

# **Time-dependent Effects of (Lisinopril) and (Valsartan) on Blood Pressure, Lipid Profile and Renal Function in Kurdish Hypertensive Patients**

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**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 12/7/2008

**Supervisor:** Dr. Ibrahim Adham Al-Bayatee  
Dr. Kassim Jaleel Al-Shamaa

## **Abstract**

### **Background:**

Accumulation of evidence supports the notion that (ACE inhibitor, lisinopril) have nearly the same favorable effects as (ARB, valsartan) in controlling BP in patients with essential hypertension. However, pharmacological profiles are substantially different between ARBs and ACE inhibitors. Clinical observations indicated that valsartan has little advantages over lisinopril in controlling BP and the incidence of severity of side effects in hypertensive patients.

### **Objective:**

In order to demonstrate the advantages of valsartan over lisinopril and relate these advantages to the different pharmacological profiles of both drugs, the present work was conducted. The study was performed at outpatient department (consultancy) of Rizgary Teaching Hospital in Hawler (Erbil) city, during the period from June to November 2007.

### **Patients and Methods:**

Forty seven patients with essential hypertension were participating in the study; twenty three patients treated with (valsartan 80 mg/day) for 9 weeks (Group One) and twenty four patients treated with (lisinopril 10 mg/day) for the same period (Group Two). Blood pressure was recorded at 0, 1, 3, 5, 7, and 9 weeks after treatment. Blood samples were withdrawn from the patients and lipid profile parameters (total cholesterol, triglyceride, serum HDL-C, and serum LDL-C) serum sodium and serum potassium were recorded at (0, 3, 5, 7, 9) week intervals. Serum urea and serum creatinine were also recorded at 0, 1, 3, 5, 7, and 9 weeks after treatment. Follow up observations for the incidence of side effects (angioedema; dry cough) also recorded.

### **Results:**

The results indicated that the diastolic blood pressure in patients treated with lisinopril was  $82 \pm 0.9$  mmHg (24.7% reduced) after 9 weeks of treatment, a value which was near up normal level, whereas the diastolic blood pressure in patients treated with valsartan was  $80 \pm 0.9$  mmHg (21.5% reduced) after 9 weeks of the treatment. However, the systolic blood pressure of patients treated with lisinopril and those treated with valsartan 9 weeks after treatment were the same (133 mmHg). Serum total cholesterol and LDL-C were significantly reduced in both valsartan and lisinopril treated groups compared to zero time values. The reduction was significant at 7 and 9 weeks in valsartan treated groups,

whereas it was significant (7.8% reduced) at 9 weeks only in lisinopril treated group; moreover in valsartan treated group the serum total cholesterol 7 and 9 weeks after treatment were  $181.4 \pm 3.4$  mg/dl and  $176 \pm 2.5$  mg/dl (6.39% and 9.1% reduced) and LDL-C, 7 and 9 weeks after treatment were  $105.4 \pm 4.7$  mg/dl and  $100.6 \pm 3.8$  mg/dl respectively (10.4 and 14.5% reduced). In contrast the serum total cholesterol at 9 weeks in lisinopril treated group was almost near the serum total cholesterol of apparently healthy normotensive individuals. Serum triglycerides showed no significant changes in both valsartan and lisinopril treated groups compared to zero level values. The present work demonstrated a significant increase in potassium ion and a non significant decrease in sodium ion in both valsartan and lisinopril treated patients compared to the zero level values, also blood urea and serum creatinine levels showed significant increase in patients treated with lisinopril or valsartan compared to zero time values. Our results clearly demonstrated that lisinopril treatment was accompanied by the presence of persistent dry cough in treated patients, while one patient only on valsartan treatment showed only occasional mild dry cough.

**Conclusion:** In conclusion, use of valsartan and/or lisinopril results in significant change in serum lipid profile toward its improvement, but depresses renal function slightly. There is significant increase in potassium ion and a significant increase in blood urea and serum creatinine levels. During the study period the only side effects presented was cough and angioedema in some cases. The study promotes the periodical biochemical check for serum potassium, serum urea, and serum creatinine.

# **Hematological and Biochemical Changes During Pregnancy at Third Trimester**

**Name:** Govand Shafeeq Tawfeeq

**Degree:** M.Sc.

**Specialty:** Physiology

**Date the debate:** 30/1/2010

**Supervisor:** Assist. Professor. Ismail S. Kakey

## **Abstract**

The effect of pregnancy at third trimester on some hematological and biochemical parameters was determined. One hundred twenty pregnant women, 16 to 46 year of age, and 20 age matched apparently healthy non pregnant women were included in this study. Pregnant women were enrolled from October 2008 to May 2009 at Maternity Hospital, Erbil city. The non pregnant women were selected from sub staff and workers of the same hospital. The results revealed that the pregnant women at third trimester had significantly lower Red Blood Cell count, Hemoglobin concentration, Hematocrit % and platelets counts, than in non pregnant women, where significantly higher values of Mean Corpuscular Volume, Mean Corpuscular Hemoglobin were observed. There were no differences between pregnant women during the 7th, 8th, and 9th months in hematological indices. The results showed non significant effect of the age on the studied parameters (WBC count, RBC count, Hb concentration, HCT, MCV, MCH, MCHC, and platelets count) in pregnant women at third trimester. There were no effects of the birth number of the pregnant women on the studied parameters at third trimester. The results of this study showed non significant effect of hypertension in pregnancy at third trimester on the (WBC count, RBC count, and Hb concentration, HCT, MCH, and MCHC), while it causes decreasing of the platelet count and MCV value. With respect to the effect of pregnancy on the studied biochemical parameter, the results showed that pregnancy cause decreased in the level of blood urea and total protein level , while it cause increasing in the level of blood sugar and globulin in the blood serum. Regarding the effect of pregnancy on the oxidative stress state in the women, the results of this study showed significant increasing level of the malondialdehyde during pregnancy at third trimester, while causing decreasing in the level of the glutathione.

# Kinetic and Thermodynamic Study for Adsorption of Antibiotics from Aqueous Solutions

**Name:** Hiwa Omer Ahmed

**Degree:** M.Sc.

**Specialty:** Physical Chemistry

**Date the debate:** 9/1/2010

**Supervisor:** Assist. Professor. Kafia M. Shareef

## Abstract

Batch equilibrium method was employed to study the adsorption behaviour of three widely used antibiotics (Cefotaxime, Ciprofloxacin, and Oxytetracycline) in Kurdistan. Four soil samples were selected for this study from different locations (Minara, Havalan, Sorbash and Runaki) in Erbil. Preliminary tests were done to find the equilibrium time, soil to solution ratio and initial antibiotic concentration. The results showed that the adsorption process of antibiotic in all soils is divided into, first, rapid initial step followed by slowly and very slowly second step. The amount of each antibiotic adsorbed ( $q_e$ ) on the studied soils from S1-S4 were; for CEF (at  $20 \mu\text{g ml}^{-1}$ ) were 84, 47.5, 70 and  $59 \mu\text{g g}^{-1}$ , for CIP ( $20 \mu\text{g ml}^{-1}$ ) were 60.36, 47, 64.4 and  $50 \mu\text{g g}^{-1}$  and for OTC ( $10 \mu\text{g ml}^{-1}$ ) were 21, 14.25, 16.87 and  $11.25 \mu\text{g g}^{-1}$ , respectively. It was noted that values of  $q_e$  increased with increasing the antibiotic initial concentration. Linear fit of our data with the first order rate expression were observed from the high values of regression factors ( $R^2 > 0.9766$ ). Our results revealed that values of  $q_e$  increased with increasing soil clay, cation exchange capacity (CEC) and soil organic matter (SOM). Linear distribution, Freundlich and Langmuir adsorption models were used to explain the adsorption equilibrium data and the data was well fitted to Freundlich model. Values of KF for adsorptions of the studied antibiotics were in the following orders for CEF 43.822, 1.448, 15.187 and 7.271, for CIP 17.676, 3.741, 52.601 and 6.513, and for OTC are 14.709, 2.884, 13.775 and  $3.466 \text{ ml g}^{-1}$  on S1-S4 respectively. Thermodynamic study of adsorption equilibrium revealed that values of equilibrium constant ( $\ln K_o$ ) were in the range 0.872 - 4.066, 1.136-5.507, and 0.590 - 10.135 for CEF, CIP and OTC respectively. The values of  $\Delta G^\circ$  indicated that adsorption of antibiotics were in order of  $\text{OTC} > \text{CEF} > \text{CIP}$ , on S1 and S3 (high SOM) while on S2 and S4 (low SOM) the order was  $\text{CIP} > \text{CEF} > \text{OTC}$ . High values of  $\Delta H^\circ$  pointed toward chemisorption mechanism. The values of  $\Delta S^\circ$  were in the range 258.291 - 190.506, 306.186 - 142.568 and 340.907 - 185.718  $\text{J mol}^{-1} \text{K}^{-1}$ , for CEF, CIP and OTC, respectively.

## **Effects of Simvastatin on Lipid Profile, Atherogenic index and Serum Transaminases in Hyperlipidemic Patients**

**Name:** Ary Aziz Salih

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date the debate:** 3/2/2010

**Supervisor:** Dr. Showan D. Husain

### **Abstract**

**Background:** Hyperlipidaemia is a condition characterized by increased concentrations of lipids including triglycerides (TG), cholesterol and lipoproteins; low density lipoproteins (LDL) and very low density lipoproteins (VLDL) in the blood and some times decreased high density lipoproteins (HDL). Many drugs have been used for treatment of this disorder. The present study was designed to estimate the effects of simvastatin on lipid profile, atherogenic index, serum transaminases, serum creatinine, uric acid and alkaline phosphatase. **Methods:** This study includes 70 subjects, 45 untreated hyperlipidemic patients, and 25 healthy subjects. They were divided into two groups, the first group included 45 patients were treated with 20mg simvastatin and second group included 25 normal healthy subjects. After 12 hours fasting, serum lipid profile (total cholesterol, TG, HDL, LDL, VLDL and atherogenic index), serum transaminases; alanine aminotransferase (ALT) and aspartate aminotransferase (AST) alkaline phosphatase, uric acid and serum creatinine were measured for the patients in 3 intervals before treatment, after 8 weeks and 16 weeks of treatment.

**Results:** After 16 weeks of therapy, simvastatin showed a significant reduction in serum (TC, TG, LDL and VLDL) and also, significant rise in serum HDL noticed. A significant reduction was observed for atherogenic index (TC/HDL) by performing a comparison between group before treatment , group after 8 weeks treatment and group after 16 weeks treatment. Serum ALT, serum AST and serum alkaline phosphatase (ALP) were significantly increased but still were within normal levels. Insignificant effect was observed from serum creatinine and serum uric acid by performing a comparison between group before treatment, group after 8 weeks treatment and group after 16 weeks treatment. Insignificant reduction was observed for body mass index (weight/ height<sup>2</sup>) by performing a comparison between group before treatment and group after 8 weeks and a significant reduction was observed between group before treatment and group after 16 weeks treatment.

**Conclusion:** Simvastatin was effective in controlling lipid profile and atherogenic index, and no cases reported with liver disease.

# **Evaluation of L-Carnitine, Multivitamins, and their Combination as Therapies for the Treatment of Idiopathic Male Infertility in Erbil Governorate- Kurdistan Region/ Iraq**

**Name:** Jehan Jalal Aram

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date the debate:** 9/12/2010

**Supervisor:** Dr. Ansam Najj Al-Hassani

## **Abstract**

Idiopathic male infertility or oligo- and/or asthenozoospermia is when a man has a low sperm count and/or poor sperm motility and the medical cause is unknown. L-carnitine is an essential cofactor of fatty acid metabolism in body tissues; it is highly concentrated in the epididymis and found to play a crucial role in sperm metabolism, motility, and maturation. The aims of the present study are to investigate and compare the efficacy of L-carnitine, multivitamins alone, and their combination therapies on semen characteristics in idiopathic male infertility in Erbil Governorate. In this study, 129 idiopathically infertile patients were randomly divided into three groups who had received three different treatment regimens for an uninterrupted period of three months: group A (45 patients) had received 2 grams daily of L-carnitine alone; group B (55 patients) had received the combination of L-carnitine (2 grams daily) plus one tablet daily of multivitamins (Stresstabs®); and group C (29 patients) had received one tablet daily of multivitamins alone (Stresstabs®). A control group was also enrolled in this study which included thirty fertile male volunteers. Patients were followed up and seminal fluid analysis was done before treatment and monthly after treatment for three months. The results were statistically analyzed for the evaluation of the effects of L-carnitine, multivitamins and their combination using paired sample t-test to compare between the values before treatment and their corresponding values after 1, 2, and 3 months of treatment and P values of  $< 0.05$  were considered statistically significant. The results of this research demonstrated that the combination therapy of L-carnitine and multivitamins was more efficient and produced more significant improvement in semen characteristics (sperm concentration, sperm count, percentage of actively motile sperm, and progressive motile sperm count) than either therapy alone, and that L-carnitine therapy was more efficient than multivitamins therapy and produced more significant improvement in the above semen characteristics using the treatment regimen applied in this study among men with idiopathic male infertility. The results also indicated that the use of the progressive motile sperm count in the seminal fluid analysis is more indicative for the improvement in semen parameters than the sperm count and percentage of actively motile sperms separately, since it represents the product of multiplying the sperm count by the percentage of actively motile sperm.

# **Evaluation of Metformin Treatment in Patients with Polycystic Ovary Syndrom**

**Name:** Thulfiqar Abdullah Mohammed

**Degree:** M. Sc.

**Specialty:** Clinical Biochemistry

**Date the debate:** 8/12/2010

**Supervisor:** Dr. Sanaa Godbaan Hama

## **Abstract**

### **Background**

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of fertile age, affecting 5-10% of the female population.

Anti diabetic(metformin) therapy has been proposed as a treatment for PCOS, a condition frequently associated with insulin resistance and metabolic syndrome.

### **Objective**

To evaluate the metabolic effects of metformin in patients with polycystic ovary syndrome.

### **Subjects and Methods**

Eighty female with a diagnosis of polycystic ovary syndrome (PCOS) were included in this study. They were selected from patients attended the infertility and Managements Clinic / Azadi teaching hospital (Kirkuk city).

At the beginning, all patients were investigated for ultrasound scanning of the ovaries, recording of menstrual pattern, anthropometric measurement (body mass index (BMI) ,waist circumference and the hip circumference), marriage state, scoring of hirsutism and involuntary childlessness period in years.

### **Results**

In our study, there was no important or statistically significant difference in median serum insulin, insulin resistance or serum leptin between study subjects using additional metformin treatment and those on usual treatment for PCOS. The median free serum testosterone was significantly lower (23 pg/ml) in those treated with metformin compared to those on usual treatment only (50 pg/ml). Also, the mean fasting serum glucose was significantly higher in group on usual treatment (without metformin) (6.46 mmol/L) compared to group with metformin (5.64 mmol/L). The mean serum HDL - cholesterol and serum total cholesterol concentration were significantly higher in the group on usual treatment (1.06 and 4.15 mmol/L respectively) compared to the group with metformin (0.88 and 3.56 mmol / L) respectively, the remaining biomarkers (serum VLDL-cholesterol and triglyceride) showed no important or statistically significant differences between two study groups.

### **Conclusion**

Metformin treatment has beneficial effects on serum free testosterone, glucose, total cholesterol and LDL-cholesterol. This finding may have clinical implication due to the role for the pathogenesis of PCOS.

# **The Effect of Preeclampsia on the Human Umbilical Cord Structure, a Quantitative Histological and Histochemical Study**

**Name:** Abd-Almuhefn Yuosif

**Degree:** M.Sc.

**Specialty:** Histology

**Date of the debate:** 17/4/2010

**Supervisor:** Assist. Prof. Fareed H. Abdul-Ahad

## **Abstract**

This study was carried out to investigate the histological and histochemical changes of human umbilical cord in pregnancy induced hypertension. The purpose was to see the effect of PE on umbilical vessels which in turn effect on fetal health.

For this purpose sixty sample from newborn of women with and with out PE (30 cases, 30 controls) were studied. Each umbilical cord was divided in to 3 segments: placental end, middle segments, fetal end .

For each segment, 5 parameters were studied for the umbilical artery and vein: The lumen diameter, total wall thickness, thickness of tunica media, number of collagen fiber layers, and the rate of Duplication of internal elastic lamina. In additional to the Wharton's jelly properties, collagen fiber content, and glycogen (polysaccharide) content using histological and histochemical stains.

The structure of the umbilical vessels changes from the placental end to the fetal end showed that the umbilical artery and vein in PE had significantly greater wall thickness, significantly increase in collagen content of arterial tunica media and a smaller luminal area than in the controls.

Non significant difference in the internal elastic lamina duplication in middle segment of both artery and vein was obtained .

The Wharton's jelly showed an increase glycogen content with an increase in collagen fibers, and have a smaller area than in controls.



## **Effects of Stabilizing Agents on the Amyloid Fibril Formation**

**Name:** Abbas Ali Braim

**Degree:** M.Sc.

**Specialty:** Biophysics

**Date of the debate:** 12/7/2010

**Supervisor:** Assist. Professor. Hisham M. Ali

### **Abstract**

Osmolytes provide a general method to protect proteins from the unfolding and aggregation induced under high temperatures. In this study, the effect of glycerol on protection of the human serum albumin (HSA) at different temperatures was investigated by a static light scattering method and spectrophotometric analysis.

At temperatures above 50°, the results showed that there is a change in the Radius of gyration (R<sub>g</sub>) and abrupt change in the molecular weight (M<sub>w</sub>). It is noted that they became double at high temperatures. The aggregation is produced. This aggregation might be due to the dimerization of HSA.

Glycerol seems to prevent HSA from thermal unfolding and aggregation in a concentration-dependent manner. Therefore, above 50°C the dimerization or aggregation was totally inhibited when the concentration of glycerol reaches 15%, since the result of the protein solution with 15% glycerol is approximately similar to the result of protein solution at 35 °C.

Amyloid fibril formation of HSA was investigated by means of absorption spectrum of Congo red (CR). The maximum wavelength spectrum of bound CR with incubated protein solution at 65 °C for 15 days shifted. This indicates that there is an amyloid fibril formation since the CR dye specifically interact with  $\beta$ -sheets. Disappearance of the red shift occurred totally in the presence of 15% glycerol with the protein solution. Therefore glycerol has ability to inhibit amyloid fibril formation.

One of the conclusions presented in our study is that the aggregation of protein plays an important role in the synthesizing or formation of the amyloid fibril. Apparently, inhibition of the amyloid formation resulted from prevention of aggregation of the protein. Therefore, fifteen percent or more addition of glycerol can prevent the amyloid fibril formation .

# **Evaluation of serum levels of homocysteine, C peptide and lipid profile in type I and type II diabetic patients in Hawler province/ Iraq**

**Name:** Abdulrahman Jawdat Muhammad

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 10/11/2010

**Supervisor:** Assist. Prof. Abdulqadir A. Alnaqshabandi  
Assist. Prof. Abdulrahman Al-Bazzaz

## **Abstract**

**Background:** Diabetes mellitus is a syndrome of disordered metabolism with inappropriate hyperglycemia caused by absence or deficiency of insulin, insulin resistance, or both.

Diabetes mellitus is typically classified into two main subtypes: type 1 or insulin-dependent diabetes (IDDM), and type 2 or non-insulin-dependent diabetes (NIDDM). Diabetes mellitus is associated with many complications such as increased risk of cardiovascular disease, even in the presence of intensive glycemic control. Homocysteine (Hcy) is an amino acid produced in the body during the breakdown of another amino acid called methionine, which is found in red meat. Numerous studies suggested that homocysteine may be a modifiable risk factor for cardiovascular disease. In experimental studies, homocysteine causes oxidative stress, damages endothelium, and enhances thrombogenicity. Homocysteine is known to take part in the development of atherosclerosis and vascular injury and it has been suggested to contribute to the atherosclerotic process of diabetes mellitus. C-peptide is peptide that is made when proinsulin is split into insulin and C-peptide. They split before proinsulin is released from endocytic vesicles within the pancreas, one C-peptide for each insulin molecule. The present study was designed to evaluate Homocysteine, C-peptide levels and lipid profile in diabetic patients.

### **Patients and methods:**

This study includes 75 diabetic patients, 35 type 1 diabetic their ages ( $49.1 \pm 10.4$ ) and 40 type 2 diabetic their ages ( $39.5 \pm 8.72$ ) and 30 control their ages ( $39.5 \pm 8.72$ ). After 12 hours fasting, serum homocysteine, C-peptide, lipid profile, HbA1c and blood glucose were measured for patients and control. The patients and control had normal kidney functions.

**Results:** The results showed that all the diabetic patients showed significantly higher serum fasting sugar and HbA1c as compared with their controls.

As all the diabetic patients under study had HbA1c more than 8% so they are all poorly controlled. Serum homocysteine levels in type 1 and type 2 diabetic patients are significantly increased as compared with their levels controls. Serum C-peptide levels in type 1 and type 2 diabetic patient show significantly low concentration as compared with their controls or between themselves although its concentration in type 2 diabetic patient is within normal range. The lipid profile showed that levels of (cholesterol, triglyceride, LDL and VLDL) are increased in diabetic patients as compared with their control

### **Conclusions:**

1. Serum homocysteine (Hcy) levels are significantly elevated in our diabetic patients also there are increases in serum levels of lipid profile including: (cholesterol, triglyceride, LDL, and VLDL) except HDL were observed to be within the lower normal limits in type 1 and type 2 diabetic patients. These increases in Hcy and lipid profile might play role in the pathogenesis of vascular complications and present a high risk of atherosclerosis .in individuals with diabetes mellitus.
2. It is better for newly diagnosed diabetic patients to measure their Cpeptide levels as a marker for distinguishing between type 1 and type 2 diabetes and to avoid misdiagnosing the type of the diabetes.

## **Glibenclamide, Metformin, or Their combination, for the treatment of newly diagnosed diabetic patients in Hawler city**

**Name:** Sazan D. Saeed

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 8/12/2010

**Supervisor:** Prof. Kassim J. Al- Shamma

### **Abstract**

Type 2 diabetes mellitus is a complex progressive disorder characterized by impaired insulin sensitivity, reduced insulin secretion and progressive failure of pancreatic  $\beta$ -cells. The standard method for identifying individuals at risk for developing type 2 diabetes include measurements of FPG, PPG and HbA1c, in addition to plasma lipid profile. Type 2 diabetes therapies are initiated with lifestyle changes (diet, exercise) and pharmacologic agents, including oral antidiabetic drug, among them: Glibenclamide, Metformin and their combination. The primary aim of the management is to compare the efficacy and safety of these drugs, both as monotherapy and in combination, and discussed evidence-based treatment

Multicentre, parallel-group trial, newly diagnosed patients with type II diabetes who were not taking any type of medication were studied. The patients were assigned into 3 treatment groups: glibenclamide 5 mg once daily; metformin 500 mg t.i.d.; glibenclamide/metformin 2.5 mg/500 mg b.i.d. Blood sample were withdrawn from the patients at pretreatment, then monthly for three months.

Forty patients with (FPG of 167.9mg/dl  $\pm$ 3.5; PPG of 276.3 mg/dl  $\pm$ 5.4; HbA1c of 8.1% $\pm$ 0.2) were received metformin, and fifteen patients with (FPG of 165.1 mg/dl  $\pm$ 4.3; PPG of 273.6 mg/dl  $\pm$ 5.5; HbA1c of 7.9% $\pm$ 0.2) were received glibenclamide both as monotherapy. Thirty five patients with (FPG of 179 mg/dl  $\pm$ 4.1; PPG of 304.4 mg/dl  $\pm$ 5.6; HbA1c of 7.9% $\pm$ 0.1) were received glibenclamide/metformin as combination therapy. Thirty healthy individuals were investigated as controls. Changes in TC, TG, LDL, HDL and BMI were measured in all of these diabetic patients as well as control.

After 3 months of treatment, patients who received glibenclamide/metformin combination had greater reductions in FPG, PPG, and HbA1c compared with metformin or glibenclamide. Metformin and glibenclamide/metformin combination had approximately similar significant effect in reduction of TC, TG and LDL, compared with glibenclamide alone. Metformin increased HDL significantly compared with glibenclamide/metformin combination or glibenclamide alone, and it also reduce BMI compared with glibenclamide/metformin and glibenclamide alone (which is associated with weight gain).

Metformin monotherapy and the combination therapy reduced plasma glucose and HbA1c significantly, and both have favorable effects on serum serum lipid profile. These two strategies are effective as an initial treatment of newly diagnosed diabetic patients in Hawler city.

## **Antibacterial Evaluation and Phytochemical screening for extracts of some plants used traditionally in Kurdistan region**

**Name:** Lana Yousif Muttalib

**Degree:** M.Sc.

**Specialty:** Pharmacognosy

**Date of the debate:** 13/10/2010

**Supervisor:** Lecturer Dr. Alaaddin M. Naqishbandi

### **Abstract**

In the present study, the antibacterial activity for twenty plants namely (*Urticadioica*, *Achilleamileforum*, *Viola odorata*, *Salvia officinalis*, *Althea officinalis*, *Malvaparviflora*, *Trigonellafoenum-graecum*, *Glycyrrhizaglabra*, *Plantago major*, *Pegunmharmala*, *Pimpinellaanisum*, *Coriandrumstativum*, *Ammivinaga*, *Nigella sativa*, *Hibiscus sabdarriffa*, *Foneuclumvulgari*, *Cichoriumintybus*, *Melissa officinalis*, *Thymus vulgari*, and *Matricariachamomilla*) were evaluated against four strains of gram negative bacteria (*Escherichia coli*, *Pseudomonas arigenossa*, *Klebsiella pneumonia*, and *Proteus spp*) and two strains of gram positive bacteria (*Staphylococcus aureus*, *Bacillus cerus*) using agar well diffusion method, and preliminary screening for main phytochemical natural product groups had been done. Later on separation and identification of the main active constituent in the active extract of sage leaves were carried out using thin layer chromatography.

Twenty plant samples used traditionally by Iraqi native people (especially in Kurdistan region) for curing a variety of illness were collected. Plant samples were extracted separately by non polar solvent (chloroform) yielding chloroform extract and the residue were extracted by hydroalcoholic solvent (75% ethanol) yielding ethanol extract using ultra sonic technique. Each plant extract were tested against selected strains of bacteria in two concentrations C1 (10mg/ml) and C2 (100mg/ml).

From the tested strains of bacteria *Staphylococcus aureus* was found to be the most susceptible bacteria that inhibited by ten extracts of forty evaluated extracts followed by *Proteus spp* which was inhibited by seven plant extracts while the *Klebsiella pneumonia* was resisted to all evaluated plant extracts.

Among the evaluated plant extracts, nine plant species showed activity against one or more of the tested bacterial strains which were (*Pegunmharmala*, *Hibiscus sabdarriffa*, *Achilleamileforum*, *Plantago major*, *Salvia officinalis*, *Matricariachamomilla*, *Nigella sativa*, *Thymus vulgari*, and *Althea officinalis*). In general chloroform extracts were found to be more active than hydroalcoholic extracts. The highest activity was exhibited by the Syrian rues which showed activity against five types of tested bacterial stains .

Minimum inhibitory concentration was determined for the active extracts by agar well diffusion method, the lower minimum inhibitory concentration was exhibited by ethanolic extract of Syrian rues against *Staphylococcus aureus* (20mg/ml) and the highest minimum inhibitory concentration was found to be for the chloroform extract of Syrian rues against *Pseudomonas arigenossa* (90mg/ml).

The preliminary screening of phytochemical natural product groups included the detection of alkaloids, cardioactive glycoside, anthraquinone glycoside, flavonoids,

condensed and hydrolysable tannins. Flavonoids natural product group was found to be the most occurring in the evaluated plant extracts while cardioactive and anthraquinone glycoside were found absent. Among the studied plants, sage leaves were found to contain the largest number of the natural product groups which were flavonoid, saponin, hydrolysable and condensed tannins.

Finally, bioactivity guided separation and identification of the main active constituents in the biologically active extract obtained from sage leaves extract by thin layer chromatography had been led to separation of six constituents (S1, S2, S3, S4, S5 and S6) their R<sub>f</sub> value were recorded as (0.81, 0.62, 0.5, 0.41, 0.35 and 0.28), from which the constituent (S3) with retardation factor value (0.5) was identified as thujone.

## **Preparation and Evaluation of Lamotrigine Water Dispersible Tablets**

**Name:** Shahla Sadeq Smael

**Degree:** M. Sc.

**Specialty:** Pharmaceutics

**Date the debate:** 7/4/2011

**Supervisor:** Prof. Alaa A. Abdul-Rasool

### **Abstract**

Lamotrigine is a novel new-generated antiepileptic drug, chemically unrelated to other anti-epileptics. It is used as an adjunctive therapy of seizure in children and adults and is effective against partial and secondarily generalized tonic-clonic seizures.

This study was done in order to prepare water dispersible tablets (WDTs) of lamotrigine. Lamotrigine WDTs were prepared by direct compression method, which are capable to disintegrate completely in water at 15-22° C (water temperature), in not more than 3 minutes and produce a smooth dispersion.

Two types of disintegrants {starch and microcrystalline cellulose PH 102 (MCC 102)}, and three types of superdisintegrants: croscarmellose sodium (CCS), crospovidone (CP), and sodium starch glycolate (SSG) in different amounts, alone and in combinations were used in this study to form 33 different formulas.

All of the prepared control (without drug) formulas were evaluated for flow properties, fineness of dispersion, tablet hardness, friability, weight variation, and disintegration time. As a result, all prepared WDTs disintegrated in  $\leq 2.24$  min (144 sec) fulfilling the official requirements ( $< 3$  min) for WDTs. All formulas exhibited a good mechanical strength (3-10 kg), except F6 which contains a high percent of SSG (12%) showed significant increase ( $P < 0.05$ ) in hardness (13.6 kg).

Among all of the prepared formulas, F12 which contains (3% SSG + 3% CP), and F19 which contains (3% SSG + 3% starch) showed a significant decrease ( $P < 0.05$ ) in disintegration time (25 sec and 23 sec), respectively and they were selected as the best formulas, because they display a good performances for the five parameters specified: hardness, friability, flow property, weight variation and disintegration time. Then 25 mg/tablet of drug lamotrigine was incorporated to them (F12 and F19) to be named as (F12L and F19L), which then evaluated for further tests such as: content uniformity, dissolution test, effect of light, and effect of temperature.

On the other hand, the hardness of marketed amoxicillin WDT (Amoxi® TD 500) was determined ( $3.9 \pm 0.01$  kg) and compared with that of the prepared lamotrigine WDTs (F12L and F19L) which was equal to ( $4.1 \pm 0.01$  and  $4.0 \pm 0.02$  kg), respectively.

In addition, a comparison was made between the dissolution rate of the prepared lamotrigine WDTs and the lamotrigine reference tablet (LOXOL® 25mg tablet). It appears that the prepared lamotrigine WDTs showed faster release rate than the marketed conventional tablet ( $P < 0.05$ ).

The overall results suggest that lamotrigine could be prepared as a water dispersible tablet.

# Design and Evaluation of Sustained Release Bilayer Tablets of Oxcarbazepine

**Name:** Naz Jamal Ibrahim

**Degree:** Master

**Specialty:** Pharmaceutics

**Date the debate:** 8/6/2011

**Supervisor:** Dr. Muath Sh.M. Ameen

## Abstract

Oxcarbazepine is a novel antiepileptic drug. It was developed as a second-generation and follow-up compound to carbamazepine. It is used as monotherapy or adjunctive therapy in the treatment of partial seizures in adults and children.

This study was done in order to formulate oxcarbazepine as an oral modified release dosage form utilizing the concept of bilayer system using direct compression method with dual compression, first layer which is immediate release layer contained 100 mg and the other layer which is sustained release matrix layer contained 200 mg. The immediate release layer consisted of four types of disintegrants; sodium starch glycolate (SSG), croscarmellose sodium (CCS), polyvinylpyrrolidone (PVP), and starch. It was found that immediate release layer contain sodium starch glycolate gave faster disintegration time. This result was introduced in preparation of bilayer tablets. On the other hand, the sustained release layer was prepared utilizing three hydrophobic polymer; two of them acrylic derivatives (Eudragit RS<sup>®</sup>, Eudragit RL<sup>®</sup>) and one cellulosic derivatives (Ethyl cellulose) as a retardant material. The prepared bilayer tablets were evaluated for flow properties, tablet hardness, friability, weight variation, content uniformity, and dissolution profile. It was found that combination of Eudragit RL<sup>®</sup> with Eudragit RS<sup>®</sup> in ratio of 2:1 gave the best retarding release profile. Moreover, it was also found that replacing of diluents of a sustain release layer from mannitol to Di calcium phosphate and binder from microcrystalline cellulose (Avicel PH 102) to microcrystalline cellulose (Avicel PH 101) gave more retardation in the release profile of the drug. Meanwhile, no significant difference was found in the release of oxcarbazepine at different pH media. According to similarity factor ( $f_2$ ) F15 which content ( Eudragit RL<sup>®</sup> and RS<sup>®</sup> in ratio of 2:1 with mannitol as diluents and Avicel 102 as binder) was selected as best formula since it showed higher similarity among all other formula equal to (87.1) comparing to reference curve. Drug released from immediate release layer within (1 hour) while from the sustained release layer within (24 hours). The mechanism of kinetic release of oxcarbazepine from bilayer tablet is mainly by diffusion rather than erosion. Furthermore, the infrared (IR) spectra shows no possibility of chemical interaction between the drug and polymers used in preparation of bilayer tablet. Study of accelerated temperature effect revealed that shelf life of drug was about 3 years and 5 months at 25°C. On the other hand, stability of selected formula in day light at room temperature revealed that oxcarbazepine is affected by light and 10% of drug lost in about 1 years and 9 months.



## **Gastroprotective and spasmolytic activity of *Calendula officinalis* extract**

**Name:** Rojgar Hamed Ali

**Degree:** Master

**Specialty:** Pharmacology

**Date the debate:** 5/7/2011

**Supervisor:** Dr. Kawa F. Dizaye

### **Abstract**

*Calendula officinalis* (Pot Marigold) has been used over decades for different therapeutic purposes and it was a target for many pharmacological studies, traditionally it's mainly used for facilitating wound healing and skin eczema, and thought to have hepatoprotective, hypoglycemic, antiinflammatory, anti-bacterial, antiseptic, antiulcer and antispasmodic activity, and recently it's been proven that Marigold also have an antiHIV and anticancer activity. In this study antispasmodic and gastroprotective effect of this plant was evaluated.

*Calendula officinalis* was effective in reduction of gastric acid secretion and preventing development of gastric ulcer in experimental mice which have been exposed to ulcer induction through the use of 300mg/kg Aspirin that has been proven to be a suitable dose for ulcer induction in mice for experimental purposes.

Hydro-alcoholic and aqueous extract of *Calendula officinalis* was failed to show any detectable effect on the motility pattern of isolated jejunum smooth muscle of rabbit, Hydro-alcoholic extract did not reverse or enhance the contraction that has been induced by pilocarpin or betahistine referring to that the Hydro-alcoholic extract of *Calendula officinalis* does not have antimuscarinic or antihistaminergic effect and does not have any effect on potassium induced smooth muscle contraction which reveals the that *Calendula Officinalis* does not posses anti-spasmodic activity.

## **Gastroprotective and Diuretic effects on Aqueous Extract of Caraway (*Carum carvi*)**

**Name:** Hogr Sabbah Saddiq Salayee

**Degree:** Master

**Specialty:** pharmacology

**Date the debate:** 9/1/2011

**Supervisor:** Dr. Kawa F. Dizaye

### **Abstract**

*Carum Carvi* has been used through centuries over the world, believed to have certain traditional action. This plant has been used since ancient times especially in the treatment of digestive disorders and as an antiulcerogenic agent.

The gastroprotective and diuretic activity of the aqueous extract of the *Carum Carvi* was evaluated in this study.

The present study showed that both aqueous extract of hot pepper and aspirin were strong ulcerogenic factors for producing lesions in the gastric mucosa of mice.

Significant and severe gastric ulcers were induced by aspirin or hot pepper. *Carum carvi* aqueous extract was effective in reducing the number of ulcer area, this result was in parallel with the similar result produced by ranitidine.

*Carum carvi* aqueous extract produced a significant increase in urine volume and urinary Na<sup>+</sup> excretion without significant changes in K<sup>+</sup> excretion rates in experimental rabbit.

## **Therapeutic and some biochemical studies of montelukast and ketotifen in children with mild asthma**

**Name:** Fareedoon Habib Mustafa

**Degree:** Master

**Specialty:** Pharmacology

**Date the debate:** 2/1/2011

**Supervisor:** Assistant Professor .Nidhal Abdul Kader Al-Saleem

### **Abstract**

**Objective:** Asthma is common chronic illness in childhood and despite significant improvements for disease control and treatment, its prevalence is increasing worldwide. The aim of this study was to compare montelukast and ketotifen efficacy and safety as controller treatment in children with mild persistent asthma.

**Patients & Methods:** 102 asthmatic children aged 2 - 12 years diagnosed with mild persistent asthma were enrolled in this study. The patients were randomly divided into three groups. The first group received montelukast and the second group received ketotifen while the third group served as control. The drugs were given once daily for 16 weeks. Data was collected through questionnaire and demographic characteristics were analyzed. Evaluations of the clinical efficacy of medications were performed by spirometric measurement of air way limitations & asthma symptoms exacerbations. Hematological, biochemical and adverse-effects were assessed at each monthly visit after starting the treatment protocol. Descriptive and inferential statistics were used to analyze the findings.

**Results & conclusions:** Asthma distribution was higher within boys than girls, equally distributed between preschool and school children, in children with own history of allergic rhinitis than atopic dermatitis and in children with maternal history of allergic rhinitis than paternal history of allergic rhinitis & asthma.

Montelukast treatment produced better improvement in pulmonary function test & reduced asthma symptoms exacerbation, peripheral blood eosinophils percentage & S.IgE than ketotifen treatment.

Both montelukast & ketotifen treatment produced significant elevation in alkaline phosphatase (ALP) activity whereas no significant differences were found in alanine transaminase (ALT) & aspartate aminotransferase (AST) activities. Weight gain was recorded after montelukast & ketotifen treatment. Agitation & sedation were the most considerable adverse-effects experienced with montelukast & ketotifen respectively but disappeared after drug discontinuation.

In conclusion, montelukast proved to be more effective than ketotifen for the prevention of mild persistent asthma in children.

# Phytochemical screening, antibacterial and antiproliferative evaluation (on cell line A549) of *Cichorium intybus* root extracts indigenous to Iraqi Kurdistan

**Name:** Aveen Nawzad Adham

**Degree:** Master

**Specialty:** Pharmacognosy

**Date the debate:** 15/9/2011

**Supervisor:** Dr. Alaadin M. Naqishbandi

## Abstract

Plants have been used for medicinal purposes since time immemorial. Natural products produced by plants have been isolated as biologically active pharmacophores. *Cichorium intybus* belongs to family Asteraceae naturally occurring in Iran, Turkey, Iraq, and other countries. In the present study the phytochemical screening for the presence of important secondary metabolites was carried out on the root of *Cichorium intybus*. Alkaloids, carbohydrates, cardioactive glycosides, steroids, and phenolic compounds were detected while anthraquinone glycosides and saponins were absent.

The main constituents extracted by soxhlet apparatus using petroleum ether, yielding (1%) petroleum ether extract, the residue re-extracted with ethanol 80% yielding (39.76%) total extract. The total extract hydrolyzed by refluxing with 5% HCl, followed by partitioning with ethyl acetate yielding (1.436%) organic fraction extract.

Antibacterial activity of total extract, organic fraction and petroleum ether extracts of *Cichorium intybus* root was evaluated at three different concentrations (500, 250, 125 mg/ml) against Gram positive bacteria *Bacillus spp*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and Gram negative bacteria *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus spp*, *Enterobacter spp*, *Pseudomonas aeruginosa*, using agar well diffusion method. Among the extracts tested organic fraction extract showed the highest inhibition zone diameter (23.5 mm). All tested bacteria found to be susceptible for organic fraction extract.

The bioassay guided separation and identification of active constituents of organic fraction extract by TLC led to separation of seven constituents OF<sub>1</sub>, OF<sub>2</sub>, OF<sub>3</sub>, OF<sub>4</sub>, OF<sub>5</sub>, OF<sub>6</sub>, and OF<sub>7</sub> their R<sub>f</sub> values were (0.09, 0.2, 0.34, 0.54, 0.61, 0.66, 0.73) respectively. From which OF<sub>2</sub>, OF<sub>4</sub>, and OF<sub>6</sub> were identified as chlorogenic acid, caffeic acid and kaempferol respectively by comparing their R<sub>f</sub> values and color properties with reference compounds.

TLC agar overlay bioautography method was performed to determine the bioactive constituents responsible for antibacterial activity. Bioautography of the three active extracts indicated the presence of a number of constituents in total extract, organic fraction and petroleum ether extracts with antibacterial activities, from which chlorogenic acid, caffeic acid and kaempferol from organic fraction extract showed inhibition against most bacterial types used.

Minimum inhibitory concentration (MIC) of the extracts and their pure constituents were determined using micro-broth dilution method. Among total extract, organic fraction and petroleum ether extracts the lowest MIC value was recorded against *Bacillus spp*, and *Staphylococcus aureus* as 15.625 mg/ml, while for pure active constituents was recorded for caffeic acid against *Escherichia coli*, and *Proteus spp*. as 0.15 mg/ml

Finally total extract and organic fraction extracts were tested at concentrations 0.2, 0.4, 0.5, 0.6, 0.8, 1 mg/ml for their cytotoxic activity against human lung adenocarcinoma epithelial cell line A549 cells at three time intervals 24, 48, and 72hr, the results showed significant decrease in cell viability with increase in concentration of extracts.  $IC_{50}$  for total extract was recorded as  $(0.703 \pm 0.047)$  on 72hr, and for organic fraction extract as  $(0.96 \pm 0.02)$  and  $(0.566 \pm 0.015)$  on 48 and 72hr respectively.

## **Serum Immunoglobulin Levels in Patients with Lymphoproliferative diseases in Erbil-Iraq**

**Name:** Karwan Bahram Maulood

**Degree:** Master

**Specialty:** Clinical Biochemistry

**Date the debate:** 3/12/2011

**Supervisor:** Ass. Prof. Abdulkader A. Alnakshabandi

### **Abstract**

**Introduction and Objectives:** Lymphoproliferative neoplasms are among the commonest human neoplasia. Immune dysregulation is frequently associated with many of these diseases, particularly those related to B-cell origin, dysregulation may lead to abnormalities of individual immunoglobulin levels or the production of abnormal paraproteins, reduced immunoglobulin levels (hypo  $\gamma$ -globulinaemia) are common in chronic lymphoproliferative diseases. This study was designed to find out the immunological status of newly diagnosed patients with lymphoproliferative disorders.

**Patients and Methods:** This study was carried out in Erbil province during the period from November 2010 to April 2011. Fifty two newly diagnosed patients with lymphoproliferative disorders referred to Nnakaly Hospital for blood disease and twenty healthy control subjects had been included in this study.

**Results:** Serum IgM and IgA level were decreased in all groups of patients with different lymphoproliferative disorders Compared to control group, while serum IgG level showed insignificant reduction in Acute lymphocytic leukemia (ALL) and Chronic lymphocytic leukemia (CLL) patients, but it was increased in Non Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL) and Multiple myeloma (MM) patients. Paraproteinemia had been seen in all patients with MM while only 10% of CLL and NHL showed Paraproteinemia, no M-band had been noticed in ALL and HL.

**Conclusion:** It was concluded that there were some conflicting data regarding serum immunoglobulin levels in newly diagnosed patients with lymphoproliferative disorders in Erbil - Iraq. Paraproteinemia is a significant feature in MM patients and its level is higher than that can be seen in other B-cell neoplasms with monoclonal gammopathies.

# **Serum Erythropoietin Levels in Type 2 Diabetes Mellitus: Relation to Development of Anemia**

**Name:** Sarmad Salam Abdullah

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 16/5/2011

**Supervisor:** Assist. Prof. Shatha H. Ali

## **Abstract**

**Background:** Anemia is common in diabetes, that is long term diabetes can affect both kidneys and nerves, which may contribute to the development of anemia. A normochromic, normocytic anemia has been observed in diabetic patients much earlier than the clinical and laboratory parameters of renal damage. The majority of type 2 DM patients with anemia have functional erythropoietin deficiency; this may be caused at least in part by efferent sympathetic denervation of the kidney leading to the loss of appropriate EPO production.

**Objective:** This study was designed to clarify the contribution of serum erythropoietin for developing anemia in type 2 diabetics with normal renal function tests.

**Subjects and Methods:** The study comprised of 54 type 2 diabetic patients (26 suffered from anemia and 28 without anemia) aging between 45 to 55 years and 28 apparently healthy subjects of comparable age and sex. Exclusion criteria were microalbuminuria, renal impairment and insulin dependent.

Fasting blood specimens were obtained for testing serum levels of: glucose, insulin, urea ,creatinine , ferritine, erythropoietin; whole blood specimens with EDTA were utilized to estimate glycated hemoglobin levels and hemoglobin concentrations. Quantitative Insulin Sensitivity Check Index and creatinine clearance were calculated.

Urine specimens were examined for the presence of ketonuria, glucosuria and microalbuminuria.

**Results:** The results showed that there was no significant difference between anemic and non anemic type 2 diabetic patients in regard to fasting serum glucose and glycated hemoglobin, renal function test (urea, creatinine, and creatinine clearance), serum insulin and quantitative insulin sensitivity check index.

Anemic diabetic patients had lower blood hemoglobin and serum erythropoietin levels, whereas mean serum ferritin levels was not significantly differ between the two groups.

Although anemic type 2 diabetic patients had significantly longer duration of diabetes than non anemic patients, but there was no significant correlation between serum erythropoietin level and duration of diabetes in both groups.

**Conclusion:** Anemic type 2 diabetic patients have significantly lower mean serum erythropoietin levels compared with non anemic diabetics. This finding suggests that the measured serum erythropoietin is an early indicator for development of anemia in type 2 diabetic patients before any detectable changes in renal function tests.

# **Clinical efficacy of Diabecon in treatment of type 2 diabetes mellitus, in newly diagnosed diabetic patients and in those on drug treatment (Glibenclamide and Metformin) in Erbil Governarate-Kurdistan Region/ Iraq**

**Name:** Mohammed Fadhil Saleem

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 5/5/2011

**Supervisor:** Dr. AnsamNaji Al-Hassani

## **Abstract**

Despite understanding the etiopathogenesis of type 2 diabetes mellitus (DM) and it accounts for 90% of DM worldwide, there is an alarming rise in the insulin-resistant cases and failure of oral hypoglycemic agents (OHAs). Various herbs have been found beneficial in the management of type 2 diabetes and are gaining considerable recognition in the management of type 2 diabetes worldwide. The present study was planned to evaluate the clinical efficacy of Diabecon (Herbal formulation) as a monotherapy and also as an adjunct with other oral hypoglycemic agents, in the management of type 2 DM. A total of 80 patients of either sex, between 30-68 years of age, in whom the diagnosis of type 2 diabetes was confirmed, and who were willing to give informed consent were included in the study.

All enrolled patients were categorized into 4 groups. Group A included 20 newly diagnosed cases who were not consuming any OHA, while group B included 20 patients who were already consuming glibenclamide but were not controlled, while group C included 20 patients who were already consuming metformin but were not controlled and lastly group D included 20 patients who were already consuming glibenclamide and metformin combination but were not controlled. Patients from all the groups were advised to consume Diabecon at a dose of 2 tablets, three times daily (30 minutes) before meal for a period of 3 months, either as monotherapy for group A or as adjunct in the other three groups.

In all the patients, fasting blood glucose (FBG) and postprandial blood glucose (PPG) were assessed at the time of enrollment and thereafter every month, for 3 months, While Glycosylated haemoglobin (HbA1c), Total cholesterol (TC), Triglyceride (TG), High density lipoprotein-Cholesterol (HDL-c), Low density lipoprotein-Cholesterol (LDL-c), Basal serum insulin, C-peptide and body weight (BW) were assessed at the time of enrollment and after 3 months.

Diabecon significantly reduced FBG, PPG and HbA1c in all groups after treatment with Diabecon, which indicating an improved glucose homeostasis under the influence of this herbal formulation. There was a mild improvement in serum basal insulin and C-peptide level after using Diabecon either as monotherapy or as adjuvant to glibenclamide, metformin or glibenclamide and metformin combination in those type 2 diabetic patients who were not controlled by such oral hypoglycemic agent. Diabecon caused improvement of lipid profile including TC, TG and LDL-c to a variable extent in all groups except for group B. Its main effect is on the reduction of TC which could be



beneficial since hypercholesterolemia is strongly associated with cardiovascular disease. A significant reduction in body weight was noticed at the end of the study among all groups except in group B who showed an increase in body weight but it was not significant. This weight reduction is a desired effect in type 2 diabetic patients and may play a role in improving insulin resistance. Most of the patients reported a sense of well-being and no side effect were recorded either by patient or observer except rare cases of gastric upset. Therefore, it may be concluded that Diabecon is clinically effective herbal formulation in the management of type 2 diabetes either as a monotherapy in newly diagnosed patients and as an adjunct therapy in patients on conventional OHAs.

# **Evaluation of immunosuppressive regimens in kidney transplanted patients in Kirkuk**

**Name:** Hemen Faik Al-Dawoody

**Degree:** Master

**Specialty:** Pharmacology

**Date the debate:** 15/2/2012

**Supervisor:** Professor. Kassim AL-Shamma

## **Abstract**

### **Background**

The availability of three immunosuppressive drug groups: calcineurin inhibitors (cyclosporine, tacrolimus), anti-proliferative agents (azathioprine, mycophenolate mofetil) and steroids (prednisolone) has led to attempt to determine which is the best maintenance immunosuppressive regimen for patients after kidney transplantation, based on efficacy and reduction of adverse effects.

### **Objectives**

The aim of this prospective study was to evaluate the efficacy and relative toxic effects of three immunosuppressive regimens used after kidney transplantation in Kirkuk.

### **Patients & Methods**

52 kidney transplanted patients their age range from 17 to 60 years ( $38.68 \pm 1.6$ ) were enrolled in this study. The kidney transplanted patients were categorized into three treatment groups. The group I included 30 patients received standard-dose of cyclosporine (3-5mg/kg), mycophenolate mofetil in combinations with prednisolone, and the group II included 15 patients received low-dose cyclosporine (1-2mg/kg), azathioprine in combinations with prednisolone, while the group III included 7 patients received low-dose tacrolimus (0.1mg/kg), mycophenolate mofetil in combinations with prednisolone. The control group consists of 30 healthy normal individuals who were free from signs and symptoms of renal disease, lipid disorders, diabetes mellitus and hypertension their ages ranged from 16 to 60 years ( $34.5 \pm 2.1$ ). The primary efficacy end point was the renal function estimated by measurement of serum urea, serum creatinine and creatinine clearance level. Secondary end points were incidence of serious adverse effects and the complication of immunosuppression therapy in transplanted recipient estimated by biochemical measurement of total cholesterol, triglyceride, HDL-c and LDL-c for lipid profile; ALP, ALT, AST, total bilirubin and bilirubin (direct & indirect) for liver function test; fasting blood glucose for hyperglycemia, and serum electrolyte (Na & K), all were assessed at each month visit for three consecutive months for patients and control healthy individuals. Independent *t* test and ANOVA statistics were used to compare the results.

### **Results & conclusions**

In patients receiving group I there were significantly increases in serum urea & creatinine, and significant decreases in creatinine clearance level. Whereas patients receiving group II there were no significant effects on serum creatinine and creatinine clearance level. Also patients receiving group III there were no significant effects on renal function parameters. The serum total cholesterol and serum triglyceride

concentrations were significantly elevated in both group I & II patients, whereas HDL-c and LDL-c concentration were not significantly elevated in both groups. While in the group III patients there were no significant changes in serum lipid profile. The serum total bilirubin and bilirubin indirect concentrations were significantly elevated in both group I & II patients, whereas hepatocellular enzymes (ALP, ALT and AST) were not significantly elevated in both groups. While in the group III patients there were no significant changes in serum bilirubin and hepatocellular enzyme (ALP, ALT, and AST). Neither group I nor group II nor group III significantly affected patients fasting blood glucose and patients serum electrolyte (Na& K). The most prominent adverse-effects associated with all the regimens were hypertension, whereas the use of cyclosporine based regimen is associated with a higher incidence of cosmetic adverse-effects (hirsutism & gum hyperplasia). Tremor and gastrointestinal adverse-effects are more frequent in tacrolimus-treated recipients than in cyclosporine-treated recipients.

In conclusion, reduced cyclosporine doses provided improvement in renal function, and immunosuppressive regimen of low-dose tacrolimus with mycophenolate mofetil in combinations with steroids provided significantly higher efficacy, as advantageous for renal function, and associated with a more favourable lipid profile and liver function, as compared with regimens containing either standard-dose cyclosporine with mycophenolate mofetil or low-dose cyclosporine with azathioprine in combinations with prednisolone.

# **The Benefit and Risk of Antihypertensive Regimens in Duhok City**

**Name:** Dlveen Mosa Sulaiman

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 2/5/2012

**Supervisor:** Prof. Kassim Al-Shamma

## **Abstract**

Hypertension is a major health problem throughout the world because of its high prevalence and its association with increased risk of cardiovascular diseases. It is defined as systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg. The ultimate goal in treatment of the hypertensive patient is to achieve the maximum reduction in the long-term total risk of cardiovascular morbidity and mortality. The aim of this study was to compare the benefit, risk and cardiovascular disease risk lowering ability, of three antihypertensive drug regimens.

A case control study was carried out on 66 hypertensive patients, 22 patients treated with angiotensin converting enzyme inhibitors (ACE inhibitors), 22 patients treated with  $\beta$ -blockers and 22 patients treated with combination antihypertensive therapy, the study also included 22 healthy individuals. Blood pressure and pulse rate were measured and blood sample was collected, and the serum processed for the measurement of lipid profiles total cholesterol, triglyceride, and high density lipoprotein cholesterol, fasting blood glucose, liver function test (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase and gamma-glutamyltransferase), kidney function test (uric acid, urea and creatinine), and electrolytes (calcium, magnesium, potassium, sodium and chloride). Cardiovascular disease risk lowering ability have been assessed by cardiovascular risk assessor computer program.

The results shows that systolic and diastolic blood pressure in three antihypertensive drug regimens treated group, were significantly higher than systolic and diastolic blood pressure in control healthy individuals indicating that these antihypertensive drug regimens were unable to reach hypertension treatment target, although ACE inhibitors and combination antihypertensive drugs reach minimal hypertension treatment target.

The ACE inhibitors regimen did not show any significant adverse effects on lipid profiles and blood glucose, while  $\beta$ -blockers regimen adversely affected it. Most predominant adverse effects that appeared, in ACE inhibitors treated group were dry cough and taste disturbances, in  $\beta$ -blockers treated group were bradycardia and sleep disturbances while in combination therapy treated group were according to the combination used. In combination containing thiazide diuretics, disturbed lipid profiles and hyperurecemia were predominant and in combination containing calcium channel blockers constipation and peripheral edema were predominant.

Coronary heart disease and stroke risk percentage in all three antihypertensive drug regimens were significantly higher compared to control healthy individuals group, and all three antihypertensive drugs regimens have the same cardiovascular risk lowering ability. In conclusion the results indicated that all three antihypertensive drug regimens used were not efficient enough to reach hypertension treatment target, the combination therapy

and ACE inhibitors regimens were only capable to reach minimal hypertension treatment target which is  $\leq 150/90$  mm Hg.

## **Assessment of some serum markers of bone metabolism in patients with type 2 diabetes in Erbil – Iraq**

**Name:** Snoor Anwer Henna

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 12/11/2012

**Supervisor:** Assist. Prof. Kamaran Y. Muhammadamin

### **Abstract**

The prevalence of diabetes mellitus (especially type 2 or non-insulin dependent diabetes mellitus) is increasing rapidly in the population, so adverse outcomes of the condition are likely to grow in importance as well. People with type 1 diabetes have been reported to have high rates of bone turnover and resorption, In addition, type 1 diabetes is associated with other risk factors for osteoporosis, such as negative protein balance and disturbances in hormonal balance. In contrast, data on skeletal abnormalities in type 2 or non-insulin-dependent diabetes appear to be conflicting, and the exact explanation of this is still unknown, Inconsistencies also exist in the available reports on biochemical markers of bone metabolism in diabetes. This study was designed to determine whether type 2 diabetes was associated with changes in bone metabolism by evaluating the differences in some biochemical bone markers between diabetic and normal subjects.

This study was carried out in Erbil province during the period from November 2010 to November 2011. Ninety five Diabetic patients with type 2 (non-insulin dependent) diabetes auditing LaylaKasem Health care Centre for diabetes disease have been included in this study. Their ages were ranged from (40-70) years the (Mean±SD) was (54.363±7.992), (40 samples) were taken males and (55 samples) from females. Forty normal subjects (27 females and 13 males) with the mean age of (52.800±6.985) years have been included in this study as a control group.

The results showed that:

1. There was a highly significant difference in (mean ± SD) for Fasting Serum Glucose level between diabetic patients ( $207.470 \pm 50.690$ ) mg/dl, and the group of control subjects ( $94.85 \pm 10.388$ ) mg/dl, ( $p < 0.01$ ).
2. The mean value of serum calcium was significantly lower in diabetic subjects ( $2.279 \pm 0.149$  mmol/L) as compared to control group ( $2.349 \pm 0.044$  mmol/L); ( $p < 0.05$ ).
3. There was a decrease in the mean of serum 25-hydroxy vitamin D concentration in patients with type 2 diabetes (non-insulin dependent diabetes) ( $19.164 \pm 4.634$  nmol/L) as compared to the control group ( $30.235 \pm 4.632$  nmol/L), this reduction was highly significant; ( $P < 0.01$ ).
4. There was an increase in the mean serum parathyroid hormone concentration in patients with type 2 diabetes ( $46.117 \pm 16.845$  pg/ml), as compared to the group of control subjects ( $43.2 \pm 12.224221$  pg/ml), but this rise was not significant.

5. Higher levels of alkaline phosphatase was observed in serum of diabetics ( $156.784 \pm 39.665$  IU/L) as compared to the group of control subjects ( $150.325 \pm 37.093$  IU/L); but this didn't reach the significant level.

6. There was a decrease in serum total proteins level in patients with type 2 diabetes mellitus ( $6.46 \pm 0.083$  g/dl) as compared to the control group subjects ( $6.535 \pm 0.334$  g/dl); but this decrease didn't reach the significant level.

# Formulation of Ketotifen Fumarate as Conventional and Hollow-Type Rectal Suppositories

**Name:** Suhail Sabah Shaba

**Degree:** M.Sc.

**Specialty:** Pharmaceutics

**Date of the debate:** 29/10/2012

**Supervisor:** Asst. Prof. Yehia I. Khalil

## Abstract

Ketotifen as a non-competitive histamine antagonist is widely used in prophylaxis and management of bronchial asthma, and some allergic conditions. It was formulated as conventional and hollow-type rectal suppositories.

The method used for preparation of suppositories was fusion method. The crushing test, disintegration time test, mass uniformity, content uniformity, and dissolution test were carried out for all prepared formulas.

Different types of suppository bases as hydrophilic bases (Polyethylene glycol 1500, 4000) alone or mixed with (Polyethylene glycol 400), and lipophilic base (Witepsol H35) alone or mixed with different non-ionic surfactants (Tween 80, 60) in different concentrations (3% w/w, 5% w/w) were used in formulations.

The formula with (Polyethylene glycol 1500) was formulated as hollow type suppositories in addition to conventional one.

The hardness of conventional suppositories formulated with hydrophilic suppository base (Polyethylene glycol 1500) was significantly less than hardness of conventional suppositories formulated with hydrophilic suppository base Polyethylene glycol (4000), but more than conventional suppositories formulated with lipophilic base (Witepsol H35), while the disintegration time was significantly less and release profile was significantly better of conventional suppositories formulated with hydrophilic suppository base (Polyethylene glycol 1500) than both last formulas.

The addition of non-ionic surfactants (Tween 80, 60) to a lipophilic suppository base (Witepsol H35) cause non significantly decrease in hardness and significantly decrease in disintegration time and significantly improve the release profile. Both non-ionic surfactants (Tween 80, 60) almost cause same effect on hardness, disintegration time and release profile. When the concentrations of non-ionic surfactants (Tween 80, 60) increase from 3% w/w to 5% w/w cause non significant decrease in hardness, while significant decrease in disintegration time and improve the release profile significantly.

The addition of low molecular weight Polyethylene glycol (Polyethylene glycol 400) to a suppository base of high molecular weight Polyethylene glycols (Polyethylene glycol 1500, 4000) in sufficient concentration causes a significant decrease in hardness, disintegration time, and significantly improve the release profile of conventional suppositories formulated with mixed hydrophilic suppository bases (Polyethylene glycols).

The formulation of Ketotifen as conventional and hollow-type suppositories using hydrophilic suppository base (Polyethylene glycol 1500) did not affect the hardness, and



disintegration time, but the release profile of Ketotifen from hollow-type suppositories was significantly better.

The storage of suppositories formulated with (Polyethylene glycol 1500) as conventional and hollow-type suppositories at  $4 \pm 1^\circ\text{C}$  for one month shows significant decrease in hardness, non significant decrease in disintegration time and improve the release profile significantly, while after one month at second and third month of storage the hardness, disintegration time, and release profile remain constant. The storage of same formulas at  $25 \pm 1^\circ\text{C}$  for the same period of time shows no effect.

The shelf life of Ketotifen in suppositories formulated with (Polyethylene glycol 1500) as hollow-type was about three years.

## **Effect of Cigarette Smoking on liver function test and some other related parameters**

**Name:** Sangar Najat Abdulrazaq

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 10/4/2012

**Supervisor:** Assist. Prof. Bakhtiar M. Ahmed

### **Abstract**

More than 3 million people die each year from cigarette smoking. Cigarette smoke consists of many chemicals, including cytotoxic, carcinogenic and free radicals, therefore it affects many organs if not all.

This work is directed to evaluate the dose response patterns of tobacco exposure (number of cigarettes smoked daily) on some serum biochemical and hematological parameters related to the liver in Kirkuk province.

This study was done in Kirkuk province. It was conducted on (110) healthy male subjects, their ages ranged from 20 to 40 years. They were divided into three groups; 40 heavy smokers, 30 moderate smokers and 40 non-smokers which served as a control group. All subjects had no history of alcohol abuse, or diseases like diabetes mellitus, hypertension, hepatic impairment, renal disease, and obesity, and not received any medications. Serum liver function test, lipid profile, iron, ferritin, protein electrophoresis, hemoglobin electrophoresis and some hematological parameters were assessed for each subjects in all groups.

There were statistically significant elevations in serum alkaline phosphatase, alanine transaminase and aspartate aminotransferase activities in heavy smokers while serum total bilirubin significantly was lower. No significant differences in serum alkaline phosphatase, alanine transaminase, aspartate aminotransferase and serum total bilirubin were observed between moderate and non-smoker groups. Serum total protein, albumin and globulin values were significantly lower in heavy smokers while there was no significant difference in albumin-globulin ratio among the study groups. Serum globulin change was not significant in moderate smokers while serum total protein and albumin levels were significantly lower in moderate smoker comparing to non-smoker group.

The results of serum protein electrophoresis show a decrease in albumin,  $\alpha$ -2, and  $\gamma$  globulins fractions in the serum of heavy smokers, while  $\alpha$ -1 and  $\beta$  globulins fractions increased in heavy smokers when compared with non-smokers. In moderate smokers, serum albumin,  $\alpha$ -2 globulin levels and  $\beta$  globulin fractions increased comparing to non-smoker group. No differences in  $\alpha$ -1 and  $\gamma$  globulin fractions were observed between moderate and non-smoker group.

The mean level of serum total cholesterol, triglyceride, LDL and VLDL was significantly higher in heavy smoker group comparing to non-smoker group while serum HDL level was significantly lower. Serum total cholesterol and LDL levels significantly higher in moderate smokers comparing to non-smoker group, while serum HDL level had a significantly lower value. There were no significant differences in mean levels of serum triglyceride and VLDL between moderate smokers and non-smoker groups.

The levels of serum malondialdehyde were significantly higher in heavy smoker group, while no significant difference was found in moderate smoker group when compared with non-smokers.

The results also showed that, serum iron level significantly elevated in heavy smoker group, while no significant difference was seen between moderate and non-smoker groups. There were no significant differences in serum ferritin and total iron binding capacity among the study groups.

Hemoglobin and packed cell volume levels were significantly higher in heavy smoker group comparing to non-smoker group, while no significant difference was found between moderate and non-smoker groups. Hemoglobin electrophoresis revealed that HbA and HbA2 percentages were significantly higher in heavy and moderate smokers comparing to non-smoker group but no difference in HbF percentage was found among the study groups.

Cigarette smoking has cumulative effects on the liver tissue, throughout affecting liver function test, lipid peroxidation, lipid profile and hematological parameters.

# **Formulation and Evaluation of Pseudoephedrine as Sustained Release Tablet**

**Name:** Ahmed Emadaddin Omer

**Degree:** M.Sc.

**Specialty:** Pharmaceutics

**Date of the debate:** 2/6/2012

**Supervisor:** Prof. Alaa A. Abdul Rassol

## **Abstract**

Pseudoephedrine is a sympathomimetic amine. Its principal mechanism of action relies on its indirect action on the adrenergic receptor system. While it may have weak or no direct agonist activity at  $\alpha$ - and  $\beta$ -adrenergic receptors, pseudoephedrine shrinks swollen nasal mucous membranes. It reduces tissue hyperemia, edema, and nasal congestion commonly associated with colds or allergies.

This study was done in order to prepare twice daily sustained release tablets containing 120 mg of pseudoephedrine by direct compression method. Two types of polymers which are hydroxyl propyl methyl cellulose (HPMC) and ethyl cellulose (EC) were used individually and in combination together in different ratios to form 12 formulas.

The prepared sustained release tablets of pseudoephedrine were evaluated for the selected formula F10 for their hardness, friability, content uniformity, dissolution profile, and flow property. It was found that the combination of (HPMC) and (EC) at concentration of 60 mg from both polymers gives the best retarding release profile. Furthermore, the effect of different variables on the release of pseudoephedrine from the prepared sustained release tablet for the selected formula F10 were studied; no significant difference was found in the release of pseudoephedrine from the prepared sustained release tablets.

According to the similarity factor ( $f_2$ ), the selected formula F10 is almost similar to the reference 94 when administered into different dissolution media. Kinetic analysis for the release of the drug showed that the release mechanism was diffusion.

Furthermore, the infrared (IR) spectra show no possibility of chemical interaction between the drug and polymers used in the preparation of pseudoephedrine sustained release tablets.

The overall results suggest that pseudoephedrine could be prepared as a sustained release tablet.

# Formulation and Evaluation of BisoprololFumarate as an Orodispersible Tablet

**Name:** Reveng Abdullah Abdulkareem

**Degree:** M.Sc.

**Specialty:** Pharmaceutics

**Date of the debate:** 7/5/2012

**Supervisor:** Asst. Prof. Yehia Ismail Al Azzawi

## Abstract

Orodispersible tablet is a dosage form, which recently got importance due to its rapid disintegration or dissolution in the mouth without the need for water. Orodispersible tablets are the most suitable choice for patients who cannot swallow conventional solid oral dosage forms, especially children and elderly.

The current work investigates the formulation and development of bisoprololfumarate orodispersible tablets prepared by direct compression technique. Different formulation parameters that influence the manufacturing process and performance of orodispersible tablets were studied.

Three types of superdisintegrants: croscarmellose sodium, crospovidone, and sodium starch glycolate with different concentrations were used to prepare nine formulas of bisoprololfumarate orodispersible tablets.

All prepared formulas were evaluated for their flow properties, weight variation, friability, hardness, disintegration, wetting time and water absorption ratio.

All formulas have a hardness of (3-4.35 Kg/cm<sup>2</sup>) which meets the required hardness for the orodispersible tablets. RF6 had a disintegration time of (18±2) sec., wetting time of (31±1.16) sec., and a water absorption ratio of about (91±0.58) %. Based on these data RF6 containing 6% w/w crospovidone has been selected for further investigations.

There were non significant changes ( $P > 0.05$ ) in orodispersible tablets hardness, disintegration time, wetting time and water absorption ratio when the concentration of crospovidone is increased to 8% w/w in RF11.

The effect of changing the ratio of mannitol: avicel PH-102 from (70:30) in RF6 to (50:50) in RF12 and to (30:70) in RF13 on different parameters were investigated. Non significant changes ( $P > 0.05$ ) were observed in hardness and disintegration time with a significant ( $P < 0.05$ ) decrease in wetting time from (31±1.16) sec. in RF6 to (25±0.57) sec. in RF12, and to (16±1) sec. in RF13, and a significant ( $P < 0.05$ ) increase in water absorption ratio from (91±0.58) % in RF6 to (98±1.4) % in RF12 and to (126±1.22) % in RF13.

Moreover, the shape of orodispersible tablets has been changed from biconvex heart shape in RF6 into flat circular shape in RF10, and again; the orodispersible tablets have been evaluated for different parameters. A non relevant change ( $P > 0.05$ ) has been found in tablet's hardness with a significant increase in disintegration time from (18±2) sec. in RF6 to (38±4.42) sec. in RF10.

RF3, RF6 and RF13 were further investigated for the content uniformity, and dissolution test. The stability test has been done for RF6 to estimate the expiry date of the

orodispersible tablets and to study the effect of the storage conditions on the bisoprololfumarateorodispersible tablets.

In addition, a comparison was made between the dissolution rate of the prepared bisoprololfumarateorodispersible tablets and the conventional tablet (Concor<sup>®</sup> 5mg). It was obvious that bisoprololfumarateorodispersible tablets showed a faster drug release than the marketed conventional tablet ( $P < 0.05$ ).

In conclusion, Bisoprololfumarate could be prepared as orodispersible tablets.

# Preparation and Evaluation of Carvedilol Sublingual Fast Dissolving Tablets

**Name:** Shakhawan Omar Ismail

**Degree:** M.Sc.

**Specialty:** Pharmacy

**Date of the debate:** 5/4/2012

**Supervisor:** Prof. Alaa A.Abdul-Rasool

## Abstract

Carvedilol belongs to beta-blocker drugs, widely used in treatment of congestive heart failure, left ventricular myocardial infarction and portal hypertension, which is highly subjected to first pass metabolism. Carvedilol insoluble in water; any improvement in dissolution may cause better bioavailability.

Sublingual fast dissolving tablet (FDT) bypass first pass metabolism, give higher dissolution profile and positive patient compliance with ingestion problems. This study was done in order to prepare carvedilol sublingual fast dissolving tablet.

Sublingual fast dissolving carvedilol tablets (FDTs) were prepared by direct compression method, which are acceptable to disintegrate completely in less than 30 seconds.

Three types of superdisintegrants were used {croscarmellose sodium (CCS), crospovidone (CP) and sodium starch glycolate (SSG)} alone in different concentrations, and in co-processed form prepared by physical mixing and evaporation methods.

All prepared formulas were evaluated for their flow properties, hardness, friability, weight variation, wetting time, water absorption ratio and disintegration time. The results indicated that most of formulas disintegrate within 30 seconds except ( $P > 0.05$ ) formula (F 7) that contain 3% SSG which require about 90 seconds. All formulas exhibited a good hardness (2.32-3.29 Kg).

On the other hand, among all prepared formulas, F5 (contains 6% CP), and F10A (contains co-processed superdisintegrant CP 3% and CCS 3%) which were prepared by evaporation method showed a significant decrease ( $P < 0.05$ ) in disintegration time (DT) (9 seconds). They were selected as the best formulas, because they display a good performance for specified parameters like: flow property, hardness, friability, weight content and disintegration time. The best formulas were subjected to accelerated stability test in order to determine the effect of temperature on disintegration time (DT) and hardness and to determine shelf lives which were 3 years for F5 and 2.6 years for F10A.

In addition a comparison was made between the dissolution rate of the best formulas of prepared sublingual fast dissolving carvedilol tablets (F5 and F10A) and carvedilol reference tablet (CarvedilolHexal 6.25mg tablet). It appears that the prepared sublingual fast dissolving carvedilol tablets showed faster release rate (more than 98% released within 15min) than the marketed conventional tablets (53% released in 15 minutes) ( $P < 0.05$ ).

The overall results suggest that carvedilol could be prepared as a sublingual fast dissolving tablet.

## **Zinc Sulphate as Add-on Therapy for Bronchial Asthma among Iraqi Patients**

**Name:** Mohammed Ibrahim Mohammed

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 8/11/2012

**Supervisor:** Prof. Marwan S. Al-Nimer

### **Abstract**

Asthma is a chronic inflammatory disease of the airways in which various resident and migrated cell-derived molecules play a role. An imbalance between oxidants and antioxidants causes inflammation and hyperresponsiveness of airways that are major features of asthma. Reactive oxygen species and reactive nitrogen species, including superoxide anion, hydroxyl radicals, hydrogen peroxide, hypochlorous acid, ozone and peroxynitrite, have been reported to play a pivotal role in the airway inflammation and pathogenesis.

The current study was designed to verify the effect of zinc sulphate as add-on therapy for bronchial asthma and to elucidate its effects on oxidative and/or nitrosative stress biomarkers. To achieve this aim, thirty eight asthmatic patients were assigned into two groups, and fourteen healthy subjects (control group) were included in this study.

Group I included twenty one uncomplicated asthmatic patients, their mean ages was  $47.28 \pm 14.44$  years. An oral single dose of 100 mg zinc sulphate tablet was administered daily for one month in addition to the conventional therapy of asthma. Group II included seventeen uncomplicated asthmatic patients, their mean ages was  $42.82 \pm 10.72$  years. An equivalent dose of single oral placebo capsule was administered daily for one month in addition to the conventional therapy of asthma.

Pulmonary function tests were carried out at the entry of the study and after one month of treatment. Blood samples were withdrawn from the patients at pretreatment and after one month of treatment for determination of serum copper, zinc, Cu/Zn ratio, malondialdehyde (MDA), nitric oxide (NO) and peroxynitrite (ONOO).

After one month, patients whom received zinc sulphate had a greater improvement of the pulmonary function test; forced vital capacity (FVC) was increased by 16%, forced expiratory volume in first second ( $FEV_1$ ) by 14.3%,  $FEV_1/FVC$  by 5%, peak expiratory flow rate (PEFR) by 40.8% and asthma control test (ACT) by 34.1% compared with placebo treatment; FVC (6.3%),  $FEV_1$  (4.59%),  $FEV_1/FVC$  (1.7%) and PEFR (5.2%) respectively. These changes are accompanied by alterations in serum zinc and copper levels. Oral zinc sulphate offered greater effect on the ACT scoring in severe asthmatics which achieved 42% improvement compared with 36.2% (moderate asthma) and 16% (mild asthma). Zinc sulphate supplementation had non-significant effect on the serum ONOO and MDA compared with controls' levels and both treatments reduced the serum NO to the same extent.



The study concludes that zinc sulphate improves the pulmonary function test in moderate to severe asthma by mechanisms seem to be not related to its effect on oxidative or nitrosative stress syndromes.

# Synthesis of Dithiocarbamate Derivatives of Thiadiazole and Triazole for Targeting Cancer Tissues

**Name:** Hayman Sardar AbdulRahman

**Degree:** M.Sc.

**Specialty:** Pharmaceutical Chemistry

**Date of the debate:** 29/3/2012

**Supervisor:** Assist. Prof. Mohammed Hassan Mohammed

## Abstract

Cancer is a large group of different diseases, all involving unregulated cell growth. In cancer, cells divide and grow uncontrollably, forming malignant tumors, and invade nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream.

Only a limited number of review studies have focused on the multiple biochemical events which could be directly implicated in the use of copper complexes in medicine.

It has been shown that copper accumulates in tumors due to the selective permeability of cancer cell membranes to copper compounds, accordingly, a number of copper complexes have been screened for anti-cancer activity and some of them were found active both *in vivo* and *in vitro*.

In the present study, dithiocarbamate derivatives of 4H-1,2,4-triazol-4-amine and 2-amino-1,3,4 thiadiazole have been designed to be synthesized for targeting cancer tissues and these were :

1. Sodium 3-mercapto-5-(5-(phenyldiazenyl)pyridin-2-yl)-4H-1,2,4-triazol-4-ylcarbamodithioate (compound A).
2. Sodium 3-(butylthio)-5-(5-(phenyldiazenyl)pyridin-2-yl)-4H-1,2,4-triazol-4-ylcarbamodithioate (compound B).
3. Sodium 5-(2-hydroxy-5-(phenyldiazenyl)phenyl)-1,3,4-thiadiazol-2-ylcarbamodithioate (compound C).

The generation of these target compounds were accomplished following multistep reaction procedures. The structure of the final compounds and their intermediates were confirmed by their infrared spectroscopy and elemental microanalysis.

## **Evaluation of Different Contraception Methods used in Erbil City**

**Name:** Ijlal Rostam Abdullah

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 8/3/2012

**Supervisor:** Prof. Kassim J. Al-Shamma

### **Abstract**

Family planning saves lives of women and children and improves the quality of life for all, the voluntary control of fertility is of paramount importance to modern society, it allows individuals and couples to anticipate and attain their desired number of children and the spacing and timing of their births. From global perspectives, countries currently face the crises of rapid population growth that has begun to threaten human survival.

The objective of this study was evaluation of five different methods of contraception used in Hawler city through estimating their efficacy, relative failure rate, percentage of use, adherence and compliance and adverse effects of each contraceptive method. In order to reach these aims, a retrospective, comparative study was conducted in Hawler city in Azadi health care center over a period of 6 months from 22<sup>th</sup> November, 2010 to 15<sup>th</sup> May, 2011 during which data collection and subjects follow up for 3 months had been achieved. A convenient sampling method was used to collect 429 married women in their reproductive age (16-39) years old. The studied population was divided into five groups according to the contraceptive method used: group (I) involved (113) women using combined oral contraceptive pills (COC), group (II) involved (38) women using depot medroxyprogesterone acetate injection (DMPA), group (III) involved (211) women using copper intrauterine contraceptive device (IUCD), group (IV) involved (11) women using vaginal spermicides, group (V) involved (56) women using male condom as a contraceptive method. The data necessary for this study had been collected by a direct interview with the women and the informations had been recorded on a questionnaire.

The study revealed that IUCD had a higher percentage of use among studied sample (49%), regarding efficacy DMPA was the most efficient contraceptive method (97.3%) with a lowest failure rate (2.6%), vaginal spermicide and the male condom showed the highest degree of adherence and compliance (100%). Male condom showed highest degree of subject's acceptability (69.9%), whereas DMPA showed lowest acceptability (21%). Regarding gynecological side effects, DMPA showed the highest degree of menstrual irregularity (81.5%) and amenorrhea (65.7%). Breakthrough bleeding, spotting and vaginal infection occurred in the highest percentage among IUCD users (43.1%), (11.8%), (59.2%) respectively. Central nervous system, gastrointestinal and dermatological adverse effects were higher in COC than DMPA users. The extent of weight gain was similar among DMPA and COC users (39.4%) and (39.8%) respectively. While hypertension was less among DMPA users in comparison with COC users. In IUCD users, (13.2%) their IUCD was expelled, (7.5%) showed increase endometrial thickness, (2.8%) had missed thread, and (1.8%) showed cervical ectropian.

In conclusion, our results were similar to that reported worldwide, although there were distinct differences in the percentage of these results. It is clear that percentage of women using different methods were greatly differ from country to another and also the percentages of efficacy, failure rate and adverse effects of each contraceptive method were different from one community to another. Therefore, one cannot conclude which method is best fit for the community.

# Preparation and Evaluation of Meloxicam orally Disintegrating tablets using natural and synthetic superdisintegrants

**Name:** Anoosh Bashir Hagop

**Degree:** M.Sc.

**Specialty:** pharmaceuticals

**Date of the debate:** 22/6/2013

**Supervisor:** Prof. Alaa A. Abdul-Rasool

## Abstract

Meloxicam is a non steroidal anti-inflammatory drug (NSAID) with analgesic and anti-inflammatory effect. It is an oxicam derivative, preferential inhibitor of cyclooxygenase-2enzyme (COX-2 inhibitor) and falls in the enolic acid group of NSAIDs. It is widely used in the treatment of rheumatic arthritis, osteoarthritis and ankylosing spondylitis.

This study was done in order to prepare meloxicam orally disintegrating tablets (MODTs), which give a high dissolution profile and better patient compliance with dysphagia problem. MODTs were prepared by direct compression method, which disintegrate completely in less than 30 seconds.

Two main types of superdisintegrants were used in this study including, a natural superdisintegrant {extracted dried mucilage powder of *Plantagoovata* seeds} and synthetic superdisintegrants {croplidone (CP), croscarmellose sodium (CCS) and sodium starch glycolate (SSG)} in different concentrations.

The natural superdisintegrant used was extracted from the seeds of a plant called *Plantagoovata* and the extracted dried mucilage powder was subjected to many pre compression parameters including physicochemical characterization like Molisch test, treatment with Benedict reagent, extraction value, loss on drying (LOD), pH, swelling index and flowability study (by measuring angle of repose).

All the prepared formulas were subjected to pre compression parameter like flowability study and post compression parameters like hardness, friability, weight variation, disintegration time (DT), wetting time and water absorption ratio. The results indicated that all the prepared formulas were disintegrating within less than 30 seconds ( $P > 0.05$ ). All the prepared formulas exhibited a good and acceptable hardness (2.30-2.73 kg).

Among all the prepared formulas, F2 (contains 6% extracted dried mucilage powder of *Plantagoovata* seeds) and F4 (contains 6% CP) were selected as the best formulas for the natural and synthetic superdisintegrants respectively, according to their physical properties like: flowability, hardness, friability, disintegration time, wetting time and water absorption ratio.

The selected best formulas (F2 and F4) of MODTs and the pure meloxicam powder were then subjected to Infrared (IR) study which indicates that there is no interaction between meloxicam and the ingredients used in the formulation of MODTs (F2 and F4). The best formulas (F2 and F4) were finally subjected to accelerated stability test in order to determine the effect of temperature on the disintegration time, hardness and drug release profile (dissolution study) and to determine the shelf lives which were 3.5 years

and 1.5 years for F2 and F4 respectively. The results indicate that both formulas (F2 and F4) were stable upon storage period of three months at different temperatures.

Collectively, the results showed that the extracted dried mucilage powder from *Plantagoovata* seeds could be used as a natural superdisintegrant in the preparation of MODTs in a concentration of (3% and 6%) as in (F1 and F2) respectively, which gives a faster disintegration time (20 and 18 sec.) respectively ( $P < 0.05$ ), compared with the synthetic superdisintegrant used like SSGas in (F7 and F8) in a concentration of (3% and 6%) respectively, with a disintegration time of (25 and 20 sec.) respectively.

The overall results suggest that meloxicam could be prepared as orally disintegrating tablets using natural and synthetic superdisintegrants.

# Synthesis of 5-Fluorouracil, 6-Mercaptopurine and Naproxen Conjugates as Possible Mutual Prodrugs for Targeting Cancer Tissues

**Name:** Soran Ali Othman

**Degree:** M.Sc.

**Specialty:** Pharmaceutical chemistry

**Date of the debate:** 22/7/2013

**Supervisor:** Assist. Prof. Mohammed Hassan Mohammed

## Abstract

Cancer chemotherapeutic agents characterized by lack of tumor selectivity and severe adverse effects on the healthy organs. These undesired properties lead to severe systemic toxicity. Targeted drug delivery, for traditional chemotherapy, can be achieved through prodrug approach by site-specific bioactivation. Several disadvantages and limitations in the parent drugs could be prevented by using prodrug manner.

Mutual prodrug is consisting of two pharmacologically active drugs covalently connected together in which each drug acts as a carrier for the other one. A chemical connection between anticancer agent and NSAID could be regarded as a mutual prodrug in which NSAID and anticancer agent serve as a promoiety for each other. In addition, several studies provide compelling evidence that NSAIDs have antineoplastic properties and thus might give synergistic action to the former drug.

In this study, two possible mutual prodrugs of naproxen with 6-Mercaptopurine and 5-Fluorouracil have been designed to be synthesized for targeting cancer tissues and these were:

Ethyl 3-((7 H-purine-6-yl) disulfanyl)-2-(2-(6-methoxynaphthalen-2-yl)propanamido)propanoate.

Ethyl 3-((2-((5-fluoro-6-oxo-1,2,5,6-tetrahydropyrimidin-2-yloxy) carbonyloxy) ethyl)disulfanyl)-2-(2-(6-methoxynaphthalen-2-yl)propanamido)propanoate.

Synthesis of these target compounds was accomplished following multistep reaction procedures. The structure of the final compounds and their intermediates were confirmed by their infrared spectroscopy and elemental microanalysis.

## **Therapeutic Drug Monitoring of $\beta$ -Thalassemic Patients Using Desferroxamine Injection In SulaimanyThalassemia Center**

**Name:** Rawa Abdullatif Ratha

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 14/5/2013

**Supervisor:** Assistant Prof. TaghreedAltaei

### **Abstract**

Therapeutic drug monitoring (TDM) is used to prevent or decrease the risk of toxic effects of medication and to obtain maximum effect. TDM begins when the drug is first prescribed, and involves determining an initial dosage regimen appropriate for the clinical condition and such patient characteristics as age, weight, organ function, and concomitant drug therapy.

$\beta$ -Thalassemia is an inherited hemoglobin disorder characterized by a significant genetic and clinical heterogeneity. Thalassemia patients can get an overload of iron in their bodies, either from the disease itself or from frequent blood transfusions. Too much iron can result in damage to the heart, liver and endocrine system, which includes glands that produce hormones that regulate processes throughout the body. The heart, along with liver and endocrine glands, is one of the main organs where iron deposition causes severe complications.

Desferroxamine was introduced in the 1960's and was the first iron chelator used for the treatment of chronic iron overload. Although effective, there are significant challenges associated with its use that can result in non-compliance. Issues regarding the appropriate age for the initiation of desferroxamine treatment, the maintenance of balance between its effectiveness and toxicity, and the problems of compliance with desferroxamine arise frequently in the management of patients with thalassemia.

Fifty-four thalassemia patients, receiving standard maintenance chelation monotherapy of subcutaneous desferroxamine (20-50 mg/Kg/day), over 8-12 hrs. for administration at home, were allocated to two groups; group one ( $G_1$ ); 30 patients missing desferroxamine dose, and group two ( $G_2$ ); 24 patients not missing desferroxamine dose. Prospectively studied the therapeutic drug monitoring and clinical outcomes of enrolled patients; assessed with adequacy of desferroxamine usage, serum peak & trough concentrations of desferroxamine, &ferroxamine with needed pharmacokinetics, cardiac parameters and biomarkers, biochemical& hematological indices were evaluated. The adverse effects/toxicity, urinary assessment of Fe, Zn, Cu and Se levels were measured, and the compliance to treatment; dose adjustment in correlation to therapeutic index, life style of enrolled  $\beta$ -thalassemia patients.

Demographic data showed no significant difference between the two groups, the peak plasma concentrations were  $36.88 \pm 6.8$ ,  $15.83 \pm 5.37$  mg/L, and the Trough concentrations



were  $86.8 \times 10^{-7} \pm 7.23 \times 10^{-7}$  ,  $83.95 \times 10^{-7} \pm 9.43 \times 10^{-7}$  mg/L of desferroxamine, Ferroxamine, respectively. The average elimination rate constant ( $K_e$ ) was  $0.02 \text{ min.}^{-1}$ , half life ( $T_{1/2}$ ) was 29 min., and volume distribution was 0.93 L/Kg. Cardiac parameters showed no significant differences between the studied groups. Comparison of the two groups; showed significant differences in Creatin Kinase-MB, and high sensitive C-reactive protein measured levels, while troponin I did not. Biochemical & hematological data showed significant differences in; serum Ferritin, Blood urea, Serum glutamate oxaloacetate transaminase, Serum glutamate pyruvate transaminase, alkaline phosphatase, Serum albumine, and Serum Calcium. Assessment of adverse effects/toxicity; showed

significant differences in urinary excretion of Fe, Cu, and Zn. Also highest incidence of arthralgia-myalgia, bone pain, growth retardation, headache, and significant differences in incidence of diarrhea & fever were seen, and at the injection site swelling, infiltration, pain, pruritus, erythema were noticed. In addition to the studied parameters, the correlation of serum ferritin to therapeutic index, and the life style; including vitamin C &/or E administration were assessed for the compliance to treatment.

In conclusion, Therapeutic drug monitoring of desferroxamine in  $\beta$ -thalassemia patients is necessary to ensure effective treatment, compliance, and to avoid adverse side effects and toxicity. The clinical pharmacist can play an important role in this aspect with medical team collaboration.

# Prediction of Cardiovascular Side Effects of Psychotropic Drugs In Psychiatric Patients

**Name:** Raz Mohammed Hamasalih

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 13/3/2013

**Supervisor:** Prof. Marwan S. M. Al-Nimer

## Abstract

Psychotropic drugs can produce cardiovascular side effects associated with a degree of cardiotoxicity. Cardiac toxicity of psychotropic drugs has well been known. This study focuses on the cardiovascular side effects of psychotropic drugs used in the treatment of mental illnesses.

A cross-section observational study was conducted in the Sulaimanyah city, 85 patients were recruited with 26 healthy controls. The patients were subdivided into three groups; group I (n=25): newly diagnosed mentally ill patients. Group II (n=30): mentally ill patients who were already on psychotropic drugs for their illnesses. Patients of this group were free from systemic diseases such as hypertension. Group III (n=30): mentally ill patients who were already on psychotropic drugs for their illnesses, these patients had a history of concomitant systemic diseases such as hypertension. Group IV (n=26): Healthy subjects served as control group. The patients and healthy individuals were subjected to electrocardiography and echocardiography investigations. Two electrocardiographic and echocardiographic records were obtained for group I patients, one before commencing drug therapy and the second after one month of treatment with psychotropic drugs. Also, biochemical analysis of nitric oxide and peroxynitrite were done for group I patients after one month of receiving treatment.

The results of the present study showed that patients were significantly overweighed compared with healthy subjects. The pulse pressures were significantly decreased in group I patients after one month of treatment ( $P < 0.01$ ) and Group II patients ( $P < 0.01$ ) compared with the controls. Electrocardiographic findings showed significant prolongation of QTc period. Echocardiographic findings showed that the dimension of left ventricle at end diastole significantly decreased and the dimension of left ventricle posterior wall significantly increased in both genders which indicated left ventricular dysfunction. Serum levels of nitrogen species in group I patients after one month of treatment showed significant increment compared with healthy subjects ( $p < 0.001$ ). There was no significant correlation between QTc period and serum nitric oxide or serum peroxynitrite in group I patients after one month of treatment.

In conclusion, the effect of psychotropic drugs on electrocardiography showed subclinical cardiotoxicity in term of prolongation of QTc period and a potential risk of torsade de pointes and echocardiograph data revealed the presence of left ventricular dysfunction.

# **Early Virological Response of the First Line Combination Therapy (Pegylated Interferon $\alpha$ -2a and Ribavirin) in Iraqi Chronic Hepatitis C Patients and Their Adverse Effects**

**Name:** Vian Ahmed W. Ismael

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 16/1/2013

**Supervisor:** Prof. Kassim J. Al-Shamma

## **Abstract**

Chronic hepatitis C is a complex life threatening disease that is marked by chronic necro-inflammatory injury to the liver. A sensitive quantitative hepatitis C virus nucleic acid determination assay is recommended for diagnosis, because it provides information on the level of virus which is helpful in management of the disease. Combination of pegylated interferon  $\alpha$ -2a and ribavirin represents nowadays the gold standard therapy and is the first therapeutic choice in chronic hepatitis C.

The aim of this study is to assess short-term outcome of chronic hepatitis C patients treated with combination of pegylated interferon  $\alpha$ -2a and ribavirin in Iraq. For this purpose 50 newly diagnosed chronic hepatitis C patients divided into three groups A, B and C, treated with equal doses of pegylated interferon  $\alpha$ -2a (180  $\mu$ g/week) and different doses of ribavirin (1200, 1000 and 800 mg/day respectively) and followed up for 12 weeks of starting treatment. Evaluations include both early virological response (EVR) and effect of combination therapy on plasma glucose level, blood count, liver enzymes, prothrombin time, international normalized ratio, serum albumin, renal function, thyroid hormone levels, body weight, psychological status and skin condition.

At week 12 (the time of achieving EVR), in all three groups, 49 patients (98%) achieved EVR, 47 of them (94%) were with complete EVR (cEVR), and 2 patients (4%) were partial responders. Among all 50 patients, only one patient (2%) was with no response.

Group A patients showed 100% cEVR. Group B patients reported 94.4% cEVR and 5.6% null response. Group C patients reported 88.9% cEVR and 11.1% partial response.

Group A patients showed significant reductions in plasma glucose level, hemoglobin, white blood cells count, %neutrophil, absolute neutrophils count, platelets count, aspartate amino-transferase level, alanine aminotransferase level, alkaline phosphatase level, serum albumin level and body weight. Group B patients showed significant changes in the same above parameters as that in group A. Significant increments in both thyroid stimulating hormone and serum creatinine levels were also reported. Group C patients showed significant changes in same parameters as that in group A, except of %neutrophil, aspartate aminotransferase and blood urea levels. Significant reduction in both prothrombin time and international normalized ratio were also reported.

Development of major depressive symptoms occurred frequently during Pegylated interferon  $\alpha$ -2a and ribavirin treatment and was predicted by baseline depression scores and higher doses of ribavirin. The prevalence of major depression 3 months after starting treatment, in group A was 28.6%, while in groups B and C were the same (27.8%).

Minor skin manifestations (like rash, dryness and spots) experienced by 34% of study participants 3 months after starting treatment.

It concludes that, treatment with combination of pegylated interferon  $\alpha$ -2a and ribavirin is highly responsive in Iraqi chronic hepatitis C patients. For achieving cEVR and minimizing adverse effects, the need for patient care, patient instruction and clinical pharmacist interventions in providing guidance, and improving adherence is mandatory.

# **Paradoxical Effects of Thiazide Diuretics in T2D and Hypertension In Reference To Metabolic Syndrome: Assessment of Interleukin- 6 and Nitrogen Species within Normal Range of Uric Acid**

**Name:** Omeed Jaleel Daloe

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 6/6/2013

**Supervisor:** Dr. AnsamNaji Al-Hasani

## **Abstract**

Thiazides are among the most commonly used diuretics as antihypertensive and have been available for over 50 years. They are recommended as a primary choice for the treatment of uncomplicated hypertension in which they are considered as one of the initial agents or recommended as the next agent added to existing therapy.

This study included 133 patients grouped into: Group I: 24 patients with type 2 diabetic (T2D) and hypertension (untreated with thiazides), Group II : 40 patients with T2D and hypertension (untreated with thiazides), Group III: 41 hypertensive patients treated with thiazides and Group IV: 28 hypertensive patients (free of thiazides). The patients were categorized according to the criteria of metabolic syndrome; blood pressure; anthropometric measurements; weight (kg), height (m), waist circumference and hip circumference (cm). Blood samples were collected and the sera was separated for determination of uric acid, glucose, lipid (triglycerides, high density lipoprotein, cholesterol), immunological tests (C-reactive protein, Interleukin-6) and nitrogen species (nitric oxide, peroxynitrite).

Group III showed significantly high atherogenic index and high serum triglycerides compared to Group IV. Groups I and III had high serum IL-6 which approximated 1.5 and 1.75 folds of Groups II and IV respectively.

Group III patients had significant ( $p < 0.05$ ) high serum uric acid level ( $5.066 \pm 1.004$  mg/dl) than Group IV patients ( $4.587 \pm 0.689$  mg/dl). Significant ( $p < 0.05$ ) high fasting serum glucose level observed in Group III compared with Group IV ( $118.6 \pm 39.2$  vs  $103.1 \pm 15.3$  mg/dl).

Significant inverse correlation observed between serum uric acid level and high density lipoprotein in Group III whereas serum uric acid level significantly and directly correlated with triglycerides in Groups III and IV. Also serum uric acid significantly and inversely correlated with peroxynitrite in Group II.

The results of this study shows that the use of thiazides in diabetic and/or hypertensive patients leads to disturbances in several immunological and metabolic variables. Thiazides probably via their effects on uric acid interact with the interleukin-6 as well as nitrogen species.

# **Clinical Utility of Altered Expressions of P53, Vascular Endothelial Growth Factor and Survivin In Serum of Patients with Bladder Cancer**

**Name:** Ahmed Nabeel Ahmed

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 7/7/2013

**Supervisor:** Ass. Prof. Shatha Rouf Moustafa

## **Abstract**

**Background and Objectives:** P<sup>53</sup>, vascular endothelial growth factor and surviving over expressions were used as biochemical markers in the investigation, prognosis and follow up of the patients with bladder cancer. The gold standard care for the detection and surveillance of carcinoma of bladder is cystoscopy which detects bladder tumors accurately but it is invasive, expensive, and represents a high burden to the patients. Also, small papillary and flat-growing carcinomas in situ are sometime missed. Regular cystoscopic examinations are performed for monitoring the patients, because the recurrence rate is high so, cystoscopy is recommended for follow up the patients, even those with low grade and stage. Therefore, a lot of researches have been done to investigate the possibilities of replacing cystoscopy with a more accurate, safe, non-expensive, noninvasive diagnostic test.

This study was conducted to find out a new approach to provide opportunities for early detection. Early diagnosis is essential and important goal to speed up the cure rate of patients. In addition to assess the aggressiveness of altered expressions of these factors in patients and correlated the expressions of these factors with histopathology characteristics. This study also focused on the effects of age – gender related variations in addition to the effect smoking.

**Patients and Methods :** This case control prospective study enrolled 50 newly diagnosed patients with bladder cancer, in addition 50 apparently healthy age – gender matched adults were also involved in this current study. Serum concentration levels of these parameters (P<sup>53</sup>, VEGF and surviving) were measured by ELISA technique. Patients had these general criteria, newly discovered cases, with no deep X-ray therapy, no chemotherapy, and no hormonal therapy with histological and cytological confirmations of bladder cancer.

**Statistical Analyses:** Data were analyzed by using SPSS vi.18.

**Results: The** mean serum levels of P<sup>53</sup>, vascular endothelial growth factor and surviving in patients and control groups were statistically increased significantly in bladder cancer patients as compared with control group  $p < 0.001$ .

**Conclusion :** The data of this study revealed for the first time the relation between altered expressions of interested parameters in combination patterns with the incidence of bladder cancer in Erbil population, which has not previously reported in all carefully reviewed scientific researches and in this region or area. A combination of these markers ( $\geq 2$ ) has synergistic effects, the higher numbers of altered biomarkers are the higher risk of disease progression. This study tested the hypothesis and supported the concept that

higher serum levels of these parameters might be pathogenic and prognostic factors and markers of tumor aggressiveness in bladder cancer.

## **High sensitive C - reactive protein for prediction of Cardiovascular risk level in patients with Metabolic Syndrome in Sulaimania-Iraq**

**Name:** Mudhafer Mohammed M.Saeed

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 22/7/2013

**Supervisor:** Assist. Prof. Abdulkadir A. Al-Naqshabandi

### **Abstract**

**Background and objective:** Metabolic syndrome is a group of characteristics which include obesity, high blood pressure, elevated blood sugar levels, and high triglycerides (fat-like substances in the blood). Having a combination of these characteristics increases risk of developing type 2 diabetes and heart disease. People with central obesity have an increased risk for developing the metabolic syndrome, type 2 diabetes and cardiovascular disease. However, a substantial part of obese individuals have no other cardiovascular risk factors, besides their obesity. C-reactive protein (CRP) is an acute phase protein that produced predominantly by hepatocytes under the influence of cytokines such as IL -6 and TNF- $\alpha$ . Determination of hs-CRP was carried out in this study to discriminate between centrally obese people with and without the metabolic syndrome.

**Patients and Methods:** One hundred and forty subject with central obesity aged 20-70 years underwent a physical examination and laboratory assays to determine the presence of the metabolic syndrome (NCEP ATP III criteria). The subjects were grouped into metabolic syndrome group and non metabolic syndrome group to decide whether CRP has an impact on development of metabolic syndrome, and further subdivision have made to sub classify them to five sub-groups according to the existence of components of metabolic syndrome .

**Results:** Mean hs-CRP levels were significantly higher in individuals with central obesity with the metabolic syndrome (n = 101; 72.1%) compared to individuals with central obesity without the metabolic syndrome (3.64 mg/L versus 1.75 mg/L (IQR 1.25-2.24); p < 0.0001). Mean hs-CRP levels increased with increasing number of metabolic syndrome components present. In univariable linear regression analyses, hs-CRP significantly correlated positively with body mass index, waist circumference, and atherogenic index, while a significant negative correlations was found with HDL-C level. All the obese participants were at risk of cardiovascular events.

**Conclusions:** The degree of central obesity (waist circumference) and BMI seemed to be the main determinant of an increased hs-CRP level. Serum hs-CRP was significantly correlated with the presence of metabolic syndrome; strong relationship between serum hs-CRP and various features of metabolic syndrome. The addition of serum hs-CRP to the present definition of the metabolic syndrome may help to identify patients at high risk for future cardiovascular disease.

**Keywords:** Abdominal obesity, Metabolic syndrome, High sensitive C-reactive protein.



# Efficiency of Cardiac Biomarkers in Identification of Patients with Acute Coronary Syndrome

**Name:** Ajeen Muhammad Ali

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 4-2-2013

**Supervisor:** Asst. Prof. Sana'a Gadbaan Hama

## Abstract

**Background and Objectives:** Biomarkers play an important role in the early diagnosis, risk stratification and management of patients with acute coronary syndrome (ACS). Heart-type fatty acid binding protein (H-FABP) and ischemia modified albumin (IMA) are relatively new biomarkers for evaluation of patients with ACS. To our knowledge, many studies have reported an analysis of study markers (troponin I, IMA and HFABP) for detection of early acute myocardial infarction (AMI) but little for differentiating AMI from unstable angina (UA). This study was to evaluate the usefulness of studying cardiac markers for recognition and differentiating patients with AMI from patients with unstable angina in Emergency Department and Cardiac Care Unit.

**Patients and Methods:** Study groups consist of 73 patients suspected of ACS. Patients were diagnosed previously as AMI (n=45) and patients with unstable angina (n=28). Serum concentration of cTnI, H-FABP and IMA were determined twice: (30minute-4 hour) and (6-12) hours after onset of chest pain. All biomarkers were measured by Enzyme Linked Immuno-Sorbent Assay.

**Result:** area under Receiver operating characteristic (ROC) curve was significantly higher for both markers (cTnI and H-FABP) at both study intervals, but ROC curve analysis failed to show significant change for IMA for diagnosing and differentiating of AMI from UA. The sensitivity and specificity of cTnI of cutoff value 1.25 ng/ml at ( $\leq$ 4) hour of chest pain was 53.3% and 100% respectively, with increase in sensitivity to 97.8% (cutoff value 1.15 ng/ml) at (6-12) hour after onset of chest pain. The sensitivity and specificity of H-FABP at ( $\leq$ 4) hour onset of chest pain was 48.9% and 100% (cutoff value 10.05 ng/ml) increased to 84.4% and 100% (cutoff value 9.15 ng/ml) at (6-12) hour after chest pain. The combination use of cTnI with HFABP enhanced sensitivity to 73.3% at first interval and 100% sensitive at second interval. **Conclusion:** combination of cardiac Troponin I and heart type fatty acid binding protein tests improve the sensitivity for early diagnosing and differentiating acute myocardial infarction from unstable angina. Ischemia modified albumin cannot differentiate patients with myocardial infarction from patients with unstable angina.

# The Effect of Omega-3, 6, And 9 Fatty Acids Mixture on Liver Functions, Lipid Profile and Protein Status in Hyperlipidemia Diabetic Menopausal Women

**Name:** Gulchin Issa Tatar

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the Debate:** 21-11-2013

**Supervisor:** Asst. Prof. Bakhtiar M. Ahmad

## Abstract

**Background and objective:** Lipids are organic compounds of biological nature. They classified on the basis of their structural, physicochemical, biological or physiological properties and these include a relatively small group of lipid monomer.

Fatty acids are the basic component of fats and oils. Certain fatty acids such as omega-3, omega-6, are essential for the body and they must be obtained from food or supplement sources. These omega fatty acids are integral to every cell in the body and offer a variety of health related benefits. Omega-9 fatty acids are also important for body health but are not considered to be an essential.

The observational studies shows that low intake of polyunsaturated fatty acids, particularly omega-3 and omega-6 associated with higher risk of many disorders like diabetic, coronary heart disease, inflammation and psychiatric disorder, because low intake of enough quantity of essential fatty acids affect receptor sites of serotonin neurotransmitter, cell functions, chemical mediator releases and hormonal changes. The aim of this study is to evaluate the effect of omega mixture on diabetic menopausal women's liver functions, lipid profile and protein status.

**Patients and methods:** This prospective study was performed on fifty two patients to evaluate the effect of daily oral administration of omega-3,6 and 9 mixture fatty acids for three months on newly diagnosed hyperlipidemic diabetic menopausal women. The biochemical studies include: estimation of serum Fasting blood glucose and Hemoglobin A1C, liver function tests; serum glutamic oxaloacetic transaminase(GOT), serum glutamic pyruvic transaminase (GPT), glutamyl transferase (GGT), alkaline phosphatase and (ALP), Serum Total bilirubin (STB), serum Lipid profiles and serum protein status, total protein, albumin, globulins and Protein electrophoresis pattern.

**Results:** The results showed that serum fasting blood glucose decreased non significantly ( $P \leq 0.05$ ) after omega fatty acids combination, while serum HbA1C percentage decreased significantly ( $P \geq 0.05$ ). The mean value of serum GOT, TSB, non significantly decreased, while S.GPT and S.GGT increased significantly. No change was observed in S.ALP three month after daily oral receiving of omega-3,6 and 9 fatty acids mixture during three months. Lipid profile showed that total serum cholesterol decreased significantly. Serum HDL-C increased significantly, while serum LDL-C decreased non significantly. No change in S.VLDL was observed. The mean of serum TG increased non significantly. Regarding serum protein status; total protein and albumin increased significantly while there was no significant change in serum globulins. Protein electrophoresis pattern showed important changes in the electrophoretic fractions concentrations.

**Conclusion:** Oral daily administration of omega-3,6 and 9 fatty acids mixture for three months has been clear effect on controlling type 2 diabetes mellitus, lipid profile and serum protein status, while It has a slight effect on liver functions.

# **"Estimation of Serum Malondialdehyde, Glutathione Peroxidase and Interlukin-18 Levels in Patients with Essential Hypertension"**

**Name:** Salar Fatih kudhur

**Degree:** M.Sc. Pharmacy

**Specialty:** Clinical Biochemistry

**Date of the debate:** 12-9-2014

**Supervisor:** Assist. Prof. Shatha Rouf Moustafa

## **Abstract**

**Background and Objectives:** The oxidative stress, antioxidant status and inflammatory process are cooperative events involved in development and progression of essential hypertension. This study was as a step for elucidating the contribution of the malodialdehyde, glutathione peroxidase, IL-18 and lipid profile in the etiology of hypertension, accordingly. So, this study was designed to examine the relation between malodialdehyde, glutathione peroxidase, IL-18 and lipid profile with the incidence of essential hypertension. The objectives of this study were: to assess the change in serum levels of malodialdehyde, glutathione peroxidase, IL-18 and lipid profile in patients with essential hypertension as compared with equal number of age–gender matched apparent healthy adult as a control group, moreover, find –out the gender-effect on the serum levels of the previous parameters, in addition, to investigate the age effect on the serum levels of studied parameters, and finally to detect the correlation between these interested parameters.

**Patients and Methods:** This study was designed to examine the associations between the interested parameters with the incidence of essential hypertension in 50 patients of both genders, and for the comparing purpose equal number of the matched age–gender also enrolled in this study as a control group, both groups completed the baseline questionnaire included self-reported questions concerning several risk factors for essential hypertension, including history of diabetes, smoking, physical activity, alcohol consumption, and hormone replacement therapy. The hypothesis that oxidant /antioxidant status and inflammatory process influence the risk of adverse clinical outcomes are worthy for investigating. Accordingly, malodialdehyde was measured by colorematic method, while, glutathione peroxidase and IL-18 were measured by ELISA technique and lipid profile was measured by using commercial kit.

**Statistical Analyses:** All analyses were performed with SPSS version 18.

**Results:** There were significance difference between patients regarding with studied parameters (malodialdehyde, glutathione peroxidase, interleukin 18 and lipid profile),

**Conclusion:** The data of the present study indicated an alteration in oxidant / antioxidant status and inflammatory process in patients with essential hypertension. This investigation provided the first evidence of the ability of MDA, glutathione peroxidase, IL-18 and lipid profile in combination patterns as a factors involved in essential

hypertension pathophysiology, etiology and are regarded as a markers of prognostic significance and potential therapeutic targets for future.

The demonstration of these parameters provided a new insights into understanding the independence of oxidative stress/antioxidant status and inflammatory pathways in essential hypertension development and progression.

# **Phytochemical Study of Some Active Constituents of *Adiantum Capillus-Veneris* Growing Naturally In Kurdistan**

**Name:** Rahwan Waisy Haji

**Degree:** M.Sc.

**Specialty:** Phamacognosy

**Date of the debate:** 3-12-2014

**Supervisor:** Assist. Prof. Abdulmutalib A.G. Nasser

## **Abstract**

In this study, two main methods have been used to separate the active constituents of *Adiantum capillus-veneris* : the first one is cold maceration method which gave us petroleum ether fraction, ethanolic fraction, ethyl acetate fraction, chloroform fraction, normal butanol fraction and water fraction extracts. The second is soxhlet method which gave us hexane extract.

Due to the large number of active constituents in *Adiantum capillus-veneris* it was necessary to make an analytical studies of its components to determine the chemical nature of these compounds, and then determine the main classes of constituents using specific chemical reagents for each class, the obtained results approved the presence of many of these compounds in *Adiantum capillus-veneris* extracts using different kinds of solvents like ethylic alcohol (ethanol 80%) to extract the largest percent of active constituents and by comparing between extracts using thin layer chromatography, and by calculating the weight percentage of each extract.

The separated compounds had been identified by using modern chromatography methods like High Performance Liquid Chromatography (HPLC) and High Performance Thin Layer Chromatography (HPTLC), and by studying some material-specific constants for each compound using Fourier transform infrared spectroscopy (FTIR), ultraviolet spectrophotometer (UV) and gas-liquid chromatography-mass spectrometry (GC-MS).

# Utility of Cardiac Biomarkers in Combination with Exercise Stress Testing In Patients with Suspected Ischemic Heart Disease

**Name:** Rawa Delshad Ali

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 22-2-2014

**Supervisor:** Assist. Prof. Sanaa Gadbaan Hama

## Abstract

**Background and Objectives:** Exercise stress test is the most commonly used non-invasive test to predict a diagnosis and risk stratification in patients with suspected ischemic heart disease. There is a controversy about cardiac biomarkers release during myocardial ischemia in the absence of myonecrosis, however little is known about the utility of biomarkers in combination with exercise stress test; this study was done to assess the role of biomarkers [Troponin I, Ischemia modified albumin(IMA) and Heart-type fatty acid binding protein(H-FABP)] and evaluate the relationship between ischemic heart disease and the change in above biomarkers level after exercise stress testing in an attempt to improve the diagnostic performance of stress test.

**Subjects and Method:** Eighty patients with suspected ischemic heart disease were enrolled in the study, they were classified into two groups: patients with positive exercise stress test results (n=40) and control group with negative exercise stress test results (n=40). Serum concentration of troponin I, ischemia modified albumin and heart-type fatty acid binding protein were measured one hour after performing stress test. Enzyme Linked Immuno-sorbent Assay was used to measure both troponin I and H-FABP levels, while IMA levels were measured by albumin cobalt binding test.

**Result:** There was no statistically significant difference in the mean concentration of troponin I between two groups ( $0.75 \pm 0.55$  ng/ml) for patients with positive test result vs. ( $0.71 \pm 0.55$  ng/ml) for negative test result group with ( $P > 0.05$ ). Contrary to our expectation, mean IMA level was slightly higher among control group ( $70.88 \pm 39.76$  U/ml) compared to ( $62.7 \pm 51.9$  U/ml) in positive test result group, but still with no statistically significant difference ( $P > 0.05$ ). Median H-FABP level was also higher among negative exercise stress testing group compared the positive one (2 ng/ml vs. 1.9 ng/ml respectively), but failed to reach statistically significant difference ( $P > 0.05$ ). When quartiles model used to explores the possible association between each study biomarkers with the others; serum H-FABP level was lowest (1.7 ng/ml) in highest quartile of IMA and lowest H-FABP (1.8 ng/ml) in highest quartile of troponin I but with no statistically significant association ( $P > 0.05$ ).

**Conclusion:** Myocardial ischemia, more likely occurred after exercise stress test, is not capable of causing troponin I release; furthermore, an increase in H-FABP and IMA levels after stress test are not reflect myocardial ischemia. Moreover, the combination of (troponin I, IMA and H-FABP) and measuring their post exercise levels does not seem to improve the diagnostic utility of exercise stress test

# **Effect of Topical Zinc Sulphate on Induced Skin Ulcers By Aspirin And Nicorandil In Rabbits**

**Name:** Shirin Sameen Hameed

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 7-4-2014

**Supervisor:** Assist. Prof. Tagreed Altaei

## **Abstract**

Wound healing is a dynamic process in which central tissue movements associated with repair, such as angiogenesis, granular tissue formation, and re-epithelialisation act together to replace necrotized and/or damaged tissue and to re-establish its integrity. Transforming growth factor- $\beta$  (TGF- $\beta$ ) has the broadest spectrum of actions, affecting all cell types that are involved in all stages of wound healing.

The assessment of wound healing activity was carried out through three models of wound induction on the back of rabbits: First, by excision model, second, by induced ulcer wound using aspirin (50mg), and third – by using nicorandil (10mg) wound. The animals were divided into eight groups: A; excision model and treated by zinc sulphate (10mg), B; excision model and treated by zinc sulphate (20mg), C; excision model and treated by zinc sulphate (30mg), D; excision model assigned as control, E; lesion ulcer induced by aspirin (50mg) and treated by zinc sulphate (30mg), F; lesion ulcer induced by aspirin (50mg) model assigned as control, G; lesion ulcer induced by nicorandil (10mg) and treated by zinc sulphate (30mg), while H; lesion ulcer induced by nicorandil (10mg) model and assigned as control.

The efficacy of topical zinc sulphate (10, 20, 30mg) on healing process of lesion induced by excision model, and the effects of zinc sulphate (30mg) on healing process of ulcers induced by aspirin (50mg), or nicorandil (10mg) models were studied by assessment of the followings: body weight change, macroscopical appearance of the induced ulcers (ulcer area and wound contraction), microscopically appearance and histopathology; as well as qualitative assessment (wound re-epithelialization; presence of new blood vessels, inflammatory cells, necrosis, and collagen deposition) were used to evaluate the histological changes of the induced ulcers during wound healing. Moreover, the effect of ulcer induction on the serum levels of TGF- $\beta$  was assessed in all groups.

In all groups, a significant reduction in ulcer area was observed compared to that of the baseline. Besides, a significant elevation in wound contraction was noticed compared to that of the baseline.

Qualitative assessment of the healing process of the induced ulcer showed discrete epithelialization in the groups A, B, C, and D; while that this was absent in the groups E, F, G, and H. It was found in all groups that the congestion is discrete, inflammation is moderate, and necrosis is discrete. Noteworthy, the intensity of collagen



occurrence was discrete in the groups A, B, C, E, F, G, and H, while that was moderate in group D.

Assessment of the  $\alpha$ -TGF- $\beta$  level in serum showed no significant elevation in those groups treated by different concentrations of zinc sulphate compared to their control, while TGF- $\beta$  level showed non-significant reduction in the group of induced ulcer by either aspirin or nicorandil and treated by topical zinc sulphate (30mg) compared to their own control. Moreover, a non-significant reduction was seen in the TGF- $\beta$  serum level for the ulcer induced by aspirin (50mg) or nicorandil (10mg) compared to those of their control (excision).

The results of this study showed that different concentrations of topical zinc sulphate has not significantly enhanced the healing of excision wounds. Additionally, 30mg zinc sulphate has not significantly enhanced the healing of lesion ulcer induced by aspirin (50mg) or nicorandil (10mg). Nevertheless, the aspirin (50mg) and nicorandil (10mg) were caused a delayed healing

## **Leukotriene D4 Antagonist as Add on Therapy for Patients with COPD in Hawler City**

**Name:** Avrs Ezat Majed

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 6-3-2014

**Supervisor:** Prof. Marwan S. M.Al-Nimer

### **Abstract**

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by chronic airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gas. Leukotriens are involved in airway inflammation and mucus hyper-secretion, characteristically present in asthma and chronic obstructive pulmonary disease.

The current study designed to evaluate the effect of leukotriene receptor antagonist (montelukast) as "add on therapy" on the current medication of COPD on pulmonary function tests, and its effect on nitrative stress biomarker (peroxynitrite) and C-reactive protein (CRP). To achieve this aim, a total number of fifty-one COPD patients (37 male and 14 females) enrolled in this study; their mean age was 63.4 years. They received 10 mg single oral montelukast daily for one month. A total number of thirty-two out of fifty-one patients completed the clinical trial for assessment of montelukast "as add-on therapy".

Pulmonary function test performed at the baseline and after one month. Blood samples were obtained from the patients at pretreatment and after one month of treatment for the determination of C-reactive protein (CRP), and the nitrogen reactive species; peroxynitrite ( $\text{ONOO}^-$ ) as biomarkers of inflammation and immune response.

Montelukast therapy for one month significantly improved pulmonary function test (forced expiratory volume in one second, forced vital capacity and peak expiratory flow rate), and its effect showed individual variation in drug response. The significant improvement of forced expiratory volume in one second ( $\text{FEV}_1$ ) that improved by montelukast is directly increased with age. Montelukast offered significant improvement in patients who were ex-smokers compared with those currently smokers. Seropositivity of C-reactive protein (from positive to negative) found in eleven out of fourteen patients, which highlights the antiinflammatory effect of montelukast. Montelukast non-significantly reduced the level of serum peroxynitrite from  $38.8 \pm 22.6\mu\text{M}$  to  $35.5 \pm 19.9$ .

It concludes that montelukast provides significant improvement in pulmonary function test, and it is of benefit in advanced age patients. These beneficial effects related to anti-inflammatory and anti-nitrative free radical effects.

# **Effect of Famotidine 40 Mg on the Clinical and Biochemical Outcomes Following Revascularization Procedures in Patients with Heart Failure**

**Name:** Sally Sameer Boya Palander

**Degree:** M.Sc.

**Specialty:** Clinical pharmacy

**Date of the debate:** 16-1-2014

**Supervisor:** Assistant Professor. Ibrahim Adham Majeed

## **Abstract**

Heart failure (HF) describes the complex clinical syndrome where the heart is incapable of maintaining a cardiac output (CO) that is adequate to meet metabolic requirements and accommodate venous return.

Cardiac myocytes secrete a BNP precursor that is synthesized into proBNP. After it is secreted into the ventricles, proBNP is cleaved into the biologically active C-terminal portion and the biologically inactive N-terminal (NT-proBNP) portion. The latter is used as a biomarker to detect level of proBNP in human blood.

The H<sub>2</sub>-histamine receptors are found in the heart, they are coupled to G<sub>αs</sub> proteins and produce chronotropic and inotropic activity. The H<sub>2</sub>-histamine receptors also subserve hypotension, increased gastric acid production, and enhanced vascular permeability. Therefore, in essence, histamine is a true neurohormone that can promote hypertrophy in heart failure patients.

Famotidine is a histamine H<sub>2</sub> receptor blocker that is used through the course of this study as a tool to examine the theory that histamine receptor blockage can have beneficial effects in heart diseases.

Twenty two patients of heart failure with an ejection fraction lower than 50 were recruited immediately after they have undergone primary coronary intervention, in order to complete this study. These patients were randomly allocated into two groups; a "Famotidine group (G1)-12 patients" and a "control group (G2)-10 patients". Famotidine 40 mg once daily for thirty days duration was added to the treatment regimen of all patients within the "Famotidine group", while no manipulation was done to the treatment regimen of patients within the "control group".

Patients' medical status was evaluated by filling a questionnaire form then a confirmatory echo study was conducted by a cardiologist for each patient in order to measure left ventricular dimensions, left ventricular ejection fraction and diastolic function.

Two blood samples, five milliliters each, were collected from each patient; one at the day of admission, the other at the day of follow up (one month after discharge). Serum creatinine and NT proBNP were measured in each sample.

Upon data analysis, no significant difference was observed in age, gender, concurrent medications, serum creatinine, random blood sugar, lipid profile, number and location of coronary lesions and stents or smoking habits. Left ventricular ejection fraction and Left ventricular systolic dimension were not different between the two groups before treatment. Famotidine administration significantly increased LVEF [EF: G1= (50.667±7.7028) vs. G2 =(41.8± 5.692), p= 0.006] and significantly decreased left

ventricular systolic dimension [LVESD, G1= (43.25±7.250) mm vs. G2 =(50.5±7.457) mm, p = 0.031].

Treatment with famotidine resulted in significant regression of diastolic dysfunction, (i.e. improvement in diastolic function) 58% of patients in (G1) achieved a regression in diastolic dysfunction, compared by only 20% of patients in (G2).

Famotidine also resulted in a significantly higher probability for patients to have a lower level of NT pro BNP [% of patients who had lower NT proBNP, G1 = 83.33 % vs G2= 40.00 %]

No significant difference was observed on left ventricular diastolic dimension after one month treatment with famotidine.

Famotidine administration for patients with heart failure increased ejection fraction, decreased left ventricular hypertrophy, promoted regression of grade of diastolic dysfunction and produced a higher probability of having a lower NT proBNP. H2 receptor blockage with famotidine may have therapeutic benefits in patients with heart failure.

# Formulation and Evaluation of Oral Fast Dissolving Film of Desloratadine

**Name:** Dina Aziz Boya

**Degree:** M.Sc.

**Specialty:** Pharmaceutics

**Date of the debate:** 5-6-2014

**Supervisor:** Dr. Yehia I. Khalil

## Abstract

Oral fast dissolving films (OFDFs) is a novel approach and the most advanced form of oral solid dosage form due to more flexibility and comfort.

The objective of this study was to formulate and evaluate oral fast dissolving film of desloratadine by solvent casting method using Hydroxy Propyl Methyl Cellulose (HPMC E15) as film base in three different concentration (40, 45, 50) % w/w with other ingredients, Propylene Glycol, Citric Acid, Sodium Saccharin, and Mannitol as plasticizer, saliva stimulating agent, sweetener and filler, respectively. Based on the peelability, thickness, disintegration time, and folding endurance, polymer with a concentration of (45% w/w) was found to be suitable and was selected for preparation of other formulas.

Three different synthetic superdisintegrants: Sodium Starch Glycolate (SSG), Crospovidone (CP), and Croscarmellose Sodium (CCS) with different concentrations (2 % w/w and 4% w/w) were used to study the effect of type and concentration of the superdisintegrants.

Control films prepared with different superdisintegrants were evaluated for their morphology, weight variation, thickness, surface pH, and disintegration time.

All formulas (F4, F5, F6, F7, F8) showed a decrease in disintegration time (49, 39, 34, 31 and 33 Sec.) respectively except F9 which contain 4% w/w CCS showed an increase in disintegration time (49 Sec.) when compared to 2% w/w CCS.

Among all the formula and based on the results of surface texture, thickness, folding endurance F8 was selected for preparation of desloratadine film.

In addition the drug release profile from the prepared Desloratadine (DSL) film was compared to that of the conventional tablet (AERIUS® 5mg) as a reference.

The result showed a significant increase ( $p < 0.05$ ) in the dissolution rate profile.

Meanwhile, the stability of the prepared Desloratadine film was conducted through storing samples at two different temperature 25 C° (room temperature) and 40 C° (accelerated temperature), which revealed that the shelf-life of prepared Desloratadine films was 3.8 years.

# **The Cardio Protective Effects of Angiotensin Receptor Blockers Compared To an Angiotensin Converting Enzyme Inhibitor in Isoproterenol Induced Cardiomyopathy in Rats**

**Name:** Jan Joseph Ghanim Al-Shmani

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 25-3-2014

**Supervisor:** Dr. Ansam N. Al-Hassani

## **Abstract**

**Background:** The presence of a wide selection of angiotensin receptor blockers and angiotensin converting enzyme inhibitors and the conflicting data regarding their cardioprotective properties, led to the attempt to evaluate the impact of a group of these agents which included irbesartan, candesartan, valsartan, telmisartan, and lisinopril on cardiac hypertrophy and remodeling, and also to conduct a comparison between them to determine the one with the most favorable cardioprotective profile.

### **Objective:**

The aim of this study is to assess the ability of these drugs to attenuate isoproterenol (ISO) induced cardiomyopathy in female Albino Rats, and to compare between them regarding their ability to modify the studied parameters and provide cardiac protection.

### **Animals and Methods**

Sixty two female Albino rats, 8-12 weeks of age, weighing 140-200 grams were used in the study. They were divided into 3 groups. The first group served as the control group (n=8) and was given 1 ml distilled water via oral gavage and 0.5 ml distilled water subcutaneously. The second group was the ISO group (n=8) and was given a daily S.C. injection of ISO at a dose of 5 mg/kg to produce cardiac hypertrophy and myocardial injury. The third group (n=46) served as the treatment group and was further subdivided into 5 groups, all of which received ISO as stated previously along with the treatment drug and they include:

Group 3.1(ISO-Irb) n=10: was given irbesartan 50 mg/kg/day via oral gavage. Group 3.2 (ISO-Cand) n=10: was given candesartan 2.6 mg/kg/day via oral gavage. Group 3.3 (ISO-Val) n=8: was given valsartan 53 mg/kg/day via oral gavage. Group 3.4 (ISO-Telm) n=10: was given telmisartan 13 mg/kg/day via oral gavage. Group 3.5 (ISO-Lis) n=8: was given lisinopril 3.3 mg/kg/day via oral gavage. All groups were treated for a period of 14 days. The drugs used in the treatment group were compared according to their ability to attenuate the deleterious effects of ISO administration through the estimation of certain parameters which included mean serum Matrix metalloproteinase 9 (MMP-9), Cardiac troponin I (cTn-I), Total cholesterol, Triglyceride (TG), Uric acid concentrations, and Heart weight to Body weight (Hw/Bw) ratio, in addition to the beneficial effects concerning the histopathological studies. Results were compared by ANOVA statistics and post hoc LSD test. Pearson correlation coefficient was used to assess the strength of the correlation between the studied parameters.

### **Results and Conclusion:**

When compared to the control group; ISO significantly increased the mean serum MMP-9 and cTn-I concentrations in the ISO group. When compared to the ISO group; irbesartan, valsartan, and lisinopril in their respective groups significantly reduced mean serum MMP-9 concentration but not cTn-I. On the other hand candesartan and telmisartan significantly reduced both MMP-9 and cTn-I serum concentrations. As for the mean serum cholesterol and TG concentrations; ISO produced a significant increase in mean serum cholesterol concentration and an insignificant reduction in mean serum triglycerides concentration. When compared to the ISO group irbesartan and valsartan had an insignificant effect on both mean serum cholesterol and TG concentrations, while candesartan and telmisartan significantly reduced mean serum cholesterol level, telmisartan and lisinopril significantly increased mean serum TG when compared to ISO group. Mean Hw/Bw ratio was significantly increased in the ISO group when compared to the control group; this ratio was significantly reduced by all the treatment drugs (irbesartan, candesartan, valsartan, telmisartan, and lisinopril). As for the mean serum uric acid concentration, only valsartan produced a significant elevation when compared to the control group. Regarding the histopathological studies; candesartan and telmisartan produced the most noticeable improvement regarding the tissue architecture, inflammation and fibrosis produced by ISO administration.

In conclusion all the treatment drugs possessed some degree of cardioprotection; candesartan being the most beneficial in ameliorating isoproterenol induced cardiac injury, while telmisartan and lisinopril increased mean serum TG concentration and valsartan increased mean serum uric acid concentration. Drugs that significantly reduced serum cTn-I levels (candesartan and telmisartan) produced the most noticeable improvement regarding the histopathological study indicating a relation between elevated cTn-I concentrations and the degree of myocardial injury.

# Phytochemical and Hypoglycemic Activity Study of *Actium Lappa* Extracts Growing Naturally In Kurdistan

**Name:** Dilbreen Hikmat Abdulqader

**Degree:** M.Sc.

**Specialty:** Pharmacognosy

**Date of the debate:** 24-3-2014

**Supervisor:** Asst. Prof. Alaadin M. Naqishbandi

## Abstract

*Arctium lappa* L. is one of the most famous plants used traditionally in folklore medicine and as an edible plant in healthy diet. Different parts of the plant have been used such as roots, leaves, seeds and fruits. It is rich in different chemical compounds belongs to different natural product groups and with different activities as antioxidant, anti-inflammatory, antidiabetic, antiproliferative, anti-obesity, hepatoprotective. *Arctium lappa* is world-widely distributed and it is native to Iraq especially to Kurdistan region. In this study, ethanolic extracts of *Arctium lappa* seeds, leaves and roots were undergo phytochemical screening using standard procedures, flavonoids, terpenoids and carbohydrates were detected in all extracts, Tannins and mucilages detected in both roots and leaves extracts, saponins are only detected in seeds extracts, phenols and resins are only detected in roots extract, alkaloids were detected in both roots and seeds extract. The antidiabetic activity of both roots and leaves extracts on albino mice were evaluated, thirty mice were divided into six groups, each with five mice, the groups I to VI were received normal saline, glibenclamide 2.5mg/kg, ethanolic roots dried extract 100mg/kg, ethanolic leaves dried extract 100mg/kg, ethanolic roots dried extract 200mg/kg, ethanolic leaves dried extract 200mg/kg, respectively. The blood samples were collected for fifteen days. *Arctium lappa* roots and leaves extracts showed dose dependent significant decrease ( $p < 0.05$ ) in blood glucose in most of the studying time periods. More reduction in blood glucose levels were obtained on longer duration of treatment, maximum reduction obtained with roots extract 200 mg/kg (35.76%), while for glibenclamide group was (45.14%) on day 13 and 14 of treatment period, respectively. Among the extracts, leave extract 100 mg/ kg was determined as the best treatment group which significantly differ from other *Arctium lappa* extracts groups. Phytochemical investigation led to separation and identification of important active ingredients using thin layer chromatography, arctiin and arctigenin were identified in seeds extract, chlorogenic acid was identified in seeds, roots, and leaves extracts, kaempferol was identified in roots extract. The separated constituents were identified by comparing with standards ran in parallel at the same conditions.



# Possible Role of Atorvastatin as Adjuvant Therapy to Improve the Lower Urinary Tract Symptoms and Serum Leptin in Benign Prostatic Hyperplasia Patients with Metabolic Syndrome

**Name:** Bootan Abdulqader Salih

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 20-12-2014

**Supervisor:** Prof. Kassim J. Al-Shamma

## Abstract

**Introduction:** Benign prostatic hyperplasia (BPH) is a common disease of the older men characterized by non cancerous enlargement of the prostate gland and is often associated with lower urinary tract symptoms. It has multi factorial etiology but metabolic syndrome is a known risk factor. There are two main group medications used in management of BPH; alpha blockers and 5  $\alpha$ -reductase inhibitors. Recently, statins (Atorvastatin) which is considered as drug with different mechanism of action and has important role to inhibiting cellular inflammation, angiogenesis and proliferation beside its dyslipidemic effects. Atorvastatin may decrease the metabolic syndrome risk in patients with BPH, so this study was designed to find out the effect of Atorvastatin on symptoms and progression of benign prostate hyperplasia in patients with metabolic syndrome.

**Patients and methods:** This study was conducted from 12<sup>th</sup> January 2013 until 17<sup>th</sup> October 2013. The study was run out in Rizgary teaching hospital in Erbil city. It involved 85 patients divided into two groups their age were (mean $\pm$ SEM) 69 $\pm$ 0.9 years and were between 55 and 85 years. The first group included 40 patients suffering from benign prostate hyperplasia, and the second group involved 45 patients suffering from both metabolic syndrome and BPH. Only 76 patients completed the study successfully, 38 patients from group one received Tamsulosin or Tamsulosin+Dutasteride while 38 patients from group two (with metabolic syndrome) received the same treatment with Atorvastatin. Prostate specific antigen, Prostate volume and International prostate symptom score were measured in all patients at diagnosis and after six months of treatment. Serum leptin and lipid profile were measured only in patients with metabolic syndrome.

**Results:** Benign prostatic hyperplasia patients with metabolic syndrome had significantly higher values of Prostate specific antigen, Prostate volume and International prostate symptom score compared to benign prostate hyperplasia patients without metabolic syndrome. Patients with MetS had significantly higher values of body mass index, low density lipoprotein, cholesterol, and triglyceride and lower levels of high density lipoprotein compared to patients without metabolic syndrome. The values of Prostate specific antigen, Prostate volume and International prostate symptom score were reduced significantly in benign prostate hyperplasia patients with metabolic syndrome treated with Atorvastatin and Tamsulosin or Atorvastatin and Tamsulosin+Dutasteride. Lipid profiles (cholesterol, low density lipoprotein, triglyceride) were reduced significantly in benign prostate hyperplasia patients with metabolic syndrome in both groups of treatment who received Tamsulosin and Atorvastatin or Atorvastatin+Dutasteride and Atorvastatin.

Serum leptin was reduced significantly in benign prostate hyperplasia patients with metabolic syndrome received Tamsulosin and Atorvastatin or Tamsulosin+Dutasteride and Atorvastatin.

**Conclusion:** Atorvastatin has a beneficial effect on symptoms and progression of benign prostatic hyperplasia patients with metabolic syndrome.

# Assessment of Superoxide Dismutase and Malondialdehyde in Rheumatoid Arthritis Patients in Erbil City

**Name:** Niaz Nasraldeen MalaAziz

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 25-5-2015

**Supervisor:** Assist. Prof. Kamaran Younis M. Amin

## Abstract

### Background and objective:

Rheumatoid arthritis (RA) is a chronic inflammatory disorder characterized by uncontrolled proliferation of synovial tissue. Rheumatoid factor (RF) and Anti-cyclic citrullinated peptide antibodies (anti-CCP) can be used with other tests and clinical examination for diagnosis of RA. Disturbance balance between oxidative stress and antioxidant may increase cause of RA.

The aim of current study was to assess the level of malondialdehyde (MDA), superoxide dismutase (SOD), Rheumatoid factor RF, erythrocyte sedimentation rate (ESR) and Anti-cyclic citrullinated peptide antibodies (anti-CCP) in patient with Rheumatoid arthritis (RA), and to compare serum level of these parameters in RA group with control group.

### Patients & method:

The study was carried out at Rizgarry Teaching Hospital from January (2014) to July (2014). This case- control study was conducted with (94) participants which distributed in two distinct groups, (58) of them suffer from RA, their ages between (23-67) years, and (36) of them are control group, their ages between (23-64). The serum MDA, SOD, anti-CCP was estimated by ELISA, rheumatoid factor estimated by latex agglutination and ESR estimated by (westergren) method.

### Results:

The results showed that the mean value of MDA ( $7.142 \pm 3.092$  mmole/L), ESR ( $36.136 \pm 21.191$  mm/hr) and anti-CCP ( $120.798 \pm 123.496$  U) were significantly

# **Effect of Small Doses of Metformin & Glimepiride on Resistin Level And Other Biochemical Markers In Overweight And Obese Female With Type 2 Diabetes Mellitus**

**Name:** Yasser Sameer Abdulrazzaq

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 4-3-2015

**Supervisor:** Assistant Professor. Ibrahim Adham Majeed

## **Abstract**

### ***Background:***

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia caused by absolute or relative deficiency of insulin. Long-standing metabolic derangement is associated with functional and structural changes in many organs; particularly those of the vascular system, which lead to the clinical “complication” of diabetes. Resistin is a member of a class of cysteine-rich proteins, Resistin has been implicated in the pathogenesis of obesity-mediated insulin resistance and Type 2 diabetes mellitus, at least in rodent models.

### ***Objectives:***

In order to compare the effect of the anti-diabetic drugs on resistin hormone level and the other parameters related to diabetes mellitus.

### ***Methods:***

Forty five female patients newly diagnosed with (T2DM) plus fifteen female healthy control subjects were included in the study. Patients distributed into three groups, received (metformin 500 mg twice daily, glimepiride 2 mg once daily and third group treated by combination of them) for three months duration, blood sample was taken before and after treatment to detect the effect of drugs on body weight, body mass index (BMI), waist circumference (WC), index of central obesity (ICO), resistin, insulin, insulin resistance, fasting blood sugar (FBS), glycated hemoglobin (HbA<sub>1c</sub>), urea, creatinine and lipid profile.

### ***Results:***

Metformin decrease body weight, BMI, WC, ICO, FBS, HbA<sub>1c</sub>, LDL-C, cholesterol and insulin resistance significantly. And decrease insulin, increase HDL-C none significantly. Glimepiride monotherapy decreases FBS, HbA<sub>1c</sub> significantly, increase body weight, BMI, and insulin level none significantly, decrease triglycerides, resistin none significantly.

Combinations of drugs resulted in increase in body weight, BMI and insulin level none significantly. It also decreases FBS, HbA<sub>1c</sub> significantly and none significantly decrease cholesterol, LDL-C, resistin, and insulin resistance.

### ***Conclusion:***

We concluded that glycemic control and insulin resistance was improved in all groups, glimepiride reduce plasma resistin and triglycerides, metformin improve obesity and atherosclerotic related factor (cholesterol, LDL-C).

# **Synthesis of Polymeric Analogue of 6-Mercaptopurine as A Possible Prodrug for Targeting Cancer Cells**

**Name:** Omar Abdulrahman Abdulqader

**Degree:** M.Sc.

**Specialty:** Pharmaceutical Chemistry

**Date of the debate:** 17-3-2015

**Supervisor:** Assist. Prof. Mohammed Hassan Mohammed

## **Abstract**

In this study, a new polymeric anticancer prodrug (VIII) was synthesized. The polymeric prodrug containing polyvinyl alcohol with many hydroxyl reactive sites along the backbone was used. The anticancer agent 6-mercaptopurine was conjugated to polyvinyl alcohol backbone. The amino acid cysteine was used as a spacer arm between 6-mercaptopurine and polyvinyl alcohol backbone to reduce steric hindrance. To increase the selectivity toward cancer cells, folic acid as a targeted moiety was attached to polyvinyl alcohol backbone through ester bond on other sites along the polymer backbone. Synthesis of the targeted compound was accomplished by multistep reaction procedures. The structure of the products and the final compound were characterized by many techniques including elemental microanalysis, <sup>1</sup>HNMR and infrared spectroscopy.

# **The Status of Atherosclerosis and Hand Muscle Strength in Ischemic Heart Disease Patients Using Statins**

**Name:** Susan Bilal Wahhab

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 28-2-2015

**Supervisor:** Professor. Marwan S. AL-Namir

## **Abstract**

### **Background:**

Statins are the most commonly prescribed lipid lowering agents. The purpose of their prescription is to ameliorate the dyslipidemia .One of the most serious adverse reactions of statins is muscle damage in term of rhabdomyositis and myopathy.

### **Objectives**

This study aimed to assess the patients with a history of ischemic heart disease treated with statins taking in consideration the atherosclerotic changes in the coronary artery (using coronary CT), peripheral artery (using ankle-brachial index) as a therapeutic effect. The skeletal muscle strength and endurance as an adverse effect in ischemic heart disease patients already treated with statins also assessed.

### **Materials and Methods:**

This observational study was conducted in the Department of Pharmacology, College of Pharmacy, Hawler Medical University and the Hospital of Specialty of Surgeries –The Cardiac Centre from January 2014

to June 2014. Sixty four patients with IHD, thirty two of them not received statins therapy (Group 1) and the other thirty two treated with statins (Group2) were enrolled in the study. The demographic characteristics that related to their illnesses were obtained and the cardiometabolic risk factors were also assessed. The anthropometric measurements, serum lipid levels profile, high sensitivity C-reactive protein(hsCRP) coronary angiograph data, calcium coronary score were determined. The ankle brachial index as an indicator of atherosclerosis in the lower limbs arteries was calculated as a ratio of systolic blood pressures at the brachial artery to the dorsalis pedis or tibialis posterior arteries. The strength of hand grip muscles was assessed as an indicator of muscle weakness was assessed by using electrical dynamometer.

**Results:**

Group 2 patients characterized by having a significant high number of risk factors and presented with myocardial infarction. Waist circumference as an indicator of central obesity is significantly higher in Group 2 compared with Group 1. There were non significant differences in the levels of lipid profile, fasting glucose and uric acid levels between Groups 1 and 2. Serum levels of hs-CRP ranged between < 0.5 to > 20.45 mg/L with a mean  $\pm$  SD values of  $6.437 \pm 6.727$  and  $7.775 \pm 7.136$  mg/L for Group 1 and Group

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respectively, a difference did not reach significant level. Significant ( $p < 0.001$ ) decrease in ankle brachial index at dorsalis pedis and tibialis posterior in Group 2 compared with Group 1. The results of hand grip strength revealed that the number of patients with a "weakness" grade is higher in Group 2 compared with Group 1 and none of patients scored "strong" grade in Group 2 while three patients from Group 1 had this grade. Significant positive correlation between the serum uric acid levels and the hand grip strength scores ( $r = 0.459, p < 0.01$ ) in Group 1 was observed. The data of coronary angiograph showed that atherosclerotic changes were observed in significant higher percents in Group 2 compared to Group 1 in left coronary artery and the mean value of coronary calcium score in Group 2 amounted three times of that in Group 1.

**Conclusions:**

The prescription of statins in coronary artery disease runs in parallel with the guidelines of statins prescription elsewhere. Statins ameliorated the cardiometabolic risk factors and possessed a beneficial effect on ankle brachial index but it carried an adverse effect on the muscle strength. They do not improve the coronary angiograph data and coronary calcium score.

# **Evaluation of Anti-Inflammatory Effects of Pentoxifylline as Adjuvant Therapy to Methotrexate in Patients with Active Rheumatoid Arthritis**

**Name:** Younis Sadiq Smail

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 24-4-2015

**Supervisor:** Assist Prof. Ibrahim Adham Majeed

## **Abstract**

### **Background:**

Rheumatoid arthritis (RA) is a common inflammatory disease associated with many articular and extra-articular features.

### **Objectives:**

The aims of the study were to evaluate anti-inflammatory effect of Pentoxifylline as adjuvant therapy to methotrexate in patients' with active Rheumatoid arthritis.

### **Methods:**

A single centre randomized single blind placebo-controlled trial of 8 weeks duration was performed. Disease activity was measured by calculating the disease activity score in 28 joints using erythrocyte sedimentation rate (DAS28-ESR). A total 40 patients who used methotrexate were screened and randomized into 2 groups to receive each day either Pentoxifylline 400mg tablet twice daily or capsules prefilled with glucose twice daily as placebo. Blood sample of both patients and controls were evaluated for erythrocyte sedimentation rate (ESR), interleukin-6 (IL-6), anticitrullinated c peptide antibody ,lipid profiles, high sensitive C-reactive protein (hsCRP), renal and liver function tests at baseline and after 8 week.

### **Result:**

Interleukin-6 (IL-6), high sensitive C-reactive protein (hsCRP), duration of morning stiffness, visual analogue scale (VAS) significantly more reduced in PTX group than placebo group after 8 weeks of treatment. statistically non-significant changes were observed in lipid profiles, anticitrullinated C peptide antibody (Anti-CCP),clinical parameter like swelling joint count (SJC), tender joint count (TJC), DAS28 and haematological parameter like erythrocyte sedimentation rate(ESR), liver and renal function test.

### **Conclusion:**

PTX was safe and well tolerated drug that has anti-inflammatory effect in patients with active RA.

**Key words:** Rheumatoid arthritis, Pentoxifylline, disease activit

# Association of N-Terminal Pro – Brain Natriuretic Peptide, Matrix metalloproteinase-9 and 8-Oxo-2-Deoxy Guanosine with the Incidence of Essential Hypertension"

**Name:** Julian Yonan Ismaeil

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 14-4-2015

**Supervisor:** Ass. Prof. Shatha Rouf Moustafa

## Abstract

**Background and Objectives:** Oxidative stress and inflammation are cooperative events involved in essential hypertension diseases incidence, development and progression. This study was as a step for elucidating the contribution of N-terminal pro-Brain natriuretic peptide, matrix-metalloproteinase-9 and 8-oxo2-deoxyguanosine to the essential hypertension.

Therefore, this study was designed to examine the relationship between the focused parameters with the incidence of essential hypertension, development and progression. The main objective of this study was to determine the serum levels of inflammatory markers N-terminal pro-Brain natriuretic peptide, matrix metalloproteinase -9, and oxidant byproduct 8-oxo-2-deoxyguanosine in hypertensive and normotensive subjects for comparing purposes. The aims of this study were to assess the association between these biomarkers with the essential hypertension, and to find out the effect of other confounding factors like stages, age and gender on serum levels of these biomarkers, and finally to find out the correlation between all studied parameters.

**Patients and Methods:** This study was designed to examine the associations between the focused parameters with the essential hypertension in 50 patients of both genders, as well as 46 of matched age-gender adults were also enrolled in this study as a control group for comparing purposes. All of patient completed the baseline questionnaire, including the self reporting questions, concerning several risk factors of essential hypertension. subject who have any other diseases, or on any kind of medications were excluded from this study. Then the blood of the participants were taken and centrifuged it, and the sera was separated, Accordingly, N-terminal pro –brain natriuretic peptide, matrix –metalloproteinase-9 and 8-oxo-2-deoxy guanosine were analyzed using ELISA technique.

**Statistical Analyses:** All analysis were performed with SPSS version 18. **Results:** Patients with essential hypertension exhibited significantly higher serum levels of N-terminal pro –brain natriuretic peptide, matrix –metalloproteinase-9 and 8-oxo2-deoxy guanosine as compared with the control group. Regarding N-terminal pro–brain natriuretic peptide the mean serum level of this parameter was  $(304.33 \pm 204.19)$  (pg/ml) in patients group and it was  $(76.52 \pm 20.98)$  (pg/ml) in control group. The mean serum level of matrix–metalloproteinase-9 was  $(2.36 \pm 1.1)$  (ng/ml) in patients group while the mean serum level of matrix –metalloproteinase-9 was  $(1.4 \pm 0.8)$  ng/ml in control group

. The mean serum level of 8-oxo-2-deoxy guanosine was (170.40±41.95) (mg/ml) in patients group and it was (84.11±34.07) (mg/ml) in control group.

**Conclusions :** 1. There were statistically significant differences between mean serum levels of NT-proBNP, MMP-9 and 8-oxo-2dG in patient's group as compared to the control group.  $p < 0.001$ . 2. The mean serum levels of NT-proBNP, MMP-9 and 8-oxo-2dG were significantly increased with the stages progression of essential hypertension.  $p < 0.0$  3. There was a significant strong positive correlation between serum levels of NT-proBNP, MMP-9 and 8-OXO-2dG.  $p < 0.001$ ,  $r > 0$ . 4. Statistically, no significant differences in the mean serum levels of NT-proBNP, MMP-9 and 8-oxo-2dG in patients and control groups regarding the age categories, so there was no age effect.  $P > 0.05$ . 5. There was no gender effect  $P > 0.05$ , there were no significant differences between men and women regarding the mean serum levels of focused parameters in patients and control groups .

# **Beyond The Local Effect Of Second Generation Mtor- Drug Eluting Stent On Proinflammatory Markers In Patients With Coronary Arteries Occlusion**

**Name:** Sham Ahmed Talaat Shareef

**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 15-1-2015

**Supervisor:** Prof. Marwan S.M.Al-Nimer

## **Abstract**

**Background:** Coronary artery disease (CAD) is the leading cause of morbidity and mortality in the world. The core to the pathogenesis of CAD is the development of atherosclerotic lesions in coronary arteries. Coronary stents elicit an initial inflammatory cell response that if excessive can lead to restenosis. The ability of drug-eluting stents to induce inflammatory response soon after implantation is not well understood.

**Objectives:** Demonstrate the effects of drug eluting stent on the circulating pro-inflammatory markers early after administration.

**Materials and Method:** This observational open label study was carried on in the Department of Pharmacology, College of Pharmacy, Hawler Medical University in Erbil, Kurdistan region from January to June 2014. The study recruited 114 patients from the surgical Specialty hospital -Cardiac Centre, who attended the hospital for managing one or more occlusion of coronary artery or its branches with a critical grade. The related risk factors, and medical history including the pharmacotherapy were obtained from each patient according to the questionnaire that designed for this purpose. Peripheral venous blood was drawn immediately after admission (baseline) and also within one week post drug-eluting stent insertion to determine lipid profile, high sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) using the technique of enzyme linked immunosorbent assay (ELISA).

**Results:** There was a non-significant decrease in the mean $\pm$  SD of serum IL-6 one week post stent application (8.71 $\pm$ 8.82 before stent Vs 7.96 $\pm$ 3.7 after stent, p=0.5). The hs-CRP level decreased after the application of the stent in both genders and reached significant level in men (7.23 $\pm$ 7.58 $\mu$ g/ml pre stent versus 5.50 $\pm$ 6.77 $\mu$ g/ml post stent application, p= 0.03). After the application of drug eluting stent, there was a positive correlation between III

IL-6 and hs-CRP ( $r= 0.349$ ) and that the level of IL-6 of 6.8 pg/ml corresponded to the zero value of hs-CRP. No relationship between the baseline data of ejection fraction and the hs-CRP ( $r=0.034$ )

**Conclusion:** Everolimus eluting stent that used in management of the majority of patients suppressed significantly the inflammatory biomarker; hs-CRP in the peripheral venous blood but not the same for IL-6. Therefore, it is possible to use hs-CRP within one week post stent application as a prognostic marker to determine the success of stent implant, but not the same for IL-6.

# Evaluation of Serum Adenosine Deaminase Activity, Some Antioxidant Status and Inflammatory Response in Breast Cancer

**Name:** Hana Mohammed Sulaiman

**Degree:** M.S c.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 2-3-2015

**Supervisor:** Asst. Prof. Bakhtiar M. Ahmed

## Abstract

**Background and objective:** Breast cancer is the most common malignancy among females world-wide. There is a relationship between cancer cells and free radicals in the body. Reactive oxygen species cause a damage to deoxy nucleic acid, thus producing mutations and formation of tumour cells. Tumour cells are known to produce more reactive oxygen species than normal cells and this lead to generation of a condition known as oxidative stress which is leading to cell proliferation and inflammatory conditions. Several studies have shown that high level of adenosine deaminase and inflammatory condition with low level of antioxidant defence system associated with increased risk of cancers.

The aim of this study is to evaluate serum adenosine deaminase activity, some antioxidant parameters and high sensitive C-reactive protein as inflammatory marker in newly breast cancer patients in order to investigate the possibility of using these parameters in the diagnostic and monitoring tools.

**Patients and methods:** This study was carried out on Forty seven newly diagnosed breast cancer women with four different clinical stages and fifteen healthy matched age and sex of control subjects. The following parameters were evaluated; the activity of serum adenosine deaminase, serum antioxidant status; serum vitamin C, uric acid, albumin, zinc and copper, and serum high sensitive C- C-reactive protein.

**Results:** The results of the study showed that Serum adenosine deaminase activity increased significantly ( $P \leq 0.05$ ) in newly diagnosed breast cancer women ( $3.84 \pm 0.40$ ), while serum vitamin C showed a non-significant decrease ( $P \geq 0.05$ ) ( $1.11 \pm 0.69$ ). Serum uric acid levels showed a non-significantly decrease

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( $P \geq 0.05$ ) in newly diagnosed breast cancer women ( $4.06 \pm 1.21$ ) with a step wise increase in the means of serum uric acid levels among the patients stages. The result of serum albumin was found to be decreased ( $P \leq 0.05$ ) ( $4.29 \pm 0.76$ ) significantly with no significant differences among patient's stages. Serum zinc concentration decreased significantly ( $P \leq 0.05$ ) in the patients ( $78.29 \pm 21.86$ ) and it showed a random change among the patients groups. Serum copper levels showed a significant increase ( $P \leq 0.05$ ) ( $166.93 \pm 47.9$ ) with increase in the mean values of serum copper concentration in patients of stage III and IV comparing to stage I and II. A significant increase ( $P \leq 0.05$ ) ( $4.29 \pm 3$ ) in level of high sensitive C-reactive protein was observed in the serum of the patients with a stepwise increase among the stages of breast cancer.

**Conclusions:**

The activity of serum adenosine deaminase, antioxidant status and the inflammatory response found to be changed in newly diagnosed breast cancer patients and among their stages. Thus these parameters may be used in diagnosis and monitoring, to confirm these findings more researches are required.



# Synthesis and Characterization of New Hybridized Molecule from 5-Fluorouracil as Possible Anticancer Agent

**Name:** Faruq Azeez Abdulrahman

**Degree:** M.Sc

**Specialty:** Pharmaceutical chemistry

**Date of the debate:** 1-6-2015

**Supervisor:** Assist. Prof. Mohammed Hassan Mohammed

## Abstract

Molecular hybridization is a new concept in drug design and development based on the combination of pharmacophoric moieties of different bioactive substances to produce a new hybrid compound with improved affinity and efficacy, when compared to the parent drugs. Additionally, this strategy can result in compounds presenting modified selectivity profile, different and/or dual modes of action and reduced undesired side effects. Therefore, in this thesis, we described several examples of different strategies for drug design, discovery and pharmacomodulation focused on new innovative hybrid compounds presenting analgesic, anti-inflammatory, platelet anti-aggregating, anti-infectious, anticancer, cardio- and neuroactive properties.

New anti-cancer drugs developed using molecular hybridization techniques to obtain multiple-ligand drugs can act at one or multiple targets, allowing for synergic action and minimizing toxicity. This work is a new anti-cancer drugs developed using the molecular modification approach.

In this study possible anticancer which are 5-FU and its sodium salts and thalidomide to be designed for synthesis of new hybridized anticancer and these were:

1. 2-[2-(5-fluoro-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-oxoethyl]-1*H*-isoindole-1,3(2*H*)-dione .[**29**]
2. 5-Fluoro-6-oxo-1,6-dihydropyrimidin-2-yl (1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)acetate .[**30**]
3. 2-{{2-(5-fluoro-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2-oxoethyl}amino}-1*H*-isoindole-1,3(2*H*)-dione .[**34**]

## **Evaluation of Superoxide Dismutase, Matrix-Metalloproteinase-9 and Interleukin -18 in the Serum Level of Type II Diabetes Mellitus**

**Name:** Shwan Ali Omar

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 1-6-2015

**Supervisor:** Assistant Prof. Shatha Rouf Moustafa

### **Abstract**

This study was designed to examine serum level Matrixmetalloproteinase-9 (MMP-9), Superoxide dismutase (SOD), Interleukin-18(IL-18) two groups. Patients group consists of 50 patients with Type-II DM of both genders and control group of 45 age and sex matched healthy subjects. Both groups will complete the baseline questionnaire included .

Both oxidative stress and low grade inflammation are involved in the pathogenesis of type II diabetes mellitus. Thus this study was designed to investigate the differences in serum levels of Superoxide dismutase as a potential marker of oxidative stress and interleukin-18 as inflammatory marker which play important roles in T2DM progression and development as compared with the control group, and investigating Matrixmetalloproteinase-9 which extracellular matrix degradation enzyme which also has important roles in the development of DM complications, and find-out their association with the blood glucose concentration.

**Methods :** Serum levels of (Matrixmetalloproteinase-9 (MMP-9), Superoxide dismutase (SOD), Interleukin-18(IL-18)) were measured using ELISA test.**Results:** the results show significant difference in serum level of all three parameters in Patients group as compared to control group, serum level of Superoxide dismutase was lower in patients group ( $301\pm 97$ ) as compared to control group ( $501\pm 162$ ) ( $p < 0.001$ ) . Furthermore, serum level of both Matrixmetalloproteinase -9 and Interleukin -18 were significantly greater among patients ( $2.632 \pm 1.745$ ) ( $93.996 \pm 21.297$ ) compared with acontrol group ( $1.506\pm 0.945$ ,  $p < 0.001$ ) ( $48.4 \pm 26.375$ ,  $p < 0.001$ ), respectively.

**Conclusion:** inflammation and oxidative stress are of major pathways of diabetes complications, also deterioration in Extracellular matrix degradation plays an important role in T2DM complications. So there is increased pro-inflammatory and inflammatory cytokines, and oxidative stress is lead to decrease in Superoxide dismutase which is a strong antioxidant.

# Changes in Atherogenic Biomarker in Patients Subjected to Percutaneous Coronary Intervention

**Name:** Hiba Shaker Boya

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 26-7-2015

**Supervisor:** Assist. Prof. Abdulkadir A.Al-Naqshabandi

## Abstract

**Background:** Acute coronary syndrome refers to a spectrum of clinical presentations includes ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction and unstable angina. Numerous studies have investigated the relationship between vonwillbrand factor plasma levels and thromboembolic cardiovascular events.

**Aim:** to assess the clotting factors status in different cardiovascular interventions and their relationship with cardiovascular risk factors with assessment of gender effect.

**Patients and methods:** This study includes 73 ischemic heart disease patients (40 men and 33 women) aged ( $58.5 \pm 8.5$ - $58.0 \pm 9.8$  years) respectively, to determine the atherogenic biomarker (von willebrand factor, hs-CRP, fibrinogen and lipid profile). The subjects were grouped in to ischemic heart disease patients without intervention and ischemic heart disease with intervention (catheterization and stent).

**Results:** The study results shows no statistically significant difference in plasma von Willbrand factor, high sensitive c-reactive protein, fibrinogen between both gender ( $20.22 \pm 11.2$  mU/ml,  $6.2 \pm 8.9$   $\mu$ g/ml,  $394.5 \pm 58.7$  mg/dl) respectively. Plasma levels of von Willibrand factor is high in Group 2A ( $22.4 \pm 10.6$  mU/ml) compared with Group I ( $20.14 \pm 11.16$  mU/ml) but it is lower in Group 2B ( $16.01 \pm 11.7$  mU/ml) compared with Group I and 2A.

**Conclusion:**The von Willbrand factor and high sensitive C-reactive protein were obviously higher in patients with coronary angioplasty compared to patients with percutaneous coronary interventions who had significant high plasma fibrinogen

# Effects of Nicorandil on Leptin and Prostaglandin E2 Levels in Albino Rats

**Name:** Asmaa Awni Haydar

**Degree:** M.Sc.

**Specialty:** Pharmacology & Toxicology

**Date of the debate:** 9-7-2015

**Supervisor:** Assist. Prof. Tagreed Altaei

## Abstract

**Background and Objective:** Many reports confirm ulcers as an adverse effect of drugs such as nicorandil and aspirin. The exact responsible mechanisms of ulceration have until now not proved. Mucosal ulcers associated with the onset of ulcer are manifested by an increase in proinflammatory cytokine production, excessive prostaglandin generation, and a marked up-regulation of Endothelin-1 level, which directly impacts the release of leptin. This study was designed to find out the effect of plasma leptin and prostaglandin levels in Albino rats and to compare between them and from control group regarding their ability to modify the studied parameters as a possible mechanism of ulcer formation and histopathological changes of tissues as an adverse effect of administration of nicorandil.

**Animal and Method:** Forty-two albino rats of both genders, aged 12-16 weeks, weighing 169-409 grams, divided into 6 groups; 0.28, 0.4, 1, and 3 mg/kg; a positive control of 5 mg/kg aspirin, and a negative control of 1 ml normal saline. All group were treated for a period of 10 days. The drugs used in treatment group were compare the efficacy of nicorandil for inducing ulceration in oral, gastrointestinal, and anal tissues was assessed by microscopic histopathology for inflammation and ulceration. Enzyme Linked Immuno-sorbent Assay (ELISA) was used to measure plasma leptin and Prostaglandin E2 and with studied parameters (gender, daily body weight change) estimated in this study. Result were compared by (t-test) was used to assess the strength between the studied parameters.

**Results:** The results demonstrated that the efficacy of nicorandil is dose-dependent, in which the microscopic examination revealed that the nicorandil affecting the tissue architecture, leading to inflammation, erosion of mucosa and ulcer induction in oral, **GIT** (gastrointestinal tract), and anal tissues of albino rats. Nicorandil significant decreased plasma leptin concentration with significant value ( $P=0.014$ ), and indicate significant reduction with doses of 1, and 3 mg/kg/day compared to the controls, while aspirin group showed a non-significant increase of plasma leptin levels.

Assessment of plasma prostaglandin E2 level showed a non-significant reduction of treated groups by tested doses of nicorandil compared to the control groups. The analysis showed that females have a significant less plasma leptin concentrations than males, and plasma prostaglandin E2 concentration was higher in female than male albino rats. Weight of rats was significantly increased in nicorandil groups compared to the significant reduction in aspirin control, which was dose-dependent.

**Conclusion:** The mechanisms of ulcer induction as an adverse effect of administering nicorandil can be related to the significant reduction of plasma leptin level, which was dose-dependent, as confirmed by studied parameters and

histopathological assay. Nicorandil causes a significant elevation of weights of albino rats. Another possible mechanism may be related to the non-significant reduction of serum prostaglandin E2 level.

# Novel Method for the Development of Immediate Release Tablets of Poorly Water Soluble Drug (Meloxicam) and Evaluating Using Invitro Dissolution Test

**Name:** Anjam Hama Abdullah

**Degree:** M.Sc.

**Specialty:** Science in Pharmaceutics

**Date of the debate:** 27-7-2015

**Supervisor:** Dr. Sabah Diyab Souliman

## Abstract

Meloxicam is a poorly water-soluble, non-steroidal anti-inflammatory drug and antipyretic agent. Meloxicam is practically insoluble in water (8-15 $\mu$ g/ml) which directly influences the bioavailability of the drug.

In recent years, the number of poorly soluble drug has been discovered. Formulation of such poorly soluble drugs for oral delivery is difficult; improvement of solubility is one of the most important ways to overcome the difficulty for the formulation development of such poor soluble drug.

Actually several methods are used in the enhancement of the solubility of poorly water soluble drugs and also were applied in the current study: (I) Addition of surfactants such as sodium lauryl sulphate (SLS) and Tween 80 (polysorbat) to enhance solubility as surface active agent at limited concentration (0.05-0.10%). (II) Complexation method by using  $\beta$ -Cyclodextrine derivatives. (III) Precipitation method: By dissolving the drug in a solvent and then, evaporation of the solvent to obtain the precipitate.

In pharmaceutical formulation, the tablets are generally prepared either by direct compression or by wet granulation. The last method depends on the dissolving of the binder inside a solution, preparation of granules and then drying of these granules by evaporation of the solvent.

This study is an attempt to use the precipitation method during the preparation of Meloxicam immediate release tablets by wet granulation: Dissolving of Meloxicam with a suitable solvent and adding it to the binder solution.

The tablets obtained with this novel method demonstrated dissolution profiles better than the tablets obtained using the conventional method when compared with the brand product. This method could be of high importance in the preparation of tablets particularly for poorly water-soluble drugs.

The recommendation for the future study is the *in vivo* Bioequivalent study for the meloxicam tablets which are prepared by novel method. Another recommendation is novel method used to prepare immediate release tablets of other active pharmaceutical ingredients which have poor dissolution rate.

# Evaluation of Efficacy and Safety of Vildagliptin Versus Glimepiride in Type 2 Diabetic Patients Inadequately Controlled on Metformin Monotherapy in Erbil City/ Kurdistan/ Iraq

**Name:** Halmat M. Jaafar

**Degree:** M.Sc.

**Specialty:** Science of Clinical Pharmacy

**Date of the debate:** 27-10-2015

**Supervisor:** Prof. Kassim Al-Shamma

## Abstract

**Background:** Diabetes mellitus is one of the common diseases world widely, despite a lot of classes of antidiabetic drugs, but still a lot of cases are not diagnosed and even most of the diagnosed cases are not controlled. In Kurdistan north of Iraq diabetes is very common might be due to lifestyle, obesity, dietary habit and poor treatment adherence and compliance. Vildagliptin is one of the Dipeptidyl peptidase-4 inhibitors that approved in 2008 in Europe for treating type 2 diabetes mellitus, alone or in combination with other anti-diabetic drugs. Till now no studies have been done on Vildagliptin in Iraq.

**Aim of the study:** To determine the efficacy and safety of Vildagliptin in comparison to Glimepiride in type 2 diabetic patients who are not controlled on Metformin monotherapy.

**Patients and methods:** This study included 50 type 2 diabetic patients, not adequately controlled on Metformin monotherapy (HbA1c between 6.5-9% despite 2000mg/day Metformin). The patients were randomized into two equal groups; Group 1 which include 25 patients, 13 male and 12 female (aged  $54.80 \pm 1.22$  and they received Metformin 1000 mg + Vildagliptin 50 mg as one pill combination twice daily) and Group 2 which include 25 patients, 13 male and 12 female (aged  $53.24 \pm 1.23$  and they received Metformin 1000 mg twice daily + Glimepiride 4mg once daily) for 12 weeks, in a randomized prospective clinical trial, in single diabetic center in Erbil city (Layla Qasim diabetic center). Blood samples from both groups were taken and evaluated for glycemic control, lipid profile, renal and liver function tests and interleukins before and after the treatment. Adverse effects were evaluated in

patients throughout the study.

**Results:** Similar reductions in fasting plasma glucose, postprandial plasma glucose and Glycated

Hemoglobin have been observed in both groups ( $p < 0.001$ ), the reductions were in Vildagliptin group

(-17.02%), (-14.74%) and 0.68%, respectively, and in Glimepiride group were (-16.03%), (-11.48%)

and 0.73% respectively. Significantly better improvement in lipid profile was reported in Vildagliptin

group in comparison to Glimepiride group regarding Total serum cholesterol, Serum triglycerides, Low

density lipoprotein, and High Density Lipoprotein, the changes in lipid profile were in Vildagliptin

group ( $p < 0.001$ ) were (-10.96%), (-13.75%), (-11.47%) and (+2.01%) respectively, and in Glimepiride

group ( $p > 0.05$ ) were (-0.76%), (-2.40%), (-0.03%) and (+0.27%) respectively.

There were significant reduction in interleukin-6 and interleukin-18 in Vildagliptin group ( $p < 0.001$ ), while there were no significant changes in Glimepiride group ( $p > 0.05$ ), where the reduction

in interleukin-6 was (-40.16%) and interleukin-18 was (-14.83%) in Vildagliptin group, while in

Glimepiride group interleukin-6 was not changed and interleukin-18 showed only (-0.39%) reduction.

No significant change ( $p > 0.05$ ) in renal function tests and liver function tests in both groups was

observed during 12 weeks of treatment.

Regarding weight changes there was a significant increase in body mass index in Glimepiride

group ( $p < 0.001$ ) which was (+4.64%) and no significant reduction in Vildagliptin group ( $p > 0.05$ ).

Hypoglycaemia was significantly more pronounced in Glimepiride group were 16 patients suffer at

least one hypoglycemia event during treatment (10 cases of mild hypoglycemia, 4 cases of moderate

hypoglycemia, 2 sever cases reported in Glimepiride group), while just 2 cases of hypoglycemia was

reported in Vildagliptin group (one mild and one moderate, with no severe hypoglycemia). The other

adverse effects (Nasopharyngitis, Dizziness, Upper respiratory tract infection, Cough, Fever, Sweating,

Tremor, Nausea, Diarrhea, Postural hypotension, Headache) were distributed in both groups ranging

from one case to 4 cases.

**Conclusion:** Vildagliptin was as effective as Glimepiride as added on therapy to Metformin, in



treatment of patients with type 2 diabetes mellitus, with lower risks of hypoglycemia and no weight gain, and better improvement of lipid profile and interleukins.

# **Evaluation the Effects of Vitamin D3 as Add on Treatment in Asthmatic Patients in Erbil Governorate/Iraq**

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**Degree:** M.Sc.

**Specialty:** Clinical Pharmacy

**Date of the debate:** 28-10-2015

**Supervisor:** Professor. Kassim Jaliil Al-Shamma

## **Abstract**

### **Background and Objectives:**

Asthma is a chronic respiratory disease characterized by airway inflammation, hyperresponsiveness and reversible obstruction. Studies suggest a link between the increased prevalence of asthma and vitamin D deficiency. This study was designed to determine the levels of vitamin D in the serum of Iraqi asthmatic patients and the effects of adding oral vitamin D3 to conventional asthma treatment to modulate pulmonary functions, asthma control, and inflammatory markers.

### **Patients and Methods:**

This single blinded randomized placebo controlled clinical trial was conducted in Rizgary Teaching Hospital in Erbil city between January 2014 and August 2014 on 40 adult asthmatic patients of both sexes, plus 20 healthy volunteer as a control group. Patients were divided equally into two groups: Group 1 received conventional asthma treatments plus 2000 IU of oral vitamin D3 tablets once daily for 2 months; and Group 2, received the same conventional asthma treatments plus placebo for 2 months. Pulmonary function and asthma control tests were conducted and serum levels of 25-hydroxy vitamin D, calcium, high sensitive C-reactive protein, IL-17A, and IL-10 were measured on both groups before and after treatment.

### **Results:**

Patients in the vitamin D3 group showed a significant improvement in their mean serum vitamin D ( $P<0.001$ ), asthma control test mean scores ( $P<0.001$ ), FEV1% predicted values mean ( $P=0.001$ ), FVC% predicted values mean ( $P=0.003$ ), FEV1/FVC ratio mean ( $P=0.048$ ), and PEF% predicted values mean ( $P<0.001$ ). While patients in the placebo group did not show significant changes. Vitamin D3 supplementation was associated with a significant decrease in mean serum levels of hs-CRP ( $P=0.006$ ), but had no significant effects on serum levels of IL-17A and IL-10. Placebo supplementation was not associated with a significant changes in serum levels of hs-CRP, IL-17A, or IL-10.

### **Conclusions:**

This study indicated a high prevalence of low vitamin D levels among Iraqi asthmatic patients and healthy volunteer, and concluded that vitamin D3 supplementation in asthmatic patients could improve pulmonary functions, asthma control, and decrease inflammation.

# Formulation Development and Evaluation of Orodispersible Tablets of Zolmitriptan

**Name:** Tariq Waece Sadeq

**Degree:** M.Sc.

**Specialty:** Pharmaceutics

**Date of the debate:** 2015

**Supervisor:** Asst. Prof. Yehia Ismail Al Azzawi

## Abstract

Orodispersible tablet bypass first pass metabolism, giving higher dissolution profile and positive patient compliance with ingestion problems. In the present study, orodispersible tablets (ODTs) of potent anti-migraine drugs of Zolmitriptan (2.5mg/tablet) as ODTs were prepared by using direct compression technique, which are acceptable to disintegrate completely in less than 30 seconds. This study was done in order to prepare Zolmitriptan Orodispersible tablet.

The superdisintegrants used were sodium starch glycolate (SSG), Croscarmellose sodium (CCS) and Crospovidone (CP). Mannitol and Avicel PH102 (microcrystalline cellulose) were used as diluents. Sodium saccharin was used as a sweetener; Magnesium stearate was selected as a lubricant and orange flavor as flavoring agent.

The blend of all powder formulations were examined for their flow properties, angle of repose, Carr's Compressibility Index and Hausner's ratio, weight variation, friability, hardness, disintegration, wetting time and water absorption ratio. It was seen that the angle of repose is  $<30^\circ$  assuming excellent flow properties for most formulations. Carr's compressibility index and Hausner's ratio were found to in a values of  $<16$  and  $<1.10$  for Zolmitriptan formulations respectively, ensuring that all the preparations resulted in good mixing, flow ability and compressible characteristics. All prepared formulas have a hardness of  $(2.17 \pm 0.1$  to  $4.42 \pm 0.12$  kg/cm<sup>2</sup>).

The results indicated that all formulas disintegrate within 30 seconds except F9 & F10. On the other hand, among all prepared formulas, containing CP, which was prepared in different concentration showed a significant decrease ( $P < 0.05$ ) in disintegration time (DT) with increasing concentration of CP from 2-6% (w/w). The tablets containing 6% (w/w) CP showed faster disintegration and better dissolution profile.

Based on the results obtained, faster disintegration and dissolution efficiency for formulation (F6) which containing CP 6% (w/w), was selected as optimized

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formula. The wetting and disintegration time for optimized formula (F6) had a  $(10 \pm 1.16)$  sec and of  $(8 \pm 2)$  sec., respectively. With water absorption ratio of about  $(46\% w/w \pm 1.56)$ .

In addition, a comparison was made between the dissolution rate of the optimized formula of prepared orodispersible Zolmitriptan tablets (F6) and Zolmitriptan reference tablet (Zomig® 2.5mg tablet), The result revealed that the prepared orodispersible Zolmitriptan tablets showed faster release rate (more than

99.2% released within 15 min) than the marketed conventional tablets (58% released in 15 minutes) ( $P < 0.05$ ).

The overall results suggest that Zolmitriptan could be prepared as ODTs, and intended as new accepted oral solid dosage form formula.

**Key words:** Direct compression, Zolmitriptan, Orodispersible, Crospovidone, Disintegration.

# Enhancement of the Dissolution Rate of Piroxicam Tablets by Using Hydrotropic Agents

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**Degree:** M.Sc.

**Specialty:** Pharmaceutics

**Date of the debate:** 2015

**Supervisor:** Professor. Alaa A.Abdul-Rasool

## Abstract

Piroxicam is a member of the oxicam group of nonsteroidal anti-inflammatory drugs (NSAIDs). It is used in bones and joints disorder. The problem with this drug is its poor aqueous solubility and dissolution rate in the biological fluid and hence poor bioavailability after oral administration.

Hydrotropic solubilization method was used to improve the dissolution rate of piroxicam tablets by increasing piroxicam solubility. Niacinamide and sodium acetate were

used as hydrotropic agents. Initially the solubility of piroxicam was determined in two types of hydrotropic solutions of each hydrotrope at the concentration of 10 % w/v and 20

% w/v using distilled water as solvent. Highest solubility was obtained in 20 % w/v niacinamide solution. Then mixed hydrotropy method was used and solutions of blend of niacinamide and sodium acetate in 1:1, 2:1 and 3:1 ratios respectively at a fixed concentration (20% w/v) were used to determine the solubility. All the blend solutions produce synergistic enhancement effect on the solubility.

A cost effective blend of niacinamide and sodium acetate in 1:1 ratio was utilized in the formulation of conventional piroxicam tablet that were prepared using direct compression method. Different formulas were prepared by physical mixing of piroxicam with the blend of the niacinamide and sodium acetate in different ratio. Drug excipients and excipients compatibility were studied using FTIR method and all the prepared formulas were evaluated for their physical, chemical properties and in vitro drug release behavior. The best formula F4 (contain piroxicam and the hydrotropes in 1:3 ratio) was used to compare between hydrotropic solubilization method and other solubility enhancement methods like complexation and micellar solubilization that they used in formulas  $\beta$  F6 & SF7 respectively. Also, F4 tablets subjected for stability study.

The FTIR study indicates the absence of any chemical interaction between the drug and the excipients. All the prepared formulas have accepted flow properties, accepted hardness, friability, weight variation, disintegration time and drug content. The dissolution

test of the prepared tablets was done using USP type II apparatus with paddle speed of 50 rpm and 900 ml of 0.1 N HCl (pH 1.2) as dissolution medium at 37  $^{\circ}$ C ( $\pm$  0.5).

After 30 minute there is a significant ( $P < 0.05$ ) improvement in the drug release profile of the prepared tablets F2, F3, F4 and F5 when compared with that of F1 (tablets without hydrotropes)

The drug release profile of F4 tablets was compared with  $\beta$  F6 & SF7 tablets and the

results indicate that hydrotropic solubilization method is superior to complexation and micellar solubilization.

After three month of storing F4 tablets for stability study, the tablets show nosignificant ( $P>0.05$ ) decrease in the drug content with significant ( $P<0.05$ ) change in tablets weight and thickness. The overall results suggest that hydrotropic solubilization method is a promising solubility enhancement method that can be used effectively to enhance the dissolution rate and bioavailability of orally administrated solid dosage form. Comparative bioequivalence study between the prepared piroxicam tablets and piroxicam capsules, orodispersible piroxicam tablets recommended for future work.

# The Efficacy of Some Drugs and Antioxidants in Doxorubicin Induced Heart Failure in Rats

**Name:** Ansam Jalal Aram

**Degree:** M.Sc.

**Specialty:** Pharmacology

**Date of the debate:** 2015

**Supervisor:** Assist. Prof. Ansam N. Al-Hassani

## Abstract

### **Background :**

Heart failure (HF) is a devastating disease that impairs the ability of the heart to respond to physiological demands for increased cardiac output. Thus led to the attempt to evaluate the efficacy of Doxycycline, L- Carnitin, Nebivolol, Rosuvastatin, spironolacton, Zinc, Omega 3,6,9 and the combination of Nebivolol and Omega 3,6,9 in doxorubicin induced Heart Failure.

### **Objective :**

The aims of this study are to assess the ability of Doxycycline, L- Carnitin, Nebivolol, Rosuvastatin, spironolacton, Zinc, Omega 3,6,9 and the combination of Nebivolol and Omega 3,6,9 to attenuate doxorubicin induced Heart Failure in female Albino Rats and to compare among them regarding their ability to cause remarkable structural, biochemical, physiological and histopathological changes that preserve normal cardiac function.

### **Materials and Methods:**

Ninety six female Albino Rats, 8-12 weeks old, weighing 140-200 grams were used in the study. They were divided in to 3 groups. The control group, the Doxorubicin group and the treatment group. All groups were treated for a period of 4 weeks. Mean serum (BNP), (CgA), (TC), (HDL), (LDL), (TG), (UA) levels and (HW/BW) ratio, in addition to the histopathological studies, are the estimated parameters used in this study.

### **Results and Conclusions:**

All drugs used in the treatment group showed a degree of cardioprotection effect against doxorubicin induced cardiotoxicity, as all of them caused a significant reduction in mean serum BNP, CgA , total cholesterol, TG, LDL, and uric acid levels and increment in HDL as compared with Doxo group. While Spironolactone appeared to be inferior in amelioration the parameters that accompanied with cardiac toxicity induced by doxorubicin, than the other drugs in the treatment group. On the other hand, Rosuvastatine and the combination of Nebivolol and Omega 3,6,9 appeared to be the most beneficial in amelioration doxorubicin induced cardiac toxicity.

# Effect of Haemodialysis on Certain Biochemical Parameters in Chronic Renal Failure Patients With or Without Diabetes Mellitus

**Name:** Lany Latif Binyamen

**Degree:** M.Sc.

**Specialty:** Clinical Biochemistry

**Date of the debate:** 2015

**Supervisor:** Assist. Prof. Abdulkadir A.AL-Naqshabandi

## Abstract

**Back ground:** Haemodialysis is a medical procedure to remove fluid and waste products from the blood and to correct electrolyte imbalances. The most common cause of kidney failure is diabetes mellitus. Among the biochemical parameters affected by haemodialysis is carnitine which is ( $\beta$ -hydroxy- $\gamma$ -Ntrimethylaminobutyric acid) and is widely distributed in food from animals source.

**Objectives:** This study was carried out to evaluate certain biochemical parameters including serum total carnitine in chronic renal failure patients managed with haemodialysis and to see the impact of diabetes on those patients. Patients and methods: This study includes fifty seven (57) participants, seventeen (17) chronic renal failure with diabetes, sixteen (16) chronic renal failure without diabetes, fourteen (14) diabetic patients and ten (10) healthy persons of same age groups served as control group.

**Results:** The results showed effective improvements in the renal function tests in both chronic renal failure patients with and without diabetes mellitus after haemodialysis respectively; in terms of decreased; urea ( $87.3\pm 34.2$ ), ( $74.4\pm 23.9$ ), creatinine ( $3.3\pm 1.0$ ), ( $3.65\pm 1.2$ ), and increased creatinine clearance ( $19.7\pm 8.9$ ), ( $20.2\pm 5.9$ ). Chronic renal failure patients without diabetes showed significant high serum level of total carnitine after haemodialysis compared with corresponding patients with diabetes ( $39.56\pm 4.9$ ), ( $53.94\pm 4.9$ ).

**Conclusion:** It was concluded that the significant favorable effects of haemodialysis on the renal function, liver function and serum total carnitine levels were related to the fact that haemodialysis process results in removal of waste products, toxic metabolites and small molecular sized particles from the body.



**Name:**

**Degree:** M.Sc.

**Specialty:**

**Date of the debate:**

**Supervisor:**