. Ruscin JM, Linnebur SA. Drug-related problems in the elderly [Online].USA: Merck Manuals; June 2014 [cited 2015 Jan 20]. Available from: URL: www.merckmanuals.com/professional/geriatrics/drug_therapy_in_the_elderly/drug-related_problems_in_the_elderly.html

Evaluating Use of Technology to Support Shared Care

Analise Said

Background: Patient information is often recorded on paper. Technology is able to provide an integrated system which will be able to reduce healthcare costs and duplicated efforts done by the healthcare team.

Objectives: To identify current shared care practices in the Maltese healthcare settings, to establish how technology is being used to facilitate shared care and to identify limitations towards achieving shared care.

Design: The Pharmacy of Your Choice scheme was observed through two observational visits in community pharmacies. Observational visits and discussion with pharmacists were undertaken at the hospital pharmacies of Mater Dei Hospital (MDH) and Rehabilitation Hospital Karin Grech (RHKG). A questionnaire was developed, validated and distributed to 109 pharmacists working in the selected healthcare settings. Data obtained was analysed using Microsoft® Office Excel 2007 and SPSS® version 20.

Setting: Twenty community pharmacies, hospital pharmacies of MDH and RHKG

Main Outcome Measure: Pharmacists' perception on current shared care systems

Results: The majority (99.1%) of pharmacists agreed that electronic medication records should be better adopted in Maltese healthcare with 97.2% stating that this would improve healthcare quality and efficiency. The majority (96.3%) also agreed that electronic health records enable better communication between healthcare professionals. Pharmacists identified the following limitations in achieving such systems: initial implementation of the system and costs involved (87.1%), difficulties in maintenance of the system (68.8%) and healthcare professionals are reluctant to accept change (51.4%). The majority of pharmacists (99.1%) agreed that data confidentiality issues are not seen as an obstacle if appropriate security measures are adopted.

Conclusion: Pharmacists are in favour of improving current IT systems. However, limitations in adopting such systems exist and need to be overcome to improve the quality and efficiency of current healthcare.

Evaluating Knowledge Available to the Public on Women's Health

Nicola Warrington

Background: Pregnancy, menopause and osteoporosis are three conditions that may affect a woman's health at different stages of her life. For this reason, it is very important that women have access to information about these conditions. The internet is a medium that offers flexibility, speed and accessibility, making it a clear route for information dissemination.

Objectives: To evaluate how informed women are about their health and to develop a website through which information about pregnancy, menopause and osteoporosis will be available.

Design: An original questionnaire was administered to 160 health professionals to determine how informed their patients are on pregnancy, menopause and osteoporosis. The responses were analysed and compared with the patient feedback obtained from a previous study conducted by Fenech.[1] Important knowledge gaps were identified and these served as the foundation on which an educational website was created.

Setting: Community pharmacies

Main Outcome Measures: To increase public knowledge on issues related to women's health

Results: Patients' knowledge on many issues related to pregnancy, menopause and osteoporosis is lacking, especially among younger age groups and low levels of education.

Conclusion: Respondents feel that their patients are least knowledgeable about how to tackle an emergency related to the pregnancy, the complications of menopause and the risk factors for osteoporosis. An emphasis was made on these issues in the website. There is no association between preferred media and region in the cases of pregnancy and osteoporosis, however there is a correlation in the case of menopause.

Reference:

1. Fenech D. Impact of an internet awareness campaign for women's health [dissertation]. Malta: Department of Pharmacy, University of Malta; 2012.

Clinical Analysis

Use of Proton Pump Inhibitors and Effects of Amylase and other Enzymes
Ritianne Cassar

Risk Assessment of the Process Involved in the Preparation of Intravenous Admixtures within an Acute Hospital Setting
Diane Saliba

Use of Proton Pump Inhibitors and Effects of Amylase and other Enzymes

Ritianne Cassar

Background: The main action of proton pump inhibitors (PPIs) is a pronounced and long-lasting reduction of gastric acid production. PPIs irreversibly block the H+/K+ -ATPase enzyme of the gastric parietal cells and allow gastric pH to be optimal for amylase activity.

Objectives: To correlate the activities of pancreatic (p-) and total (t-) amylase in relation to the patient's drug history, presenting complaints and diagnosis.

Design: Amylase activity analysis was carried out with the Reflotron® device using a previously designed methodology.[1] Amylase activity is being carried out for p- and t- amylase.

Setting: Endoscopy Unit, Mater Dei Hospital; Research laboratory, Department of Pharmacy, University of Malta

Main Outcome Measures: Correlation between patient drug history, gastric pH, amylase activity and PPI therapy.

Results: Thirty-four patients were taking PPIs whilst 16 patients acted as a control group. The age of the patients ranged from 29 to 88 years. Pearson correlation coefficient showed a positive relationship between gastric pH and amylase activity ($p<0.05$). Independent samples t-test indicated that PPI patients have a significantly higher p- and t- amylase activity when compared to control patients (p-value for both tests <0.05).

Conclusion: Treatment for patients should be based on the relationship of gastric pH, amylase activity and pathology for better long-term treatment and knowledge of the disease. In 6 patients who had stopped PPI treatment, amylase was still active in their gastric juice during analysis. This must be further analysed to identify the duration of action after cessation of treatment and how this varies with different PPIs.

Reference:

1. Zammit K. Determination of α-amylase in gastric juice [project]. Msida (Malta): Department of Pharmacy, University of Malta; 2010.

Risk Assessment of the Process Involved in the Preparation of Intravenous Admixtures within an Acute Hospital Setting

Diane Saliba

Background: An essential element of centralised preparation of intravenous (IV) admixtures is preparing these products aseptically under controlled conditions. This may be an effective means to enhance patient safety.[1]

Objectives: To develop a reproducible risk assessment by evaluating risk factors, including risk elements on the functionality of the aseptic dispensing system (impact on capacity), risks to efficacy (turnaround time between drug order to availability at clinical area) and classical risks to patient safety.

Design: The medications analysed were chosen from a list of 223 products used to prepare IV admixtures at Mater Dei Hospital. A risk assessment tool was developed using Microsoft Access 2013. A record was created for each medicine formulation. Information in the form of 'risk number' for each formulation was generated. The risk factors were obtained from the National Patient Safety Alert 20 risk assessment tool for injectable medicines.[2] The total number of risk factors of each product were added. If a product has 6 to 8 risk factors, it is considered as a high risk product and risk-reduction strategies are required. If a medication has 3 to 5 risk factors, it is classified as a moderate-risk medicine. Low-risk products are those that have only 1 or 2 risk factors.

Setting: Mater Dei Hospital

Main Outcome Measures: Development of risk assessment tool, creation of a record for each medicine formulation, generation of information in the form of 'risk number' for each formulation

Results: Out of the medications assessed and analysed, 7 medications were found to be low risk medications, 8 medications were found to be of moderate risk and 5 medications were found to be high-risk medications.

Conclusion: This risk assessment tool identifies the high risk IV medications that might benefit from improved risk profiles if they are prepared in the pharmacy rather than within clinical areas.[1] However, such controls may not always enable the timely availability of all medicines within an acute setting.

References:

1. Beaney AM, Black A. Preparing injectable medicines safely. Nursing Times. 2012; 108(3): 20-23.
2. National Patient Safety Agency (NPSA). Promoting safer use of injectable medicines: Patient safety alert 20 [Online]. UK: NPSA; 2007 [cited 2015 Jan 20]. Available from: URL: http://www.nrls.npsa.nhs.uk/resources/?entryid45=59812

Industrial Pharmacy and Regulatory Affairs

Self-Auditing in Good Distribution Practice
Stephen Charles Bartolo

Factors Influencing Synthesis of Steroids
Conrad Cassar

Business Plan for an Eco-Friendly Mini-Scale Production Facility
Maria Mercieca

Regulatory Challenges and Innovations in a Small Member State: A Case Study of the Malta Medicines Authority
Benjamin Micallef

Self-Auditing in Good Distribution Practice

Stephen Charles Bartolo

Background: Recent advances in practices for the wholesale distribution of medicinal products were published in a revised European Commission guideline[1]. The revised guideline became enforced by the European Commission and consequently by the Inspectorate and Enforcement Directorate of the Malta Medicines Authority, as of 24th November 2013. The revised guideline replaced guideline 94/C 63/03 in accordance with Article 10 of Council Directive 92/25/EEC of 31st March 1992[2].

Objective: To create a self-auditing system for wholesalers to ensure that their practices of storage and distribution are in accordance with revised guidelines.

Design: Differences between the old and the revised guidelines were compiled, validated and used to generate checklists. Checklists were used to create the self-auditing system which was tested and validated in collaboration with a local wholesale dealer who had recently updated its SOPs to meet the requirements of the new GDP guidelines. Materials used to compile data include the European Commission Guidelines of 5th November 2013 on Good Distribution Practice (GDP) of medicinal products for human use[1] and guideline 94/C 63/03 in accordance with Article 10 of Council Directive 92/25/EEC of 31st March 1992.[2]

Setting: Local wholesale dealer

Main Outcome Measures: Creation of a self-auditing system

Results: A validated self-auditing system was compiled covering all areas of wholesale distribution described by the revised guidelines.

Conclusion: An effective self-auditing system is one which includes all the requirements described in the revised guidelines. The developed self-auditing system was effective in auditing the practices of a local wholesale dealer.

References:

1. European Commission. Guidelines of 5 November 2013 on Good Distribution Practice of medicinal products for human use (Text with EEA relevance) (2013/C 343/01). Official Journal of the European Union 2013; C 343/1.
2. European Commission. Guidelines on Good Distribution Practice of Medicinal Products for Human Use (94/C 63/03) (Text with EEA relevance). 1994.

Factors Influencing Synthesis of Steroids

Conrad Cassar

Background: The 17α-monoester steroid molecule bears a primary hydroxyl group at C21 and a secondary one at C11. It is being used as a starting material in the synthesis of a 17α,21-diester.

Objectives: To review methods describing acylation reactions at hydroxyl groups andto identify factors affecting the selective acylation of a hydroxyl group at C21 of a 17α-monoester.

Design: The method by Procopiou et al[1] was adopted and modified. The 17α-monoester dissolved in dichloromethane was reacted with acetic anhydride in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) or sodium bicarbonate[2] ($NaHCO_3$) as catalysts at 0 – 5°C. Thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) were used to monitor the reaction and assess synthesis of a specific steroid molecule.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Synthesis of a17α,21-diester steroid

Results: A review article of the literature discussing acylations at hydroxyl groups published between 1996 and 2013 has been prepared. The reaction with TMSOTf was completed within few minutes whilst that with $NaHCO_3$ was carried out for several hours. TLC analysis of reaction mixtures revealed two spots, one of which matched that of the reference standard.

Conclusion: TLC results show that the steroid molecule of interest may have been synthesised as the retention factor (R_f) of the reference standard matched that of the product. HPLC results correlate with those of TLC as a peak for both the product and the reference standard were obtained at the same retention time.

References:

1. Procopiou PA, Baugh SP, Flack SS, Inglis GG. An extremely powerful acylation reaction of alcohols with acid anhydrides catalyzed by trimethylsilyl trifluoromethanesulfonate. J Org Chem. 1998;63(7):2342-7.
2. Lugemwa FN, Shakih K, Hochstedt E. facile and efficient acetylation of primary alcohols and phenols with acetic anhydride catalysed by dried sodium bicarbonate. Catalysts. 2013;3:954-965.

Business Plan for an Eco-Friendly Mini-Scale Production Facility

Maria Mercieca

Background: Malta's strategic position and its legal and regulatory framework have attracted several industries, including pharmaceutical industries, to the island. A new way of ensuring efficient and prudent use of land is being sought to juggle between the needs of the industry and the island's limited land space.

Objectives: To plan and design an Oral Solid Dosage (OSD) form facility on a multi-storey basis, to draw up estimates as part of the capital expenditure and to estimate the running costs incurred in one year.

Design: A green facility is designed vertically, with special focus on material, waste and personnel flow. Professionals in the pharmaceutical industry validated the plans to ensure GMP regulations were adhered to. Fixed capital investment (FCI) was established using the "detailed-item estimate" method[1], through quotations from local suppliers. Running costs for the first year are estimated.

Setting: Local pharmaceutical companies, Malta Enterprise and Malta Medicines Authority

Main Outcome Measures: Incorporation of sustainable characteristics to the design; estimation of FCI and running costs; SWOT analysis as part of the business plan.

Results: The proposed multi-purpose OSD small scale production facility was designed on a land footprint of 4710m^2, with a total area of 7828m^2 spanning on four levels. The estimated capital expenditure is €12,970,067 excluding VAT. The running cost to produce 100 million OSD is €3,636,282.06.

Conclusion: Since there are no imposed height restrictions in industrial parks, a vertical facility will safeguard the relatively limited land space available. This facility will also reduce the carbon footprint by embracing renewable energy sources and products. It is imperative to note that investing in efficient infrastructures will contribute to the local growth of the pharmaceutical industry.

Reference:

1. Peters MS, Timmerhaus KD, West RE. Plant design and economics for chemical engineers. 5th ed. Singapore: McGraw-Hill; 2004.

Regulatory Challenges and Innovations in a Small Member State: A Case Study of the Malta Medicines Authority

Benjamin Micallef

Background: The Malta Medicines Authority (MA) was established in 2003 and its mission is to protect and enhance public health through the regulation of medicinal products and pharmaceutical activities.

Objectives: To accurately represent the complexities and challenges faced by the MA and to explore innovative solutions adopted by the same authority.

Design: A case study approach was used to holistically reflect the activities of the MA. Non-probability sampling was used and grounded theory was applied. Seven semi-structured interviews were carried out with the directors of the MA and three professional staff from different directorates. A focus group involving four inspectors was established. All interviews and the focus group were carried out on the MA premises between July and December 2013.

Setting: The Malta Medicines Authority

Main Outcome Measures: Interview transcripts were coded and the framework approach was used to display prominent themes.

Results: Innovative solutions include use of joint packs for medicinal products and a fast track procedure in line with article 126a of Directive 2001/83/EC to enhance access to medicines (4536 authorised products as on 31/12/2013). Involvement in centralised, decentralised and Mutual Recognition Procedure are used as a way to create impact at EU level and attract new revenue. Participation in 214 inspections, and management of 150 ICSRs and 349 ADRs by post-licensing, ensured that pharmaceutical activities were regulated and supported in 2013. To optimise regulatory efficiency and to respond to Malta's pharmaceutical needs, regular communication and feedback exercises are being carried out with stakeholders.

Conclusion: The MA achieved its objectives by adopting innovative solutions to deal with the challenges and has managed to balance core business and its responsibilities to stakeholders with additional positive initiatives that benefit the patient.

Medicinal Chemistry and Drug Design

Design and Optimisation of Novel Anti-Prostate Cancer Drugs capable of CYP17A1 Receptor Modulation using Galeterone as a Lead Molecule
Marie Claire Bonanno

Design and Optimisation of Novel Huperzine A Analogues capable of Modulating the Acetylcholinesterase Receptor for the Management of Alzheimer's Disease
Sara Bonavia

Design and Optimisation of Novel Structures Capable of Modulating a Homology Model of the Human M1 Receptor for the Management of Alzheimer's Disease
Neil Bugeja

Design and Optimisation of Novel Antihistaminic Agents Using the Doxepin Scaffold as a Probe
Rachel Camilleri

Optimisation of Novel Selective Cyclooxygenase-2 Inhibitors using Resveratrol Analogues as Lead Molecules
Clarissa Caruana

Design and Optimisation of Novel Structures Capable of Epidermal Growth Factor Inhibition for the Management of Neoplastic Disease
Marie Claire Farrugia

Design and Optimisation of Novel Lead Carbonic Anhydrase Inhibitors for the Management of Neoplastic Disease
Jessica Marie Muscat

Design and Optimisation of Novel Human Dihydrofolate Reductase Inhibitors for the Management of Proliferative Disease
Graziella Portelli

Design and Optimisation of Novel Structures Capable of Modulation of a Homology Model of the Human β1-Adrenergic Receptor for the Management of Hypertension
Astrid Marie Sant

Design of Novel Structures Capable of Inhibiting *Mycobacterium tuberculosis* Replication using the Azole Antifungals as Lead Molecules
Caroline Spiteri

Design and Optimisation of Novel Anti-Prostate Cancer Drugs capable of CYP17A1 Receptor Modulation using Galeterone as a Lead Molecule

Marie Claire Bonanno

Background: Androgen receptor antagonists are used clinically in the management of prostate cancer and the discovery of new molecules in this area generates increasing interest.

Objective: To use galeterone as a lead molecule for further iterative design of novel anti-prostate cancer drugs which modulate the CYP17A1 receptor.

Design: Protein Data Bank (PDB) crystallographic deposition describing the bound co-ordinates of galeterone and the CYP17A1 enzyme was selected as a template. Galeterone was examined from a structure activity relationship point of view, the moieties vital for ligand binding were identified and retained for the *de novo* drug design process using LigBuilder® v1.2. Sybyl® was used to obtain the apo form of the enzyme which was then used to map the ligand binding pocket. The binding affinity between galeterone and the CYP17A1 enzyme was predicted using X-SCORE® v1.3. The steroid nucleus of galeterone was removed, thus creating a seed. Novel structures with different pharmacophores were generated and further analysed to determine factors such as LogP, binding affinities and compliance with Lipinski's rules.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display, modelling, seed generation and Ligand Binding Affinity calculation.

Results: Eight families of molecules, comprising of a total of 65 novel structures were generated. Each family of molecules exhibits a different pharmacophoric structure, with the molecules in any one family differing only in the additional groups bound to the pharmacophore.

Conclusion: Prostate cancer research will benefit from structure-based drug design as it is expected to contribute to the future development of inhibitors that bind to the CYP17A1 enzyme and inhibit its androgen generating activity.[1]

Reference:

1.De Bono JS, Logothetis CJ, Molina A, Fizazi K, North S, Chu L et al. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med. 2011;364:1995–2005.

Design and Optimisation of Novel Huperzine A Analogues capable of Modulating the Acetylcholinesterase Receptor for the Management of Alzheimer's Disease

Sara Bonavia

Background: Huperzine A is a natural cholinesterase inhibitor derived from the Chinese herb *Huperzia serrata*. Huperzine A presents acetylcholine to enhance brain performance and shows promise for reversing or slowing down Alzheimer's disease.

Objective: To use *in silico* studies to design high affinity novel ligands for the ligand binding pocket of the acetylcholinesterase receptor with predicted adequate *in vivo* bioavailability and non-toxicity.

Design: The X-ray Crystallographic model of the *Torpedo californica* acetylcholinesterase complexed to Huperzine A was identified from the Protein Data Bank (PDB ID 1VOT). Two seed structures were constructed in Sybyl® 1.2 according to a methodology that took into account the relationship between molecular structure and biological activity as described in literature. Based on SAR data derived from Huperzine A, the points considered to be critical for binding were retained in each seed and planted into the AChE_LBP with growth being allowed according to defined parameters utilising the GROW module of Ligbuilder® v1.2.

Setting: Department of Pharmacy, University of Malta.

Main Outcome Measures: Molecule display, modelling, seed generation, Ligand Binding Affinity (LBA) calculation and *de novo* design.

Results: The *in silico* LBA of Huperzine A to the AChE_LBP was calculated to be 6.45. The result was the identification of 200 and 600 *de novo* designed structures from Seeds A and B respectively with a predicted *in silico* LBA (pKd) ranging between 6.30 and 10.00. Their molecular weight ranged from 300 to 526. A smaller cohort from Seed A (n=15) and Seed B (n=45) was also compliant to more stringent rules[1] with respect to central nervous system drugs.

Conclusion: Novel structures compliant to Lipinski's Rule of 5 may be promoted to second level drug design which could lead to identification of novel AChE inhibitors with better potency and a low side effect profile.

Reference:

1. Lipinski CA. Drew University Medical Chemistry Special Topics Course; July 1999.

Design and Optimisation of Novel Structures Capable of Modulating a Homology Model of the Human M1 Receptor for the Management of Alzheimer's Disease

Neil Bugeja

Background: "The link between M1/M3 receptors and Alzheimer's disease has been proposed to explain the progressive tau pathology that is characteristic of this disease".[1]

Objective: To create a novel drug to modulate an *in silico*-created homology model of the M1 receptor to manage Alzheimer's disease.

Design: The preliminary part of this study involved the creation of a homology model of the M1 receptor. 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 results.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measure: Creation of a drug which modulates an *in silico*-generated homology model of the M1 receptor to manage Alzheimer's disease.

Results: A homology model for the M1 receptor was created. Analysis of the ligand binding pocket resulted in 12 varying conformers. The conformer with optimal binding affinity was chosen to create a seed. This generated 200 molecules classified into 12 chemical families, 124 of which conform to Lipinski's Rules.[2] Highest and lowest-ranked molecules in each chemical family were structurally analysed, which yielded chemical moieties responsible for optimal chemical binding.

Conclusion: The *de novo* molecules created and optimised *in silico* present viable leads for high-throughput screening in subsequent drug-design studies, leading to identification of novel M1 muscarinic receptor subtype modulators for the use in managing Alzheimer's disease.

References:

1. Avila J. Muscarinic Receptors and Alzheimer's Disease. Future Medicine Ltd. Neurodegenerative Disease Management. 2011;1(4):267-269.
2. Lipinski CA. Lead- & Drug-Like Compounds: The Rule-of-Five Revolution. Drug Discov Today Technol. 2004;1(4):337–41.

Design and Optimisation of Novel Antihistaminic Agents Using the Doxepin Scaffold as a Probe

Rachel Camilleri

Background: H1 receptor antagonists are used clinically in the treatment of histamine-mediated allergic conditions. Apart from identifying molecules which are selective to the receptor, rational design of novel H1 antagonists aims to design molecules with reduced lipophilicity. This decreases their penetration through the blood-brain barrier with the consequent effect of sedation reduction.

Objectives: *In silico* design of novel H1 receptor antagonists with reduced lipophilicity and a lower side effect profile specifically with respect to sedation was undertaken.

Design: Protein Data Bank crystallographic deposition 3RZE showing the structure of the H1 receptor complex with doxepin was identified and selected as a template for this study.[1] Desloratadine, levocetirizine and fexofenadine were sketched in Sybyl® and docked into the H1 receptor Ligand Binding Pocket. Conformational analysis was performed in each case and the optimum conformation identified and used as a scaffold for novel molecular growth.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Seed generation, generation of novel H1 receptor antagonists and Ligand Binding Affinity (LBA) calculation

Results: Two seed structures (one for levocetirizine and one for fexofenadine) were constructed. Novel molecular growth was carried out using the Grow algorithm of LigBuilder®. Two hundred novel structures were generated for each seed with a LBA (pKd) ranging from 7.88 – 9.71 for the seed deriving from fexofenadine and 6.37 – 8.53 from the seed deriving from levocetirizine.

Conclusion: This study managed to identify a series of novel high affinity structures for the H1 receptor. These must be further analysed with an emphasis on logP such that molecule with utility as H1 antagonists may be identified.

Reference:

1. Shimamura T, Shiroishi M, Weyand S, Tsujimoto H, Winter G, Katritch V et al. Structure of the human histamine H1 receptor complex with doxepin. Nature. 2011;475(7354):65-70.

Optimisation of Novel Selective Cyclooxygenase-2 Inhibitors using Resveratrol Analogues as Lead Molecules

Clarissa Caruana

Background: Hydroxylated analogues of resveratrol represent a novel class of selective COX-2 inhibitors. 3,3',4',5-tetrahydroxystilbene and 3,3',4,4',5,5'-hexahydroxystilbene are highly COX-2 selective, with the latter being more selective than celecoxib.[1]

Objectives: To design and optimise a series of molecules which have a high affinity for COX-2, using 3,3',4',5-tetrahydroxystilbene and 3,3',4,4',5,5'-hexahydroxystilbene as molecular templates.

Design: In the first part of the study, X-ray crystallographic deposition 3LN1 describing the bound coordinates of celecoxib with COX-2 was used as a template. The bound coordinates of celecoxib were used to dock the two resveratrol analogues into the COX-2 active site, resulting in the generation of binding conformers. The best conformers were edited to create seeds capable of sustaining molecular growth. In the second part of the study, *de novo* design was performed. The seed structures were allowed to undergo growth, generating new molecules.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Accelrys Discovery Studio®: Molecule Display; Sybyl®: Molecular modelling; X-Score®: Ligand Binding Affinity (LBA) calculation; LigBuilder®: Ligand Binding Pocket elucidation.

Results: The binding affinities of the generated molecules compliant with Lipinski Rules[2] ranged from 9.71 to 10.00.

Conclusion: The *de novo* designed molecules with high LBA for COX-2 and oral bioavailability are suitable for inclusion into libraries of molecules which bind to the active site and selectively inhibit the receptor.

References:

1. Murias M, Handler N, Erker T, Pleban K, Ecker G, Saiko P, et al. Resveratrol analogues as selective cyclooxygenase-2 inhibitors: synthesis and structure-activity relationship. Bioorg Med Chem. 2004;12(21):5571-8.
2. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings.Adv Drug Deliv Rev. 1997;23(1-3):3-25.

Design and Optimisation of Novel Structures Capable of Epidermal Growth Factor Inhibition for the Management of Neoplastic Disease

Marie Claire Farrugia

Background: Overexpression of epidermal growth factor receptors (EGFRs), due to gene amplification, results in a number of tumours of an epithelial origin, such as breast, lung, colon, ovarian and bladder.

Objectives: To assess the ability of 2-O-caffeoyl tartaric acid, 2-O-feruloyl tartaric acid, emetine and rosmaricine, which were identified from Traditional Chinese Medicine (TCM), for their ability to antagonise the EGFR[1].

Design: The X-ray crystallographic deposition 2ITY describing the bound co-ordinates of gefitinib to EGFR was selected. The ligand was extracted from the binding site and its bound co-ordinates were used as templates for the conformational analysis of 2-O-caffeoyl tartaric acid, 2-O-feruloyl tartaric acid, emetine and rosmaricine. The best conformation was identified using X-Score® and Sybyl®. Seed structures were then generated and used for the *de novo* structure generation.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display, Ligand Binding Affinity (LBA) calculation, de novo design

Results: The best LBAs (pKd) for 2-O-caffeoyl tartaric acid, 2-O-feruloyl tartaric acid, emetine and rosmaricine were predicted to be 4.81, 4.81, 5.48 and 6.13 respectively. Seed molecules were then designed based on the best conformations identified.

Conclusion: Sixty-six, 16, 17 and 55 novel Lipinski Rule compliant molecules were generated from the 2-O-caffeoyl tartaric acid, 2-O-feruloyl tartaric acid, emetine and rosmaricine scaffolds respectively. These candidate molecules are recommended for synthesis and *in vitro* validation tests.

Reference:

1. Yang SC, Chang SS, Chen HY, Chen CY. Identification of potent EGFR inhibitors from TCM Database@Taiwan. PLoSComput Biol. 2011 Oct; 7(10):e1002189.

Design and Optimisation of Novel Lead Carbonic Anhydrase Inhibitors for the Management of Neoplastic Disease

Jessica Marie Muscat

Background: Carbonic anhydrase inhibitors (CAIs) are of utility in the management of solid tumours. Specificity for the carbonic anhydrase IX (CA IX) is associated with enhanced clinical outcomes.[1]

Objectives: To design novel CAIs to inhibit the growth of tumour cell lines *in vitro* and *in vivo*.

Design: Protein Data Bank (PDB) crystallographic deposition 3IAI[2] describing the bound coordinates of CA IX complexed with acetazolamide (AZM) was used as a template. The catalytic domain of the receptor was identified. Binding affinity between CA IX and AZM was estimated and used for the comparison with the binding affinity of the designed molecules. Sulphonamide moiety on AZM was identified as responsible for the inhibition and retained as a vital moiety when 3 seed structures were designed. Molecular growth was guided through the positioning of .hspc atoms on which fragments were introduced until novel molecules were obtained. Sybyl-X® v1.1 was used to extract AZM from CA IX and for the generation of 3 seed molecules. The binding affinity between CA IX and AZM was estimated using X-Score v1.3. LigBuilder v1.2 was used for molecular growth

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: The binding score, partition coefficient and molecular weight were calculated in Ligbuilder and were analysed.

Results: Four hundred and sixty five molecules out of the generated 600 molecules complied with Lipinski's rules, with a binding score significantly higher than that of AZM.

Conclusion: Results indicate that the novel molecules had increased positive interactions with the binding pocket. Unsaturation and a decrease in number of alkyl groups contribute to decreased molecular weights and partition coefficients, further predisposing to enhanced oral bioavailability.

References:

1. Supuran C. Carbonic anhydrase inhibitors. Science Direct 2010; 20(12):3467-74.
2. Alterio V, Mika H, Di Fiore A, Supuran CT, Pan P, Parkkila S et al. Crystal structure of the catalytic domain of the tumour-associated human carbonic anhydrase IX. PMC 2009; 106 (38): 16233-8.

Design and Optimisation of Novel Human Dihydrofolate Reductase Inhibitors for the Management of Proliferative Disease

Graziella Portelli

Background: DNA synthesis requires the co-enzyme tetrahydrofolate (THF) to act as a 1-C donor, where THF becomes reduced to the inactive dihydrofolate (DHF). Dihydrofolate reductase (DHFR) enzyme recycles DHF back to THF via a redox reaction with nicotinamide adenine dinucleotide phosphate (NADPH). Inhibiting DHFR exhausts cellular growth, making DHFR an ideal target in proliferative disease. Methotrexate (MTX) is a classic example of a drug which inhibits the DHFR enzyme.[1]

Objectives: To discover and optimize *in silico* high binding affinity antifolate ligands.

Design: Protein Data Bank (PDB) crystallographic deposition 1U72 describing MTX and NADPH bound to hDHFR was modelled in Sybyl, where only the moieties fundamental for biological activity were retained from the bioactive conformation of MTX. Seven seeds were generated by Sybyl using MTX as the reference molecule. Using LigBuilder the POCKET algorithm delineated the key site of the hDHFR-LBP and proposed a general pharmacophore for novel structures.[2] The seed structures were individually planted into this space where user-directed molecular growth was carried out according to the position of the pre-established Hspc atoms by GROW algorithm. The PROCESS module then organised the novel structures into families based on structural similarity.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecule display with modeling seed generation; Ligand Binding Affinity (LBA) calculation

Results: Using visualisation programmes, 14000 generated results were analysed. The general pharmacophore of each family was established and the top pharmacophore for each seed selected on Lipinski's Rules.

Conclusion: The crucial bonds necessary for inhibition between the selected 7 pharmacophores and the receptor are recognised and further optimised for the generation of the best conformer.

References:

1. Oefner C, D'Arcy A, Winkler FK. Crystal structure of human dihydrofolate reductase complexed with folate. Eur J Biochem 1988;174(2):377-85.
2. Wang R., Gao Y, Lai L, Ligbuilder: A Multi-Purpose program for Structure-Based Drug Design. JMolModel 2000;6:498-51.

Design and Optimisation of Novel Structures Capable of Modulation of a Homology Model of the Human β1-Adrenergic Receptor for the Management of Hypertension

Astrid Marie Sant

Background: The design of novel high affinity β1-antagonists with acceptable bioavailability could result in dose reduction and provide effective management of hypertension. The 3D structure of human β1-adrenoceptor has not yet been crystallographically elucidated.

Objectives: To construct a homology model of the β1-adrenoceptor and to design *in silico*, novel structures capable of its inhibition.

Design: A homology model was constructed using Protein Data Bank (PDB) ID 2YCW[1], describing turkey β1-adrenoceptor bound to antagonist carazolol, as template and the amino acid sequence of human β1-adrenoceptor. Conformational analysis following the docking of carazolol into the homology model's ligand binding pocket (LBP) yielded 19 conformers and for each, the ligand binding affinity (LBA), expressed as pKd, and the ligand binding energy (LBE), expressed in kcal/mol, with the homology model was calculated. The study was carried out using computational tools: UCSF Chimera, Sybyl-X and XScore.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Homology and molecular modeling; LBA calculation

Results: Five homology models were generated. Of these, Model 3 with a low root-mean-square deviation of 5.673Å was selected as the most viable. The LBP on the selected model was identified as the 3D space within which carazolol was to be docked. The conformer with a high LBA (pkd) and a low LBE (Kcal/Mol) was selected as a scaffold for novel analog screening.

Conclusion: This study has been successful in generating a viable homology model for the human β1-adrenergic receptor. Carazolol, a β-blocking agent was successfully docked into the generated LBP with the optimal conformer being identified. This latter will be used as a template for the generation of novel β1-selective analogues with predicted adequate *in vivo* bioavailability.

Reference:

1. Moukhametzianov R, Warne T, Edwards PC, Serrano-Vega MJ, Leslie AGW, Tate CG et al. Two distinct conformations of helix 6 observed in antagonist-bound structures of a β1-adrenergic receptor. Proc Natl Acad Sci USA. 2011; 108: 8228-232.

Design of Novel Structures Capable of Inhibiting *Mycobacterium tuberculosis* Replication using the Azole Antifungals as Lead Molecules

Caroline Spiteri

Background: *Mycobacterium tuberculosis* (Mtb) has been difficult to eradicate due to the constant emergence of resistant strains. Bound conformations of azole antifungals were used as templates for the *in silico* design of novel agents capable of superior inhibitory activity at the CYP450 enzymes prevalent within Mtb, due to their high affinity and *in vitro* inhibitory activity at this locus.

Objective: To create novel structures containing the azole pharmacophore which are capable of antagonising the Mtb CYP450 enzymes and be lethal to the organism.

Design: Protein Data Bank (PDB) crystallographic deposition 2IJ7 describing the bound coordinates of Mtb CYP121 enzyme with fluconazole, as documented in the literature[1], was selected as a template to create novel structures via a *de novo* drug design approach. Moieties critical for binding, according to the structure activity relationship of fluconazole bound to the CYP121 enzyme, were retained and the rest of the molecule was altered accordingly by adding novel moieties.

Setting: Department of Pharmacy, University of Malta

Main Outcome Measures: Molecular modelling was carried out in SYBYL®-X and ligand binding affinities were calculated *in silico* using X-Score®. LigBuilder® v1.2 was used to plant the seed structures into the Mtb CYP121 ligand binding pocket for growth into novel structures.

Results: Each seed structure generated a number of molecules with novel structures, which were grouped in families according to a unique pharmacophoric structure.

Conclusion: Azole antifungals were proven to be effective antimicrobacterial agents against Mtb CYP 121 which resulted in the possibility of novel anti-tubercular drugs.

Reference:

1.Seward H E, Roujeinikova A, McLean K J, Munro A W, Leys D. Crystal structure of the mycobacterium tuberculosis P450 CYP121-fluconazole complex reveals a new azole drug-P450 binding mode. J Biol Chem 2006; 281:39437-43.

Pharmacoeconomics

The Economics of Medicine Use in *in vitro* Fertilisation
Christina Noella Abela

Cost Reduction related to Temperature Control in Community Pharmacies
Kristina Baron

The Economics of Medicine Use in *in vitro* Fertilisation

Christina Noella Abela

Background: In November 2013, the first free *in vitro* fertilisation (IVF) cycles were initiated at Mater Dei Hospital (MDH) following the introduction of the Embryo Protection Act in 2012.

Objective: To carry out feasibility costing for state-funded IVF treatment in Malta

Design: Local prices of IVF medicines were gathered and a database was compiled. Two IVF protocols were formulated. The 'Gonadotropin Releasing Hormone (GnRH) Agonist Protocol' is widely recognised as the gold standard treatment and was chosen as a template on which the cost of each IVF cycle could be estimated.

Setting: Obstetrics and Gynaecology Unit, MDH

Main Outcome Measure: IVF treatment algorithms with wholesale medicine prices

Results: The average cost of 1 IVF cycle based on the GnRH Agonist Protocol, using exclusively proprietary products, is approximately €1,900. As of November 2014, 333 couples had enlisted to make use of this free service.[1] To be able to supply the medicines to these couples free-of-charge, a financial burden of approximately €640,000 would need to be incurred by the government.

Conclusion: In view of the fact that the IVF budgetary allocation for 2015 was €500,000, it is currently not feasible to offer both the hospital services and the medication for free without a 228% increase in funds.[2] Alternatively, treatment may be replaced by the novel GnRH Antagonist Protocol that is recognised as being more cost-effective. If these proposals prove to be unsustainable, patient affordability needs to be addressed. Statistics show that the average monthly gross wage in Malta is currently €1,311 which only covers 57% of the total cost of the medicines, assuming that the couple will only need 1 cycle for IVF to be successful. In conclusion, unless governmental initiatives are put forward towards this proposal the average citizen will not afford to undergo such treatment.

References:

1. 333 couples apply for hospital IVF service. The Times of Malta. 2014 Nov 11 [cited 2015 Jan 14]. Available from: URL: http://goo.gl/JQFTEr
2. Ministry for Finance. Financial Estimates 2015. 2014 Nov 17 [cited 2015 Jan 14]. Available from: URL: http://goo.gl/hEZgil

Cost Reduction related to Temperature Control in Community Pharmacies

Kristina Baron

Background: Legal requirements stipulate that a community pharmacy must be maintained at temperatures not exceeding 25°C. This temperature is exceeded during five months in the local scenario[1] resulting in a large investment in energy expenditure.[2]

Objectives: To quantify the cost of abiding by statutory requirements and to investigate the disposition of pharmacy managers to the potential introduction of energy saving methods in their own establishments.

Design: The first phase of the study consisted of analysis of yearly expenditure linked to cooling and its relation to other operating costs. The second phase comprised the development of a questionnaire to gather the opinion of managing pharmacists with regards to such costs. Two community pharmacies were analysed in phase 1 as selected via accessibility sampling. The questionnaire devised was sent electronically to 80 community pharmacy managers.

Setting: Community pharmacy

Main Outcome Measures: Cost reduction needs and exploration of possible energy saving methods.

Results: The average yearly cost of temperature control was established at €2587.25 representing 66% of the total cost expended on utilities and 8.2% when compared to the total operating expenses of pharmacies. Forty managing pharmacists completed the questionnaire. Responses indicate a strong interest in reducing costs related to temperature control. Pharmacists were open to implementing alternative methods to do so and suggestions of energy saving techniques were put forward.

Conclusion: The cost of cooling a community pharmacy resulted in a notable financial issue for proprietors. The application of energy efficient practices and techniques is the rational step for resolving this recognised issue.

References:

1. Galdies C. The Climate of Malta: Statistics, Trends and Analysis 1951-2010. Valletta: National Statistics Office Malta; 2011.
2. Coleiro D. Storage of Medicines [dissertation]. Msida (Malta): Department of Pharmacy University of Malta; 2012.

M.Sc. Pharmacy
Dissertation Descriptions

The Availability of Medicinals as Affected by Regulation
Anna Maria Cassar

Evaluation of After-Hours Pharmaceutical Services in a General Hospital
Jeffrey Cassar

Proposing Guidelines for Responsible Person Eligibility in Malta
Simon Corrieri

The Use of Internet Pharmacies by the Maltese Public
Elaine Gatt Baldacchino

Applying Quality Systems to Computerised Stock Management Systems
Joseph Giglio

The Impact of Pharmacist Advice on Metabolic Syndrome
Stephanie Magro

Pharmacist Intervention in Patient Monitoring in a Psychiatric Setting
Maria Mamo

The Availability of Medicinals as Affected by Regulation
Anna Maria Cassar

Regulation aims to ascertain the quality, safety and efficacy of medicinal products, however it may have negative consequences on their availability and accessibility. This study aims to evaluate the local scenario by analysing the list of medicinal products authorised in Malta to identify products according to the Anatomical Therapeutic Chemical Classification System which are not licensed or marketed. Factors influencing availability are identified following discussion with marketing authorisation holders and the implications of new licensing methods are assessed.

Evaluation of After-Hours Pharmaceutical Services in a General Hospital
Jeffrey Cassar

Mater Dei Hospital operates a 24-hour pharmacy service on shift basis, including after-hours drug information (DI) services. A data collection form was developed to evaluate DI requests encountered during one shift. A focus group consisting of six pharmacists and four pharmacy technicians is formed with the purpose of evaluating after-hours pharmaceutical services. The resulting outcomes are used to conduct a SWOT analysis highlighting the strengths, weaknesses, future opportunities and threats of the services.

Proposing Guidelines for Responsible Person Eligibility in Malta
Simon Corrieri

Maltese legislation requires the holder of a wholesale dealer licence to have a responsible person overseeing the distribution activities of the Licence Holder. This Responsible Person must be a pharmacist, and there is no indication on experience or training required. A focus group with various stakeholders from the industry was formed and results were used to prepare recommendations and guidelines

The Use of Internet Pharmacies by the Maltese Public
Elaine Gatt Baldacchino

There is an increase in the number of people using the internet to purchase pharmaceuticals. The purpose of this study was to determine the percentage of the Maltese population who purchase medicines over the internet and to educate the public on how to distinguish a legal from a ‘rogue’ internet pharmacy. The awareness of doctors and pharmacists of the possibility of patients using this route to purchase medicines, with the risk of adverse drug reactions and interactions with medications they may recommend, was also assessed.

Applying Quality Systems to Computerised Stock Management Systems
Joseph Giglio

The introduction of quality systems in stock management systems improved data reliability. A margin of error remains, when employees do not comply with established quality systems. Quality systems’ implementation for computerised stock management systems is essential to guarantee batch traceability and enable Good Distribution Practice requirements to be satisfied.

The Impact of Pharmacist Advice on Metabolic Syndrome
Stephanie Magro

Patients with metabolic syndrome are predisposed to cardiac problems due to diabetes, abdominal obesity, high cholesterol levels and high blood pressure. Fifty overweight patients who suffer from either two of the aforementioned conditions were recruited. Weight, blood pressure, blood glucose and cholesterol are monitored and assessment of medication compliance, side-effects, self-monitoring, lifestyle and risk factors is performed using a questionnaire. Patients were given advice on medication and lifestyle modifications.

Pharmacist Intervention in Patient Monitoring in a Psychiatric Setting
Maria Mamo

In psychiatric care, developments in psychotherapeutic agents and use of these medicinal products in patients with co-morbidities have inadvertently led to complex patient scenarios. A patient review tool was developed and psychometrically evaluated to enable pharmacists to carry out patient monitoring in an orderly manner and to allow for documentation of pharmaceutical care issues. The tool was used to monitor patients in an acute ward at Mount Carmel Hospital and to evaluate rational use of psychotherapeutic treatment.

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

Pricing of Medicines
Dillon Attard

Procurement of Medicinal Products in Governmental Health Services
Nicolette Bezzina

Packaging and Labelling in a Partial Manufacturing Unit
Melissa Ceci

Risks in Pharmaceutical Processes
Diane Camilleri

Medicine Reimbursement Systems
Cherieanne Giles

Packaging and Labelling in Parallel Importation of Medicinal Products
Valerie Mifsud

E-Pharmacy Services
Mark Sean Zammit

Pricing of Medicines

Dillon Attard

Medication pricing is influenced by various factors depending on the effectiveness and medical need; however the increasingly high cost of medication is posing a problem to many low income households resulting in patients forgoing treatment or skipping medication. An assessment of the approaches taken to overcome high pricing of medication is carried out; including the effectiveness of the pharmacy benefit scheme, elimination of pay-for-delay strategies and insurance coverage and subsidies increasing utilisation limitation.

Procurement of Medicinal Products in Governmental Health Services

Nicolette Bezzina

Effective health services depend on efficient supply of medicinal products. Medicinal shortages are increasing internationally and it is essential to take a proactive approach to managing or avoiding shortages. This study aims to understand the reasons for shortages on a local and international level and to map out strategies that can limit this problem. The study takes a qualitative approach, with document review and interviews as data gathering tools. Published standards and guidelines on shortage management form the basis of the research undertaken.

Packaging and Labelling in a Partial Manufacturing Unit

Melissa Ceci

The packaging and labelling processes undertaken within the Partial Manufacture Area (PMA) were assessed. The study includes a critical evaluation of the procedures followed at the PMA in relation to established national and international laws and guidelines. Areas of improvement within the current system were identified and suggestions based on published evidence were put forward.

Risks in Pharmaceutical Processes

Diane Camilleri

Risk scenarios in different pharmaceutical processes of community pharmacies are assessed. Such risk scenarios include risks in pharmacist prescribing. Risks during the medicine dispensing process of prescription and over-the-counter medications are evaluated. The knowledge, perception and practice of pharmacovigilance are assessed using a questionnaire disseminated to all local community pharmacies. The outcome of the questionnaire is to evaluate Good Pharmacovigilance Practice amongst pharmacies in Malta.

Medicine Reimbursement Systems

Cherieanne Giles

This research will address the Maltese reimbursement system and its advantages and disadvantages. Particular focus will be attributed to medicinal products present on the Government Formulary List (GFL) for instance, statin tablets (i.e. Simvastatin, Fluvastatin, Atorvastatin, and Rosuvastatin). Reimbursement systems in other European countries are analysed and assessed. Moreover, possible opportunities for cost savings to the Maltese system are explored.

Packaging and Labelling in Parallel Importation of Medicinal Products

Valerie Mifsud

This project compares parallel imports with originator products. A survey is conducted on which medicines and formulations are imported into Malta and which require re-packaging. A study of Malta and EU legislation on parallel imports is undertaken. A questionnaire is given to pharmacists about parallel imports, their packaging and labelling. Evaluation of the questionnaire should show the knowledge and preference of parallel imports by pharmacists and patients, thus the influence of parallel imports, in their final packaged and labelled state, on the local pharmaceutical market.

E-Pharmacy Services

Mark Sean Zammit

The purpose of this project is to compare and critically appraise the various types of medically-related applications that are used on smartphones and tablets, based on a number of criteria using various online reviews. The application types include drug interaction apps, medication trackers and reminders, disease and conditions management apps, drug dose calculators, formularies and pharmacopoeias. These are judged using the following criteria: cost and availability, reliability, usefulness, accessibility and ease of use. A review comparison is then compiled for all of them.

Fourth Year Students
Project Descriptions

Pharmacist Manpower
Petra Abdilla

This study aims to analyse the satisfaction of pharmacists in their specific roles. A validated questionnaire was distributed to all registered pharmacists to understand better their current employment structure. Only 110 out of 935 pharmacists completed the questionnaire to date, where 31% described their career choice as very satisfactory, 61% are satisfied with their area of employment and 9% are not satisfied. Of the not satisfied group, 5 were community pharmacists, who stated that they are not well respected by patients and underpaid for the advice they offer.

Pharmacist Prescribing
Abigail Aquilina

Guidelines for pharmacist prescribing in hospitals were compiled based upon reviewed models of pharmacist prescribing, along with guidelines for managing oral anticoagulation, hypertension and diabetes. An expert panel consisting of five pharmacists and five physicians is formed for evaluation of such guidelines. Case studies on the conditions mentioned were compiled and disseminated to the expert panel for comparison of pharmacist and physician prescribing. Questionnaires are developed to identify for which other conditions pharmacists are willing to prescribe.

Drug Design in Order to Modulate the PDE4 Receptor
Daniel Attard

Cyclic nucleotide phosphodiesterase 4 (PDE4) isozymes catalyse the hydrolysis of cAMP. They are located within brain and immunocompetent cells. The PDE4B subtype is a well-validated target for modulating inflammation, as selective inhibition is shown to preserve cAMP and suppress TNF-α and other pro-inflammatory cytokines. Molecular seed structures were obtained and used with permission from the Faculty of Pharmacy, Jagellonian University, Poland. The structures were docked to the PDE4B subtype (Protein Data Bank deposition 4MYQ), and optimised to result in superior ligands capable of antagonising the PDE4B.

Pharmacy Of Your Choice - Where Are We Going? Patient and Pharmacist Forum
Hannah Bonnici

The Pharmacy Of Your Choice Scheme aims to improve the delivery of free medication to patients, to expand the pharmacists' role and to better the relationship between pharmacists and patients. A pilot study forum was created in two sessions. In the first, all 11 participants said that the relationship has improved but 2 of the 6 patients said that there is still lack of communication. Nine participants would like medication reviewing to be launched. In the second session, all 6 participants were in favour of electronic prescribing. Although 2 of the 3 pharmacists have separate areas for consultation, they said that privacy is still an issue.

Evidence Based Use of Herbal Medicines
Justine Borg

The study aims to identify the knowledge of pharmacists and patients vis-à-vis herbal medicines and their use in the Maltese community. Literature research was conducted and analysed to identify whether herbal medicines have truly an evidence-based use or otherwise. A questionnaire was conducted in Maltese or English. Twenty-two pharmacies were selected randomly, where 50 pharmacists took part in the study. An average of 20 patients from each pharmacy will be participating.

Design of Novel Structures With an Aminopiperazinone, Aminoimidazole and Aminoquinazoline Scaffold Capable of Inhibiting the β-secretase Enzyme for the Management of Alzheimer's Disease
Luke Borg

Current treatment for Alzheimer's disease based on NMDA antagonists and acetylcholinesterase inhibitors is symptomatic, failing to reverse the condition. The β-secretase enzyme is cited in literature as being a potential disease modifying target for this condition. This project aims to utilise the aminopiperazinone, aminoimidazole and aminoquinazoline scaffold for the creation of seed molecules based on Structure Activity Relationship understanding. The seed molecules are then used for the *in silico* design of novel structures capable of inhibition of the β-secretase enzyme.

Use of Compliance Devices in Psychiatry
Estelle Borg Falzon

Use of compliance devices in psychiatric outpatients and those in domiciliary care is analysed. A group of psychiatric patients is chosen by convenience sampling from Mount Carmel Hospital and patients are given a 7 Day Multi Dose Pill Box to use for a specific time frame. The impact of the introduction of such a device within this patient group is evaluated with respect to practicality, cost-effectiveness and rate of compliance by conducting interviews before and after the administration of the compliance device.

Pharmacist Services in Community Pharmacies
Andrew Busuttil

The study aims to identify which services take up most of pharmacists' time by conducting a time-motion study of pharmacists in 22 pharmacies for three hours each. Novel services are recommended for the Maltese scenario and techniques which could improve time efficiency of pharmacists are suggested. A discussion on the importance of the availability of patient information will take place.

Multidisciplinary Tasking in Cancer Patient Management
Ann Camilleri

Cancer care requires complex management due to the involvement of combination therapy administered by multiple providers. A questionnaire intended for health care professionals was developed to study the intervention by the pharmacist in patient education and counselling, drug-related problems and administration of oncology medication. A pilot study was carried out by an expert panel to determine its validity.

Methadone Dispensing Services
Mark Caruana

The methadone dispensing services (MDS) in Malta and other countries were investigated. A questionnaire was developed and distributed, via the pharmacy council, to pharmacists registered in Malta. Fifty responses were collected and statistical analysis was performed. Forty pharmacists are willing to take part in a professional training program on MDS. Forty-two pharmacists agreed that they should be provided with the appropriate training required to dispense methadone.

Association of Medicinals to Sleep Apnoea
Yanica Cassar

A total of 183 medical records of patients that were referred to Mater Dei Hospital Sleep Lab were reviewed for their drug history, Epworth Sleepiness Score and Apnoea Hypopnoea Index (AHI) score. Two groups of patients were formed, group A patients diagnosed with obstructive sleep apnoea (OSA) (n=170) and group B patients not diagnosed with OSA (n=13). Antidiabetics and antihypertensive agents were amongst the agents found to be associated with the presence of OSA. This identified the need to screen for untreated OSA especially in patients suffering from hypertension and diabetes mellitus.

Risk Management in the Pharmaceutical Industry
Matthew Chircop

Stability of medicinal products is compromised if they are not stored within the correct upper and lower limits of the prescribed temperature by the appropriate pharmacopoeia. This project aims to address the influence of temperature fluctuation on stability of medicinal products by applying techniques of risk management. A temperature logging exercise was carried out on 14 temperature probes, placed at the CPSU warehouse and data was collected hourly over a period of six days. The data was then analysed using IBM SPSS® version 20 creating box plots and comparing means. The average probe temperature obtained was of 21.05 degrees Celsius.

Quality and Safety of Pharmaceutical Solvents used in the Pharmaceutical Industry
Darren Cioffi

Solvent selection in drug synthesis should have a minimal environmental impact. A review was done to find greener alternatives to dichloromethane. Drug synthesis was carried out using ethyl acetate as the green solvent. Samples taken during the reaction were analysed by thin layer chromatography (TLC). The product was purified by evaporating the solvent using a rotary evaporator. TLC showed that all of the starting material was used in the reaction and that the desired product may have been synthesised since the retardation factor of the reaction sample matched with that of the standard.

Design of Novel Anti-prostate Cancer Drugs which Modulate the CYP17A1 Receptor using Abiraterone as Lead Molecule
Kurt Degabriele

The X-ray crystallographic model (Protein Data Bank (PDB) ID 3RUK) describing the drug abiraterone bound to the CYP17A1 enzyme was identified from the PDB. The ligand-receptor complex was read into Sybyl-X and modelled such that the protein and abiraterone were separated. The apo protein and the extracted small molecule were used to calculate ligand binding affinity and ligand binding energy using X-SCORE. LigBuilder was used to analyse the key site and pharmacophore for 3RUK whilst seed structures were created and processed in LigBuilder to generate *de novo* designed structures for further analysis.

Professional Development of Pharmacists
Amanda Farrugia

Information on how continuing professional development in pharmacy is carried out in different countries around the world was compiled. Comprehensive updates on breast cancer, mood disorders and arrhythmias are currently being developed for the local scenario, with emphasis on the management and medications used in these conditions. The updates are prepared according to an already established template and are then reviewed by an expert panel. The updates are presented to pharmacists and evaluated. The perception of pharmacists on the updates is studied.

Use of Non-Steroidal Anti-Inflammatory Drugs
Jessica Farrugia

The local use of non-steroidal anti-inflammatory drugs and occurrence of unwanted effects and risk of interactions are evaluated. The data is collected using a patient-directed questionnaire. Patients are recruited from community pharmacies. Pharmacist and physician views are determined through another specific questionnaire.

Drug Induced Effects and Hospital Admissions
Nicola Farrugia

This study aims to investigate the occurrences of medication errors related to hospital admissions. On the post-admitting days of five selected medical consultants, each patient file was read and points noted through the use of a Data Collection Form. When the cause of admission was due to a drug-induced effect, an interview with the patient was carried out. These admissions are classified into categories depending on the medication error that occurred. Three hundred thirty three admissions have been observed, 54 of which were due to drug induced effects, with 29 being due to cardiac drugs.

Medication Reconciliation During Transfer of Care
Tresha Formosa

Pharmacist intervention in history-taking on admission was noted. One hundred patients are interviewed to obtain the best possible medication history (BPMH) using a structured data collection form. This medication history is compared to the one already taken by the admitting healthcare professional and any discrepancies are categorised. The vast majority of discrepancies have been omissions. Through the BPMH an overall larger number of medications were identified when compared to the other medication history. The clinical impact of these discrepancies is assessed.

Partial Manufacturing Within the Pharmacy Of Your Choice
Matthew Gatt

The project investigated the partial manufacturing (PM) carried out in the Pharmacy Of Your Choice (POYC) system. Operations, processes and environments in the PM area within the POYC are analysed. Patient and pharmacist perception about the labelling and packaging of products within the POYC were analysed through questionnaires. Questionnaires were distributed to two pharmacies in each of the 12 districts. There were 20 patient questionnaires handed per pharmacy. From current results more than 80% of pharmacists want better labelling of POYC products hence creating an improved system.

New Drug Distribution Regulations
Luca Giudice

The newly implemented Good Distribution Practice (GDP) guidelines provide wholesale dealers with the appropriate tools necessary to carry out their activities. These include the following revisions: written documentation of all processes to avoid errors by spoken communication; the presence of a Responsible Person (RP) who must implement and maintain a quality system and formal processes to deal with customer complaints, returns and suspected counterfeit medicines. The effect of these recent changes in GDP guidelines on the pharmaceutical industry is being investigated.

Design of Novel Anti-Prostate Cancer Drugs which Modulate the CYP17A1 Receptor using Ketoconazole and Orteronel as Lead Molecules
Michael Grima

Protein Data Bank deposition 3RUK describing the CYP17A1 receptor bound to abiraterone was identified and modelled in Sybyl® to measure the *in silico* affinity of the components. The structurally similar molecules orteronel and ketoconazole were sketched in Sybyl® and subjected to conformational analysis such that the optimum scaffolds from which seed structures were created were identified. Novel *de novo* structures based on each scaffold with high affinity for the target receptor and predicted *in vivo* bioavailability were generated in LigBuilder®. The optimum structures were proposed for *in vitro* validation.

Drug Design at the Sphingosine-1-Phosphate Receptor for the Management of Multiple Sclerosis
Daphne Gusman

Fingolimod is an immunomodulating drug approved for the treatment of multiple sclerosis. It is a sphingosine-1-phosphate receptor (S1PR1) antagonist. This project used fingolimod as a lead molecule for the design of novel modulators of S1PR1. The X-ray crystallographic model of S1PR1 was identified from the Protein Data Bank (3V2Y). Seeds were constructed *de novo* in Sybyl® and novel structures were generated using LigBuilder®. These structures were evaluated with emphasis being placed on ligand binding affinity and Lipinski Rule compliance with optimal structures being recommended for *in vitro* validation.

Yield in Synthesis of Active Pharmaceutical Ingredients
Christopher Davis Mallia

Synthetic processes for the production of active pharmaceutical ingredients were studied to improve product yield. Synthesis of 17α, 21-orthoestersteroid was carried out by reacting a 17α,21-dihydroxysteroid with the corresponding orthoester using an acid catalyst. The acid catalysts p-toluenesulfonic acid and pyridinium p-toluenesulfonate were used. The yield may be improved by varying reaction conditions such as temperature and concentrations of reagents. Thin layer chromatography was used to monitor reaction progress and high performance liquid chromatography was used to quantify products formed.

Use of Protocols in Community Pharmacy
Kyle Marston

Protocols can support professional services in diagnosing conditions and dispensing medicines in the community pharmacy. Locally published protocols were streamlined and compared to international versions. The booklet developed consisted of five sections each related to different conditions related to responding to symptoms in a community pharmacy. This comprehensive set of local protocols for responding to symptoms applicable to the local scenario was evaluated by an expert group and feedback was collected using a questionnaire.

Drug Design at the HIV Reverse Transcriptase Enzyme
Marie Mifsud

The discovery of novel drugs capable of managing the HIV virus is important, given that the resistance of this virus to drugs in current clinical use remains a consideration. This study used the reverse transcriptase (RT) enzyme as a target, for which novel antagonist molecules from the non-nucleoside reverse transcriptase inhibitors class could be designed. Both investigational, as well as FDA approved drugs were modified, to increase their potential to modulate this receptor. On completion of this study, a series of novel structures which can be compiled into a library for high throughput screening processes will be designed.

Design of Novel Non-Steroidal Structures capable of Antagonism of the Oestrogen-Related Receptor Alpha for the Management of Breast Cancer
Keith Muscat

This study considers oestrogen-related receptor alpha (ERRα) as a target for the design of drugs capable of treating breast cancer. The experimental steroidal drug SR16388 is used as a template to design novel structures devoid of the steroid nucleus which are capable of antagonising this receptor. These structures will be optimised and proposed for inclusion in libraries for high throughput screening.

Management in Chemotherapy Admixtures
Dylan Said

Cytotoxic drug residual waste of part-used vials at Mater Dei Hospital (MDH) and Sir Paul Boffa Hospital (SPBH) compounding units was captured. Monthly estimates of €12,244 (August 2014) and €6,219 (September 2014) worth of viable treatment were discarded at MDH and SPBH respectively, with bortezomib and trastuzumab being the predominant agents. Economic analyses and risk assessments are performed for the advanced batch preparation and shelf-life extension of reconstituted chemotherapy. Proposed strategies will take into consideration quality of admixture, cost savings and patient waiting times.

Medicinal Plants Research in Malta: Role of the Pharmacy Department and Argotti Gardens
Katrina Saliba

Research was carried out on ten studies which were conducted by past pharmacy students about herbal plants and products. These were compared to seven related studies undertaken by biology students. All the methods, results, discussions and conclusions were reviewed. The differences, similarities and consistency in results of these projects were analysed. Essential oil extraction and analysis were common to all the seventeen projects. Five out of the seventeen students did not conduct antimicrobial tests on the essential oils. Germination inhibition tests were done by the biology students only.

Drug Design at the Human Fatty Acid Synthase Enzyme using Orlistat as Lead Molecule
Ramon Sciberras

Orlistat, an anti-obesity drug, is being considered as a potential anti-cancer agent due to its ability to modulate the fatty acid synthase enzyme which is over-expressed in many tumours. In this study, orlistat was docked into the fatty acid synthase ligand binding pocket, subjected to conformational analysis, and the optimal conformer obtained was used to create seed structures onto which novel molecular growth was allowed. These new molecules are being analysed from a binding affinity and Lipinski Rule compliance perspective with the aim to promote for subsequent in-vitro testing.

Formulary for Non-British National Formulary Items
Timothy Scicluna

The Maltese Medicines Handbook is a publication giving information about medicinal products found locally which are not listed in the British National Formulary (BNF). The list of products issued by the Medicines Authority was used to identify the products to be included. Information was obtained from the Summary of Product Characteristics, while prices were identified from pharmacies. Out of 1000 products, 384 entries have their active ingredient and/or trade name not found in the BNF. From these, 51 entries have active ingredients not listed in the BNF while the other 333 entries have their trade name not listed in the BNF.

Waste Management in Pharmaceutical Processes
Shirley Tabone

In 2012, 339 tonnes of solvent waste were sent abroad from Malta for recovery. Currently, there are no facilities for the recovery of solvent waste available locally therefore solvents are sent abroad where they are recycled or incinerated. Since different types and amounts of solvent waste are generated by local pharmaceutical industries, vacuum distillation would be the most appropriate method for recovery. The cost-benefit analysis showed that it is not feasible and cost-effective to build a Solvent Recovery Plant locally. EU funding will only be considered if the project proves to be sustainable.

Pharmacist-Led Adherence Clinics for Chronic Conditions
Jessica Vella

The pharmacist's intervention in improving medication adherence at the Medical Investigations and Treatment Unit (MITU) at Mater Dei Hospital was investigated. The Morisky 8-item adherence questionnaire was used to evaluate medication adherence. Patients were given a leaflet and an individualised treatment chart. Follow-up was done after 6 weeks and reassessment was undertaken using an extended version of the questionnaire to evaluate the pharmacist's intervention. There was an increase in medication adherence from n=38 (week 0) to n=41 (week 6) for non-Hodgkin's lymphoma (p=0.042) and from n=2 (week 0) to n=5 (week 6) for Hodgkin's lymphoma (p=0.035).

Drug Extraction from Biological Fluids
Maria Vella

A literature review of previously published methods for the extraction of ciprofloxacin and clindamycin was done. A robust and reproducible procedure for the extraction and analysis of ciprofloxacin from human skeletal tissue was developed and validated. Fifty eight patient samples were collected. Most of these patients underwent minor lower limb amputation, whilst 6 underwent debridement. Of these patients, 39 had severe peripheral arterial disease (PAD). The samples will be analysed to determine the pharmacokinetics of ciprofloxacin in patients suffering from PAD.

Design of Novel A2A Adenosine Receptor Antagonists for Treatment of Parkinson's Disease
Yana Vella
Parkinson's disease is a chronic neurodegenerative condition caused by dopaminergic cell death. The A2A receptor has been identified as a target, with antagonists of this receptor being associated with attenuation of symptoms. This study used the scaffold of the experimental drug SCH-412348 to create seed structures capable of sustaining molecular growth with the A2A receptor ligand binding pocket. This process led to the identification of a cohort of structurally diverse high affinity molecules with the potential for *in vivo* bioavailability and antagonism of this receptor.

Human Papillomavirus Vaccination
Bettina von Brockdorff

Various factors related to the use of Human Papilloma Virus (HPV) vaccines available, their clinical benefits and pharmacoeconomic impact on the local health care system are studied. Perception of HPV vaccines amongst pharmacists, gynaecologists and patients of different specified social groups are assessed. Administration schemes of these vaccines in several countries and the impact of vaccinating males are studied. Awareness regarding these vaccines is established in the selected population sample and expedient recommendations will be devised for application in the local setting.

Drug Design at the Angiotensin-Converting Enzyme using Rubiatriol as Lead Molecule
Althea Marie Xuereb

Angiotensin-converting enzyme (ACE) is responsible for the regulation of blood pressure. Literature indicates that rubiatriol a naturally occurring triterpene, shows ACE-inhibitory effects. The protein data bank crystallographic deposition 2C6N was used to delineate the ligand binding pocket into which rubiatriol was docked. It was used as a scaffold from which seed structures were generated and onto which novel growth could be sustained. The molecular cohort obtained will be analysed with respect to affinity and Lipinski Rule compliance such that the optimal structures will be proposed for *in vitro* validation.

Pharmacists Intervention in the Use of Diuretics
Katya Xuereb

Patients with congestive heart failure on diuretic treatment were investigated. This study aims to examine the impact of a pharmacist-led intervention on pharmacotherapy of heart failure. Diuretic compliance and reasons for non-compliance were studied amongst hospitalised patients and patients identified at the community pharmacy by using the Morisky medication adherence questionnaire.

Drug Design at the β–Secretase Enzyme for the Identification of Novel Structures for the Treatment of Alzheimer's Disease
Keith Xuereb

The beta secretase enzyme is an aspartic acid protease, important for the formation of myelin sheaths in peripheral nerves. It has been implicated in the formation of the amyloid beta plaques found in the brain that characterise Alzheimer's disease. This project aims to discover newly obtained and optimised molecules which inhibit, or at least decrease, the formation of the amyloid beta plaques. These molecules will be used to design novel inhibitors with potential for clinical use in the therapeutic management of Alzheimer's disease, which act by blocking the β–secretase enzyme.

Medication Administration Systems at Mount Carmel Hospital
Nicola' Xuereb

A study of current medication administration systems at Mount Carmel Hospital (MCH) was undertaken. Observations of medication preparation and administration processes were carried out on three different wards at all administration times. A check list was developed and used to document these observations. Individual medication preparations (170) and administrations (172) were observed. Preliminary results revealed that 42 treatment charts contained illegible entries; in 71 cases of medication administration, nurses identified patients by calling out their name and surname.

Drug Design at the Oestrogen Receptor
Sharon Zammit

The experimental drug GW5638 has been reported to be of use in the management of breast cancer by antagonising the oestrogen receptor (ER) through a novel binding modality. This molecule was used as a template to design novel structures with potential clinical use in the management of tamoxifen-resistant breast cancer. Its scaffold was modelled in SYBYL to create a number of seed structures which were allowed to sustain molecular growth with the ER ligand binding pocket which lead to identification of novel antagonists with *in silico* demonstrable high affinity and bioavailability.

Third Year Students
Project Descriptions

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

P-glycoprotein is an efflux transporter which is commonly overexpressed in cancer cells, resulting in resistance to chemotherapy. Literature indicates that verapamil shows P-glycoprotein inhibitory effects if given in sufficient concentrations. *In silico* techniques are used to create verapamil analogues and identify molecules with the greatest predicted affinity.

Monitoring of Patients with Heart Failure
Rebecca Bugeja

Heart failure patients discharged from Mater Dei Hospital are divided into a control and study group. Pharmacist intervention is carried out by providing medication charts to study group patients with the aim of improving their understanding of the medications they are being prescribed and medication compliance. Usefulness of the medication chart is assessed using a questionnaire.

Development and Evaluation of the Pharmacy Practice Resource Unit
Francesco Cassar

A review of the development of the Pharmacy Practice Resource Unit (PPRU) at the Department of Pharmacy and literature about units developed in other countries is compiled. A questionnaire is distributed to students in the Department of Pharmacy to obtain feedback about the PPRU and to evaluate students' desired outcomes. Changes are implemented according to the feedback obtained.

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

K-RAS proteins serve as signalling messengers in response to extracellular stimulation. Inhibition of the signalling pathway of mutated K-RAS is associated with the mitigation of tumorigenesis. Polyphenolic extracts are used as leads in the *in silico* design of novel structures capable of inhibiting these molecules.

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 proteasome inhibitor with a β-lactone-γ-lactam bicyclic ring structure obtained from the marine organism *Salinispora tropica*. Inhibition of the 20S proteasome causes a build-up of proteins which induces apoptosis. The binding modality of NPI-0052 with the yeast 20S proteasome is determined from crystallographic data and used to design novel ligands with anti-tumorigenic properties.

Evaluation of the Affinity of the Small Molecule Maltanedienol for Farnesyl 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 (FPPS). *In silico* evaluation results show that maltanedienol binds with high affinity to the FPPS enzyme. The binding modality of maltanedienol to the FPPS enzyme is evaluated and novel analogues proposed.

Interdisciplinary Management of Arthritis in Children
Julian Fearne

Paediatric rheumatology patients are followed up by an interdisciplinary team at the Mater Dei Hospital paediatric out-patient clinic. Documentation forms used by the pharmacist to record pharmaceutical care issues are reviewed, updated and validated to further improve seamless care. A pharmaceutical care plan is compiled and submitted for further review and validation.

Validation Instruments for Community Pharmacy: An Update
Hannah Flynn

The quality system 'Validation of Community Pharmacy' developed locally and updated in 2011 is reviewed and implemented through the elaboration of an electronic platform. Implementation as a self-reporting exercise by community pharmacists is studied whilst analysis of pharmacist perception and professional services regulation is performed.

Implications of Regulation for Medical Devices
Jasmine Marie Gauci

The process by which a medical device is affixed with a CE marking is analysed. The role of the notified body and feasibility of establishing notified bodies for medical devices in Malta are examined. Identification of medical devices which should be dispensed from a community pharmacy as 'Pharmacy Only' items and those which should require a prescription is carried out.

Shared Care Guidelines in Rheumatology
Daniel Joseph Grixti

Shared care guidelines (SCGs) assist healthcare professionals and patients in clinical decision making, including enhanced practice of pharmaceutical care. A SCG for infliximab based on guidelines established by NHS UK, Janssen approved by US FDA and Mater Dei Hospital Malta is developed and evaluated. Similar processes are conducted for other drugs used in rheumatology.

Drug Design at the Human Glucocorticoid Receptor
Sean Meachen

Glucocorticoids are involved in a variety of drug functions and their chronic use is associated with a plethora of side effects which greatly limit their use. Novel structures capable of superior modulation of the aforementioned protein target are identified using specialised software such as VMD® and LigBuilder®.

Drug Design at the Adenosine A_{2A} Receptor using Caffeine and Limonene as Lead Molecules
Danica Micallef

The adenosine A_{2A} receptor has potential in neurodegenerative diseases when antagonised and has potential as a regulator of inflammation when agonised. X-ray structures of the A_{2A} receptor complexed with various antagonists and agonists were identified using the Protein Data Bank. This *in silico* drug design study aims to identify novel structures capable of modulating this receptor by using caffeine and limonene as lead molecules.

Procurement of Medicinal Products and Medical Devices
Caroline Muscat

Uninterrupted availability and accessibility of medicines is considered to be a citizen's right in Malta. The Maltese formulary and procurement system are assessed through a pharmacoeconomical approach to investigate the innovativity and cost-effectiveness of drugs in addition to drug management and supply. These are compared to international health care system procedures and improvements are suggested.

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

Alcohol dehydrogenase, thioredoxin reductase and RNA polymerase are cited as potential targets for allicin, an antibacterial garlic compound. An *in silico* conformational and binding analysis of allicin with these enzymes and comparison with known enzyme ligands are performed. The resulting data is used to generate new and improved inhibitors of these enzymes.

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

Databases covering individual chapters of the British National Formulary (BNF) created by M.Pharm students are currently being checked for updates in Protein Data Bank entries and for errors against the latest BNF version. These databases are collated into one searchable tool. Its utility is validated by both a panel of expert educators and students to include assessment in the classroom scenario.

Patient Monitoring of Out-Patients at the Rheumatology Clinic
Jonathan Vella

Considering that rheumatology patients are treated with drugs which are highly immunosuppressant, it is important for the pharmacist to collaborate within a team to improve patient safety. This is achieved by reviewing guideline algorithms for patient monitoring, designing patient information booklets and developing a quick method to alert health professionals regarding abnormal laboratory blood test results.

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. The prenyl-binding protein facilitates diffusion of this K-RAS protein through the cytoplasm. The deltarasin scaffold is used to design novel therapeutic agents capable of inhibiting this prenyl-binding protein.

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

Diallyl Disulphide (DADS) is a major organosulfur constituent derived from garlic with documented ability to stop cancer cell proliferation through the inhibition of histone deacetylase. A crystal structure was identified from the Protein Data Bank. It describes the bound coordinates of the histone deacetylase enzyme receptor complexed with the DADS ligand. The molecular modelling computer programme Sybyl® was used to model this holostructure.

Second Year Students
Project Descriptions

Pharmaceutical Care Processes used in Psychiatric Institutions
Roberto Briffa

The study addresses processes undertaken in pharmacotherapy management, medication administration and patient follow-up monitoring for inpatients at Mount Carmel Hospital. Improvements are proposed, discussed and evaluated.

Health Economic Study of the Use of Warfarin
Grazielle Camilleri

This study presents case studies of patients on warfarin, monitoring their progress and treatment outcomes. The pharmacist's role in this scenario is studied. The present system is analysed and compared to other countries.

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

Leishmania affects approximately 12 million people globally. Leishmania kinases have been identified as critical in the life cycle of this protozoan. The aim of this project is to design *in silico* novel kinase inhibitors using the suramin *in silico* scaffold as template.

Medicine Use and Access Intelligence
Stefan Cassar

The intelligent use of medicines and access to these medicines is analysed. Case studies about factors which could improve access to medicines are recorded, grouped and analysed to devise and propose responses to research questions.

Registration of Medicines
Francesca Cilia

All medicines marketed in Europe require a marketing authorisation. This process is analysed, highlighting the bureaucracy in the registration of medicines related to small countries. Alternative procedures with the aim of simplifying the registration process are proposed.

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

Quercetin is a naturally occurring flavonoid which through histone deacetylase inhibition, mitigates tumour growth. The quercetin scaffold is used for the *in silico* design of novel inhibitors.

***In silico* Interaction of Oleuropein With the MMP-9 Receptor for the Management of Breast Cancer and Alzheimer's Disease**
Matthias Karl Farrugia

Oleuropein inhibits breast cancer proliferation by inhibiting matrix metalloprotease (MMP) enzymes. Protein Data Bank crystallographic depositions describing these enzymes bound to small molecule inhibitors are used in the design of novel antagonists derived from the oleuropein scaffold.

Use of Medicines in Older Patients in Long-term Care Facilities
Tiziana Fenech Caruana

An analysis of the medicine use processes carried out in long-term facilities of the elderly is carried out. A comparative approach is undertaken and models of best practice are proposed. Pharmacist intervention in pharmacotherapy management and medication review are assessed.

***In silico* Design of Phytoalexin Resveratrol Polyphenolic Analogs as Inhibitors of Histone Acetyl Transferase for the Management of Tumour Growth**
Rebecca Hammett

Histone acetyl transferase inhibition is associated with tumour growth suppression. This study uses resveratrol as a probe molecule in the design of novel inhibitors for these enzymes.

***In silico* Design of Diallyl Disulphide Analogs as Inhibitors of Histone Deacetylases for the Management of Tumour Growth**
Christian Mercieca

Diallyl disulphide (DADS) and its analogues are known to inhibit histone deacetylase enzymes, and consequently tumour growth. This *in silico* study will design novel DADS based inhibitors.

***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 uses the olaparib scaffold for the *in silico* design of novel inhibitors.

Pharmacovigilance
Philip Paris

Pharmacovigilance is the pharmacological science which focuses on the detection and assessment of adverse effects of drugs. The study investigates the practice of pharmacovigilance in Malta.

Patient Management With Use of Lithium
Julia Pirotta

Lithium treatment entails patient monitoring due to its pharmacological profile. Patient management with regards to use of lithium is analysed. The submission of pharmacovigilance reports within the system are assessed and the importance of follow-ups is highlighted.

***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 uses the crystallographic co-ordinates of known histone deacetylase inhibitors to predict the binding modality of epigallocatechin-3-gallate at this locus and to use its scaffold to design novel structures with potential clinical use for neoplastic disease.

Pharmacist Intervention in Ambulatory Care of Older Persons
Rebecca Zammit

Pharmacist intervention in the monitoring of older persons to understand needs, distribution of medicines and medicine review is evaluated. By dividing and investigating different models, proposals are made to improve ambulatory care for older persons through follow-ups and direct patient feedback.

M.Pharm. Dissertation Title Index in Alphabetical Student Surname Order