ABSTRACTS

ESPET 53RD ANNUAL CONFERENCE, APRIL 13TH 2013
BRITISH UNIVERSITY IN EGYPT (BUE)

EGYPTIAN JOURNAL OF BASIC AND CLINICAL PHARMACOLOGY
EJBCP

Editor -in- Chief
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Abstracts of the General Lectures

L 1. Important aspects in the treatment of Hepatitis C infections

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L 2. Medical co-morbidities of Obesity

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The prevalence and severity of obesity is increasing allover the world. In Egypt, the prevalence of overweight / obesity % is about 43 for males and 41 for females. Both BMI and a measure of fat distribution (waist/hip ratio) are important for calculation of obesity comorbidities which are many (The first three letters in diet are DIE). The metabolic syndrome is a variably defined aggregate of disorders related to: central obesity, insulin resistance, diabetes type 2, hyperlipidemia, hypertension and a recently added hepatic component NAFLD.

The central and visceral adipose tissues are not inert fat, but act as endocrine organ, leading to lipotoxicity of metabolic syndrome, through the production of adipocytokines, leading to diabetes, CVD and NAFLD. The prevalence of NAFLD and NASH is highest in obese and diabetic patients. Pediatric NAFLD and NASH also increase with the increase in obesity. The spectrum of NAFLD and NASH includes steatosis, steatohepatitis, fibrosis, cirrhosis and HCC can also follow.

The prevalence of chronic hepatitis C in Egypt is very high (about 15 %).The presence and severity of hepatic steatosis associating chronic hepatitis C correlates with:

- Stage of the hepatic fibrosis and marker of progressive liver disease
- Virologic response to anti-HCV therapy

Hepatic steatosis is a potential predictor of the severity of diabetic dyslipidemia; NAFLD may be not only a marker but also an early mediator of atherosclerosis. Among men with diabetes, the risk of NAFLD and HCC is doubled. Cancers of the colon, breast, endometrium, kidney, and esophagus are solidly associated with obesity; a link to prostate cancer is controversial.

There is a 50–60% increase in cancer mortality among persons with BMI exceeding 40 kg/m^2

The link between obesity, T2D, and cancer is related to insulin resistance, hyperinsulinemia, and increased levels of IGF1, as well as augmented levels of steroid and peptide hormones and inflammatory markers.

Finally Obesity, metabolic syndrome and diabetes therapeutic strategies are highlighted.

L 3. Novel formula of Iron Based Nanocomposites for Rapid and Efficient Treatment of Iron Deficiency Anemia*

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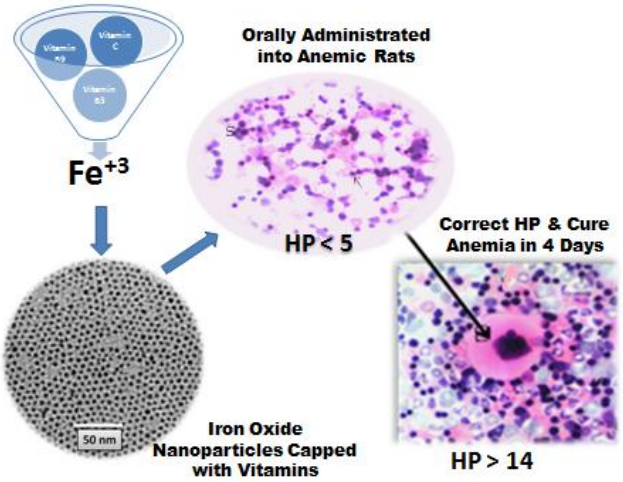
New formulae of Iron oxides nanoparticles capped with a mixture of multivitamins such as folic acid, Nicotinic acid (vitamin B9) and Ascorbic acid (vitamin C) has been developed for the rapid and efficient treatment of life threatening iron-deficiency anemia.

We found that a small single dose of iron oxides-multivitamin nanocomposite (as low as 25 mg elemental iron per dose) is sufficient to increase the hemoglobin level from 4.4 g/dl up to 14.6 g/dl within only four days of administration. We found that multivitamins, which used in this nanocomposite enhances iron absorption significantly and elevated the concentration of hemoglobin. We developed two dosage forms of Iron nanocomposites; gel capsules and aqueous solution for oral administration. Our animal trials studies revealed that introducing single dose of Iron 0xide-vitamin nanocomposites containing 2.57 mg elemental iron per kg rat body weight (equal to 25 mg in human) is sufficient to correct the hemoglobin level and cure Anemia via oral administration.

Our toxicity studies reveal that the LD50 of our new iron nanocomposite is 1425.3 mg/kg rat body weight. This means that the LD50 of nanosized iron nanocomposites in standard human (60 kg weight) is 13,854 mg. Thus, the single dose required for rapid treatment of iron deficiency anemia is 554 times less than the LD50 in human.

No obvious sight of toxicity has been detected on hematological, biochemistry or histopathology studies. Moreover, the histopathology study of the bone-marrow suggested that the used iron oxides –vitamin nanocomposites increased the number of the RBCs precursors which stimulated the bone-marrow to produce more RBCS.



***** Patent pending, the application number EG 371-2013

L 4. Interactive Computer Simulated Practical Pharmacology

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The use of computer in education is growing, increasingly widespread and became an essential requirement for education quality. Computer assisted learning is interesting to students and best suited for them to acquire and understand the knowledge and also easier for the lecturer to deliver that knowledge. There is an obvious trend toward simulation of practical experiments, particularly those wasting animals. There is no doubt that simulation saves animals, time as well as other financial resources. Although, there are many simulation programs for some pharmacological experiments, we have designed new software to simulate in vitro experiments which are currently involved in practical pharmacology syllabus for undergraduate students of Faculty of Pharmacy, Cairo University. This software is called Interactive Computer Simulated Practical Pharmacology (ICSPP). ICSPP does not depend on a database storing figures for different responses, as it is designed to be interactive so that gives variable responses through mathematical equations that take into account; nature, concentration, dose of added drug as well as presence or absence of another drug on the isolated preparation that may affect the drug response. ICSPP also gives the possibility for coding names or concentrations of drugs allowing a coding for practical exams. In addition, it records potential procedural mistakes made by students, so that staff members can properly assess the student's work. Finally, the software can be modified to simulate other in vitro
dose-response experiments according to the required educational syllabus.

Abstracts of Oral Presentations

O 1. Behavioral and Neurochemical Effects of Repeated Exposure to Low Doses of Bacterial Lipopolysaccharide 'LPS' in Wistar Rats: Reversibility by Imipramine and Pentoxifylline

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Background: Several evidences suggest that acute immune challenge by bacterial lipopolysaccharide (LPS) causes short-term depression-like behavior.

Aim of the study: The present study designed to examine the hypothesis that repeated challenge by low doses of LPS might induce behavioral, neurochemical and TNF-α gene expression changes that are comparable to those induced by chronic mild stress (CMS), an animal model of depression. Additionally, the effects of chronic administration of tricyclic antidepressant, imipramine and anti-TNF-α, pentoxyphylline were investigated.

Methods: Wistar rats were exposed to either repeated LPS (50 μg/kg i.p.) over 2 weeks, CMS protocol for 4 weeks or LPS over 2 weeks then 4 weeks CMS. Two groups of rats were exposed to LPS-then-CMS protocol and treated with either imipramine or pentoxifylline. Rats were examined for behavioral, neurochemical and gene expression changes.

Results: Animals exposed to LPS-then-CMS elaborated depressive-like symptoms with significant increase in both serum corticosterone and TNF-α level compared to saline, LPS and CMS groups Hippocampal kynurenine/tryptophan ratio and TNF-α gene expression showed significant increase in the LPS-then-CMS model compared to saline, LPS or CMS groups. Chronic treatment with imipramine or pentoxifylline significantly reversed behavioral, neurochemical and TNF-α gene expression changes induced by LPS-then-CMS protocol.

Conclusion: This study gives a clue to the neurobiological processes underlying at least subtypes of depressive disorders. It highlights the possible interaction between stress and immune-inflammatory pathways in the pathogenesis of depression and suggests a new animal model of depression that addresses these pathways.

O 2. Molecular mechanisms of PDGF-AA expression induced by The dsRNA-mimetic poly (I:C) and IL-18

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Background: PDGFs particularly A and B have been found in atherosclerotic lesions in high levels compared with normal vessel wall. A number of animal studies suggest a role of PDGF in atherosclerosis. The mechanisms leading to increased PDGF expression in conjunction with atherosclerosis are not known. Previously, it has been reported that IL-18 has a pro-atherogenic character. Furthermore, animal studies support the concept that IL-18 participates in the pathogenesis of atherosclerosis as demonstrated by a reduction in atherosclerosis in IL-18-deficient $ApoE^{-/-}$ mice. Recently, it has been shown that herpes viruses are able to intiate and accelerate atherosclerosis in animal models.

Aim of the study: Elucidation of PDGF-AA production under the influence of IL-18 and the dsRNA-mimetic poly (I:C) [PIC].

Methods: Cell culture: Cultivation of KG1cells.

Western blot analysis: For analysis of p38 MAPK, JNK, IκBα, and β-actin

ELISA: For detection of PDGF-AA levels in cellular supernatant.

EMSA: To evaluate whether the increasing in I□B□ degradation is functionally linked to a rise in DNA binding capacity of NF-κB.

Reporter plasmids and transient transfection of KG1 cells: To evaluate whether the DNA-binding capacity of NF-κB induced by IL-18 and PIC would correlate with an increase in NF-κB-controlled gene expression.

Statistical analysis was performed using the ANOVA test for significance.

Results: PIC and IL-18 have the ability to release PDGF-AA in cellular supernatant. Furthermore, costimulation of KG-1 cells with both IL-18 plus PIC shows an additive effect on PDGF-AA levels in cellular supernatant. Neither p38 nor SAPK/JNK is required for PDGF-AA production by both PIC and IL-18. However, NF-κB is essential for PDGF-AA production by IL-18 and PIC in KG-1 cells.

Conclusion: This study demonstrates that the byproduct of viral replication, dsRNA [poly (I:C)], and IL-18 have the ability to release PDGF-AA in NF-κB-dependent manner. Furthermore, costimulation of KG-1 cells with both IL-18 plus PIC shows an additive effect on PDGF-AA expression which might help to understand the pro-athrogenic character of IL-18 and molecular mechanisms of viral infection-induced atherosclerosis.

O 3. Aqueous extract of propolis has anti-apoptotic effects in radiation induced mucositis in rats

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Background: Intestinal mucositis is a common adverse effect in patients undergoing radiotherapy. The search continues for agents that could protect against the development of intestinal mucositis in such patients. Propolis is a honey bee product which contains many active compounds, such as flavonoids, organic acids, phenols and minerals. Propolis has previously been shown to possess anti-oxidant and anti-inflammatory properties.

Aim of the study: The present study was intended to investigate the anti-apoptotic effect of aqueous propolis extract (AEP) on mucositis induced after total body irradiation.

Methods: Intestinal mucositis was induced in rats by exposure to whole body gamma-irradiation from a Caesium^{-137} source at radiation dose levels of 4, 6, and 8 Gray. Rats were treated orally with AEP (450, 650 and 850 mg/kg) for three days prior to irradiation and for two days after. One day later, rats were sacrificed and segments of small intestine were examined histologically. Intestinal homogenates and serum samples were used to assess relevant parameters for apoptosis and different markers for inflammation and oxidative stress.

Results: Exposure to different degrees of radiation produced dose-dependent extents of intestinal mucositis histologically. Apoptotic changes were associated with an increase in cytosolic calcium, depletion of mitochondrial cytochrome c, B-cell lymphoma-2 and complex I. Inflammation markers (tumor necrosis factor and myeloperoxidase) and indices of tissue damage (serum diamine oxidase and lactate dehydrogenase) were increased. Oxidative stress parameters (reduced glutathione, thiobarbituric acid reactive substance and nitric oxide) were deranged. AEP protect to a large extent against histological changes and counteracted the deranged parameters.

Conclusion: The findings provide supportive evidence for the beneficial anti-apoptotic, anti-inflammatory, and anti-oxidant effects of AEP against intestinal radiation damage.

O 4. Telmisartan, an AT1 receptor blocker and a PPARγ activator, alleviates liver fibrosis induced experimentally by Schistosoma mansoni infection in mice

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Background: Hepatic schistosomiasis is considered to be one of the most prevalent forms of chronic liver diseases in the world due to its complication of liver fibrosis. The demonstration of the pro-fibrogenic role of angiotensin (Ang) II in chronic liver diseases brought up the idea that anti-Ang II agents may be effective in improving hepatic fibrosis by either blocking Ang II type 1 (AT1) receptors or inhibiting the angiotensin converting enzyme. Peroxisome proliferator-activated receptors gamma (PPARγ) activation has been also shown to inhibit hepatic stellate cell (HSC) activation and fibrosis progression.

Aim of the study: The present study has aimed at testing the anti-fibrogenic effects of telmisartan; an AT1 receptor blocker and a PPARγ agonist, alone or combined with praziquantel on acute and chronic stages of liver fibrosis induced by Schistosoma mansoni infection in mice.

Methods: To achieve the aim of the study, treatment with telmisartan (10 mg/kg/day, p.o., for 5 weeks) was initiated at the 10th and 15th weeks post infection to assess the drug efficacy in acute and chronic stages of liver fibrosis, respectively. Praziquantel (500 mg/kg/day, p.o.) was given at the 7th week post infection for 2 consecutive days. Parasitological (hepatomesenteric worm load and oogram pattern), histopathological, morphometric, immunohistochemical (hepatic expressions of matrix metalloproteinase-2; MMP-2 and tissue inhibitor of metalloproteinase-2; TIMP-2), and biochemical (serum transforming growth factor-beta 1; TGF-β1 and liver function tests) studies were performed.

Results: Telmisartan failed to improve the parasitological parameters, while significantly ($P<0.05$) decreased the mean granuloma diameter, area of fibrosis, and serum TGF-β1. Additionally, telmisartan increased MMP-2 and decreased TIMP-2 hepatic expressions. Combined treatment failed to show any additive effects, yet it did not affect the anti-schistosomal activity of praziquantel.

Conclusions: These results suggest potential anti-fibrotic effects of telmisartan in acute and chronic stages of liver fibrosis induced by Schistosoma mansoni infection in mice which could be attributed to blocking the AT1 receptors as well as activating the PPARγ receptors.

O 5. Effect of Moterlokast and/or Irbesartan in Metabolic Syndrome

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Background: Metabolic syndrome (MS) is a worldwide problem that includes obesity, dyslipidemia, hypertension, and insulin resistance. Elucidation of the role of inflammatory and immune mediators in pathogenesis of MS suggests a variety of potential therapies worthy of testing.
Aim of the study: The present work investigated the effect of the interleukine antagonist (monterlokast) and/or angiotensin-2 receptor blocker (irbesartan) in prevention of fructose-induced MS in rats.
Methods: Rats were divided into 9 groups: 1) normal control; 2) high fructose fed (HF) (received 20% fructose) to serve as MS group; 3-5) monterlokast-treated (treated with monterlokast, 5, 10, and 20 mg/kg/day, respectively); 6-8) irbesartan-treated (received irbesartan 15, 30, and 45 mg/kg/day, respectively); 9) monterlokast-irbesartan-treated (co-treated with both monterlokast 5 mg/kg and irbesartan 15 mg/g). Visceral fat weight /body weight ratio, insulin resistance (fasting glucose and insulin level), serum lipid profile, oxidative stress (malondialdehyde (MDA), reduced glutathione (GSH), and catalase), inflammatory parameters (uric acid, C-reactive protein (CRP), and tumor necrosis factor- α (TNF-α)) were measured.
Results: The results showed that monterlokast, irbesartan, and their combination prevented the development of high fructose-induced MS as indicated by significant attenuation in visceral fat/body weight ratio, insulin resistance, and lipid profile. Their protective effect was associated with significant improvement in serum levels of MDA, GSH, catalase, uric acid, CRP, and TNF-α. The combination between monterlokast and irbesartan added no significant benefit over their single use.
Conclusion: These results indicate that monterlokast and irbesartan represent potential therapies in treatment of MS.

O 6. Protective Mechanisms of Thymoquinone on Methotrexate-induced Intestinal Toxicity in Rats

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Background and aim of the study: The objective of this study is to investigate the mechanisms by which the anticancer drug methotrexate (MTX)-induced intestinal damage could be prevented by thymoquinone (TQ), an active ingredient of Nigella sativa.
Methods: TQ (10 mg/kg/day) was given orally for 10 days, and, in independent rat groups, MTX toxicity was induced via a single i.p. dose of 20 mg/kg at day 3 of experiment, with or without TQ pre-treatment.
Results: MTX caused intestinal damage, represented by distortion in normal intestinal histological structure, with significant oxidative stress, exhibited as decrease in reduced glutathione (GSH) concentration and catalase activity, as well as significant increase in malondialdehyde (MDA) level compared to control group. MTX also caused nitrosative stress evident by increased nitric oxide level in intestinal tissue, with up-regulation of inducible nitric oxide synthase (iNOS) expression shown in immunohistochemical staining. In addition, MTX caused inflammatory effects as evident by up-regulation of intestinal necrosis factor-kappa beta (NF-κB) and cyclooxygenase (COX)-2 expressions, which were confirmed by increased intestinal tumor necrosis factor-alpha (TNF-α) level via ELISA. Furthermore, MTX caused apoptotic effect, as it up-regulated intestinal caspase 3 expression. Concomitant TQ significantly reversed MTX-induced intestinal toxic effects as it improved intestinal architecture and significantly reverted all oxidative and nitrosative stress markers tested, as well as inflammatory and apoptotic signs caused by MTX alone.
Conclusion: TQ may possess beneficial intestinal protective effects as an adjuvant co-drug against MTX intestinal toxicity during cancer chemotherapy. TQ protection is conferred via antioxidant, anti-nitrosative, anti-inflammatory and anti-apoptotic mechanisms.

O 7. Immunostimulatoty and antioxidant effect of statins, fenofibrate and triton in infection

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Background: Statins and fibric acid derivatives are the most effective pharmacological agents used to treat hyperlipidemia. Better understanding of various pleiotropic effects of simvastatin and fenofibrate has prompted a new surge of interest in their use to treat or prevent a wide range of chronic and life-threatening disorders.
Aim of the study:, the effects of triton (a hyperlipidemic-inducing agent), simvastatin and fenofibrate on the acquired immunity as well as on the oxidative stress were evaluated. These effects were investigated in presence and absence of infection, to confirm whether these effects were affected by infection or not.
Methods: Male Swiss albino mice were used. Animals were classified into 14 groups. Seven groups were treated with either heat killed E. coli (to induce infection), while the rest were given saline. All groups were then injected by triton in a low or high dose (200 and 400 mg/kg, respectively, three times weekly for 3 weeks). Animals were also injected by 100mg/kg/day of either simvastatin or fenofibrate beginning after the 1st triton injection. The effects of simvastatin and fenofibrate in triton-induced hyperlipidemia on the lipid profile, interferon-gamma (IFN-γ), total immunoglobulins and total antioxidants activity were examined in both non-infected and infected mice.
Results: Triton administration induced a significant rise in the lipid profile (triglycerides, total cholesterol, and LDL), IFN-γ, and total immunoglobulins in immunized (infected) animals as compared to non-immunized (non-infected) animals. On the contrary, it didn't increase the antioxidant activity compared to the saline treated groups (immunized and non-imunized control groups) Moreover, there was a significant increase in IFN-γ, total immunoglobulins and the total antioxidant activity upon treatment with either simvastatin or fenofibrate in non-immunized and immunized hyperlipidemic mice. However, this significant increase was more pronounce in infected animals.
Conclusions: these findings revealed that treatment of hyperlipidemia by either simvastatin or fenofibrate increased the acquired immunity by increasing the level of interferon-γ and total immunoglobulins. In addition, these antihyperlipidemic drugs increased the antioxidant activity during infection.

O 8. Dexamethasone induces the conversion of embryonic pancreatic cells to hepatocyte-like cells

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Background: Transdifferentiation is defined as the direct conversion of one differentiated cell type into another. Usually transdifferentiation occurs in cells originating from adjacent cells in the developing embryo. Transdifferentiation can also be induced experimentally by overexpressing the expression of 'master switch genes' or a single transcription factor. It is important to study the transdifferentiation state as it will be very useful in designing potential methods for cell therapy.

Aim of the study: The main aim was to investigate the transdifferentiation of embryonic pancreatic cells to hepatocyte-like cells using the synthetic glucocorticoid Dexamethasone (Dex).

Methods: Dorsal pancreatic buds were isolated from day 11.5 embryos and cultured in the absence and presence of Dex. Indirect Immunostaining was done on the tissue cultures. Liver & pancreas cultures were stained for both hepatic and pancreatic markers. Finally, reverse transcriptase polymerase chain reaction (PCR) was carried out to confirm the expression of hepatic markers.

Results: In pancreatic buds treated with Dex, epithelial branching was inhibited and the appearance of hepatocyte-like cells was induced. By immunostaining we observed an increase in the expression of some hepatic markers (e.g.:transferrin (TFN), Alpha-1- antitrypsin (α-1at) and Cyp2E1) and reduction in pancreatic markers(e.g. : insulin and glucagon) in Dex-treated tissues. However, amylase was expressed at similar level to control tissues but with different distribution. Finally by Reverse transcriptase polymerase chain reaction (PCR) we confirmed the hepatic markers expression increase in the pancreatic cultured tissues.

Conclusion: The present demonstrated that Dex treatment of pancreatic buds induced morphological changes from pancreas to hepatocyte-like cells probably due to the transdifferentiation process. It was also shown that pancreatic cells expressing liver markers AFP, TFN, GS and CPS after Dex treatment while reducing the expression of insulin and glucagon.

O 9. Importance of Time Dimension: Reconsideration of Chronopharmacology

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Chronopharmacology is the investigative science that elucidates the biological rhythm dependencies of medication, i.e. it concerned with the variations in the pharmacological actions of various drugs over a biological timings and endogenous periodicities. Chronopharmacology is further subdivided into chronotherapy, chronopharmacokinetics and Chronotoxity. Most prescribers are currently more concerned with "what" to prescribe rather than "when" to prescribe. There is convincing scientific work to indicate that more attention should be given to the timing of drug administration. The goal of chronotherapeutics is to optimize the efficacy and reduce the adverse effects by timing the drug to match rhythms of the disease. This concept is based on observation that there are interdependent relationship between the peak-to through rhythmic activity in the disease and risk factors, pharmacodynamics and pharmacokinetics of different drugs. There are extensive studies to develop and improve various technologies such as time-controlled formulas, pulsed and programmed drug delivery devices……etc. Application of these technologies will be expected to provide much benefit in many diseases, regarding that our entire body is in an interactive state with time.

Keywords: Chronopharmacology, chronotherapy, chronopharmacokinetics, Chronotoxity, Chronobiology

Abstracts of Poster Presentations

P 1. Antiulcer activity of mirtazapine, escitalopram and venalfaxine on oxidant and antioxidant parameters in stomach tissue of depressed rats

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Aim of the study: This study was performed to evaluate the gastroprotective effects of commonly used antidepressants in rat model of depression**.**
Methods: For the induction of depression, each rat in the experimental group was injected with clonidine intraperitoneally (0.8 mg/kg). After the confirmation of depression, groups were treated with the drugs for 30 days. Group 1: received saline and serve as normal control. Group 2: receive saline and serve as depressive control. Group 3,4 and 5: received mirtazapin (10 mg/kg), escitalopram (20 mg/kg) and venalfaxine (30 mg/kg) respectively. Group 6: received ranitidine (50 mg/kg). On day 30, gastric ulcer was induced using indomethacin (20 mg/kg) in all groups except the normal group. After 4 hours, animals were sacrificed, stomachs removed and ulcer scores were determined and reduced glutathione (GSH), malondialdehyde (MDA), nitric oxide (NO), tumor necrosis factor alpha (TNF-alpha) and interleukin 10 IL-10) levels were measured in the stomach homogenates.
Results: In the behavioral despair test (also known as the forced swim test), mirtazapin (10 mg/kg), escitalopram (20 mg/kg) and venalfaxine (30 mg/kg) enhanced the mobility of rats. Pretreatment with all drugs produced significant reduction in gastric ulcer number and severity and a reduction in the malondialdehyde levels and serum tumor necrosis factor (TNFα). However, there was a significant increase in gastric reduced glutathione, nitric oxide and IL-10 levels.
Conclusion: We concluded that tested antidepressants have antiulcer effects, and that these occur by a mechanism that involves activation of antioxidant parameters and inhibition of some toxic oxidant parameters as well as the modulation of inflammatory markers.
Key words: antidepressants, forced swimming test, ranitidine, indomethacin-induced ulcer, oxidative stress.
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P 2. Role of ursodeoxycholic acid in prevention of Liver injury caused by Ceftriaxone in Albino Rats

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Background and objective: Ceftriaxone causes partial damage in the liver as a result of transient elevation in some biochemical parameters and liver injury appears after 9–11 days. In this study, our aim was to investigate the role of Ursodeoxycholic acid (UDCA) in prevention of hepatotoxic effect and biochemical alterations induced by ceftriaxone in rats.

Methods: Rats were divided into 6 groups (control, UDCA, ceftriaxone 180 mg/kg, ceftriaxone 360 mg/kg, UDCA + ceftriaxone 180 mg/kg and UDCA + ceftriaxone 360 mg/kg). Ceftriaxone was injected intraperitoneally and UDCA was given orally daily for four consecutive weeks. Blood and liver samples were collected for quantitative determination of some biochemical parameters and histopathological examinations.

Results: Treatment of animals with UDCA and ceftriaxone resulted in a significant decrease in the elevated liver enzymes; alanine aminotransferase, aspartate aminotransferase, as well as total bilirubin level. In addition, UDCA significantly decreased the elevated nitric oxide, malondialdehyde content and significantly elevated glutathione content.

Conclusion: The present data suggest that UDCA acts as an effective hepatoprotective agent against liver dysfunction caused by ceftriaxone and this effect might be related to its antioxidant properties.

Key words: Ceftriaxone, Ursodeoxycholic acid, Hepatotoxicity, Liver.

P 3. Diacerein: a potential therapy for insulin resistance

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Background: Insulin resistance (IR) is a worldwide problem that plays a pivotal role in the pathophysiology of the most common human diseases including diabetes mellitus and cardiovascular diseases. The subclinical systemic inflammatory status is a central pathogenic factor associated with IR.

Aim of the study: This study investigated the effect of the anti-inflammatory interleukien-1(IL-1) inhibitor, diacerein, on high fructose-induced IR in rats.

Methods: Adult male Wistar rats allocated into 6 groups and treated for 6 weeks as follow: normal control, high fructose-fed (FF), FF plus diacerein 5, 10 and 50mg/kg/day, respectively, and FF plus metformin to serve as metformin control group. Body weight, visceral fat weight index (visceral fat weight (g)/100 g body weight ratio), insulin resistance indices (fasting blood glucose, fasting serum insulin and homeostasis model assessment of insulin resistance (HOMA-IR)), serum levels of lipids (triglyceride (TG), and high density lipoprotein (HDL)), oxidative stress (malondialdehyde (MDA), reduced glutathione (GSH) and catalase), uric acid, and tumor necrosis factor- α (TNF-α) were measured.

Results: Diacerein in 50 mg/kg/day prevented high fructose-induced IR indicated by significant decrease in IR indices. The protective effect of diacerein was associated with significant attenuation in oxidative stress as well as significant decrease in serum levels of uric acid and TNF-α. Interestingly, it decreased body weight and visceral fat index.

Conclusion: Our results indicate diacerein prevented high fructose-induced IR possibly via antioxidant and anti-inflammatory effects. The beneficial effect of diacerein suggests that it might be a potential therapy for IR.

P 4. Effect of Atorvastatin on Phenytoin- Induced Osteoporosis in Adult Albino Rat, a Pharmacological, Light and Electron Microscopic Study

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Background: Phenytoin (PHT), as one of antiepileptic drugs (AEDs), might affect bone structure and mineralization. Epileptic patients, who take AEDs, are at increased risk for falls and fractures. Therefore, there is a great need to a new approach to increase bone health in these patients.
Aim of the work: To weigh up if statins could prevent bone loss associated with antiepileptic drugs or not.
Methods: Thirty male adult albino rats were divided into five equal groups. Animals, receiving daily treatment by gastric gavage for 5 weeks, were classified as following: group I (control group), group II in which phenytoin was given as 20mg/kg b. wt, then 3 groups which received phenytoin as in group II with atorvastatin 5 mg/kg b. wt (group III), 10 mg/kg b. wt (group IV), 20 mg/kg b. wt (group V). Biochemical assays, bone minerals, both light (LM) and scanning electron microscope (SME), morphometric and statistical studies were done.
Results: The present work demonstrated that atorvastatin in a dose-dependent manner significantly ($P<0.001$) prevented the decrease in serum and bone calcium and phosphorus and bone specific alkaline phosphatase that were associated with phenytoin administration. There was also a graded improvement in either osteocalcin (a marker for osteoblastic activity) or TRAP (a marker for osteoclastic activity). Moreover, atorvastatin significantly inhibited the loss in bone weight, volume and density. By LM and SEM examination, atorvastatin showed a gradual improvement of tibia bone with higher doses as there were a significant increase ($P<0.05$) in trabecular and cortical bone thickness and a significant decrease ($P<0.05$) in osteoclast numbers per area of bone surface in the metaphysis, as well as, improving the growth of epiphyseal plate, compared to phenytoin-treated group.
Conclusion: Atorvastatin could be considered as a beneficial drug used for treatment of osteoporosis in epileptic patient using phenytoin.
Keywords: phenytoin; osteoporosis; atorvastatin; scanning electron microscope; rat.
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P 5. Protective effect of hydrogen sulfide against cold restraint stress-induced gastric mucosal injury in rats

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Background: Hydrogen sulfide (H_2S) is an endogenous gaseous mediator plays a potential role in modulating gastric inflammatory responses. However, there is a controversy regarding its putative protective role and diversity actions in gastric ulcer

Aim of the study: The present study aimed to evaluate the role of the exogenously released and endogenously synthesized H_2S on cold restraint stress (CRS)-induced oxidative gastric damage in rats.

Methods: Rats were restrained, and maintained at 4°C for 3h. The H_2S donor, sodium hydrosulfide (NaHS) (60 µmol/kg) was injected intraperitoneally (i.p.) before CRS.

Results: Our results showed that NaHS significantly attenuated ulcer index, free and total acid output, and pepsin activity in gastric juice in addition to gastric mucosal carbonyl content. This was accompanied by increases in gastric juice pH and mucin concentration along with gastric mucosal reduced glutathione (GSH) content and catalase (CAT) activity. NaHS preadministration reduced the serum tumor necrosis factor (TNF-α) compared to CRS-non-treated. Moreover, NaHS preadministration significantly attenuated the inflammatory and the deleterious effects of CRS on gastric mucosa. Pretreatment with the inhibitor of the H_2S- synthesizing enzyme cystathionine gamma lyase (CSE), beta-cyano-L-alanine (BCA, 50 mg/kg, i.p.) reduced the gastroprotection afforded by the endogenous H_2S. The protective effects of H_2S were confirmed by gastric histopathological examination.

Conclusion: Our results provide important evidence that while the exogenous H_2S effectively ameliorated stress-associated gastric mucosa ulceration, blockade of the endogenously released gastric H_2S exacerbates the ulcer lesion. This gastroprotectionis probably attributed to its anti-oxidant, anti-inflammatory effects and increased mucin level.

P 6. Vascular, renal and placental effects of thymoquinone in preeclampsia rat model

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Background: preeclampsia (PE) is due to many factors and affects many organs, despite improvements in the diagnosis and management of PE, severe complications can occur in both the mother and the foetus. The initiating event in PE has been postulated to involve reduced placental perfusion which leads to widespread dysfunction of the maternal vascular endothelium. While the mechanisms are not clear, they are likely to involve a delicate balance of vasodilators such as NO and prostacylin and vasoconstrictors of which the potent vasoactive peptide, endothelin may play an important role. Placental ischemia, results in increased synthesis of tumor necrosis factor-alpha, interleukin-6 and thromboxane. Elevations in these factors are proposed to result in endothelial dysfunction by decreases in bioavailable NO and increased reactive oxygen species (ROS), which in turn results in altered renal function, increased total peripheral resistance and ultimately hypertension.

Aim of the study: The aim of this work was to investigate the vascular, renal and placental effect of TQ on PE induced by LNAME in pregnant rats.

Methods: Females rats were divided into five groups, non pregnant, pregnant control, pregnant treated with TQ, pregnant treated with LNAME, pregnant treated with TQ and LNAME.

Results: PE produced worsening in the maternal BP and HR, decrease in maternal, renal weight, increase in urinary protein and creatinine, serum uric acid, BUN and creatinine levels, decrease in urine volume and creatinine clearance .. Also, PE produced decrease in placental and foetal weights. In addition, PE increased renal and placental TBARS contents and decreased renal and placental NO contents compared to pregnant control group. Furthermore, PE decreased renal and placental SOD and GST activities as compared to pregnant control group. Finally, PE produced hyalinizations in the trophoblasts and trophospongium with ischaemia in the labyrinth of placenta as regarding to the histopathological alterations, while, treatment by TQ, improved all previous parameters.

Conclusion: TQ produced previous beneficial effects on preeclamptic female rats since it had cardiovascular-, reno- and placental- protecting effects. Antioxidant action had been reported to play an important role in these protecting effects.

P 7. The protective effect of sarpogrelate in high fructose – induced MS

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Background: Metabolic syndrome (MS) contributes greatly to development of cardiovascular diseases and type 2 diabetes mellitus. There are clinical and epidemiological evidence suggesting an association between the progressive development of metabolic syndrome and high consumption of fructose. MS patients usually have elevations in fibrinogen and other coagulation factors leading to prothrombotic disorders. Sarpogrelate is a (5-HT2A) antagonist that inhibits platelet aggregation, vasoconstriction, and vascular smooth muscle proliferation.
Aim of the study: The present study investigated the effect of sarpogrelate, alone or in combination with pioglotazone (as well known insulin sensitizer) on metabolic disorders in high fructose-induced MS in rats.
Methods: Wistar rats allocated into 5 groups and treated for 6 weeks as follow: normal control, high fructose-fed (FF), FF plus sarpogrelate (30mg/kg/day), FF plus pioglotazon to serve as control group (10mg/kg/day), FF plus sarpogrelate and pioglotazon**.** Body weight, visceral fat, liver index, insulin resistance (IR) indices (fasting glucose, fasting insulin and HOMA-IR), oxidative stress parameters (MDA and catalase), serum lipid profile (TG, and HDL) were measured.
Results: Sarpogrelate in 30 mg/kg/day prevented high fructose-induced MS indicated by significant decrease in IR indices, decreased body weight and visceral fat index, and improved lipid profile. The protective effect of sarpogrelate was associated with significant attenuation in oxidative stress.
Conclusion: These results indicate that sarpogrelate might be a protective drug for MS induced by high-fructose diet.

P 8. Melatonin Protects Against Diazinon-Induced Brain Toxicity In Rats

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Background: Diazinon (DZ) is an organophosphorous pesticide with a prominent toxicity on many body organs. Multiple mechanisms contribute to diazinon-induced neurodevelopmental abnormalities including inhibition of cholinesterase and consequent cholinergic hyperstimulation. The toxicity of diazinon is mostly mediated via the formation of reactive oxygen species. On the other hand, melatonin (MT) is a pineal hormone with a well-known potent antioxidant activity. Moreover, it affects some behavioral processes.

Aim of the study: The study was performed to investigate the possible modulatory effects of Melatonin on Diazinon-induced brain toxicity and behavioural changes in rats.

Methods: To achieve the previously mentioned goals of the study, brain MDA, TNF-α contents, brain glutathione-peroxidase activities in addition to brain monoamines were measured. Behavioral tests namely the elevated plus maze and open field tests were also performed.

Results: Results showed that DZ- induced oxidative stress, and inflammation in brain tissues observed as elevation in brain MDA and TNF-α contents in addition to reduction in brain glutathione-peroxidase activities. Diazinon-induced behavioral changes in the rat brain were observed as increase in anxiety behavior evidenced by changing parameters measured in elevated plus maze and open field tests. Investigating the underlining causes of these behavioral changes revealed that DZ changed the brain monoamines contents of nor-epinephrine; dopamine, and serotonin. Co-administration of MT significantly ameliorated all the above measured behavioral and biochemical parameters.

Conclusion: The present study showed that Melatonin can offer significant protection against the deleterious effects of Diazinon in rat brain and ameliorate Diazinon-induced anxiety behaviour in rats.

P 9. L-arginine reduces colonic damage in acetic acid-induced ulcerative colitis via modulation of NF-κB in rats

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Background: The transcription factor, nuclear factor-κB (NF-κB) is a key inducer of inducible nitric oxide synthase (iNOS) gene expression. The role of NF-κB in inflammatory bowel (IBD) disease seems to be controversial and a matter of debate. NF-κB is a key regulator relevant to the pathogenesis of IBD, being activated markedly in IBD and in turn promote the expression of various proinflammatory genes (Atreya et al., 2008). Furthermore, NF-κB activation was demonstrated both in macrophages and epithelial cells of biopsy specimens from inflamed mucosa (Rogler et al., 1998; Schreiber et al., 1998) resulting in high level of expression of iNOS (Singer et al., 1996) and excessive production of NO (Perner et al., 2002). Conversely, NF-κB simultaneously stimulates the expression of different protective molecules that inhibit inflammatory responses (extensively reviewed in (Sartor, 2006). Therefore NF-κB appears as a very promising target for therapeutic intervention in IBD.

Aim of the study: The aim of the present study is to investigate the potential protective effect of L-arginine (NO precursor) and aminoguanidine (iNOS inhibitor) against acetic acid (AA) -induced ulcerative colitis in rats., as well as the elucidate the molecular mechanisms regarding the modulatory effect of L-arginine on NF-κB on the inflammatory effect of AA- induced UC in rats.

Methods: Ulcerative colitis (UC) was induced by intra-rectal inoculation of rats with 4% acetic acid for 3 consecutive days. The effect of L-arginine and aminoguanidine on nitric oxide (NO) levels was assessed by Greiss assay. NF-κB protein expression was also investigated by immunohistochemistry (IHC).

Results: Intra-rectal acetic acid caused a significant increase in body weight loss and colon weights. L-arginine at 100 mg/day for 7 days prior to induction of colitis diminished the changes in both body weight loss and colon weight. Moreover, L-arginine attenuated the colonic tissues macroscopic and microscopic damage induced by acetic acid. In addition, i.p. aminoguanidine 100 mg/Kg administred during and after induction of colitis recovered the colonic ulcerative lesion induced by acetic acid. The probable modulatory effect of L-arginine and aminoguanidine on the expression of the nuclear factor-kappa B (NF-κB) in the colon tissues, evaluated by IHC, was dependent on dose and duration of administration.

Conclusion: Our results suggested that L-arginine treatment can reduce the inflammation associated with UC as confirmed with histopathological investigations. L-arginine inhibited the acetic acid-induced UC though NF-κB pathway.

P 10. Impact of Lamotrigine on Epileptogenesis and Cardiovascular Risk Markers in a Rat Model of kindling seizures

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Background: Enzyme -inducing antiepileptic drugs (AED) and epilepsy itself might be associated with increased vascular risk over time.

Aim of the study: We sought to determine whether non-enzyme-inducing AED lamotrigine (LTG) has different effects on markers of vascular risk in pentylepentetrazol (PTZ) kindling seizures.

Methods: 4 groups of rats were used. Vehicle control group; PTZ group (alternate day PTZ, 30mg/kg, i.p); LTG alone group (20 mg/kg/day p.o.) and LTG with alternate day PTZ group. The study period was 5 weeks. Serum lipid profile and levels of total homocysteine (tHcy), malondialdehyde (MDA) and glutathione (GH) were measured. Endothelial function studies and histopathological examinations of the brain, aorta, heart and coronaries were conducted.

Results: Serum total cholesterol (TC), triglyceride(TG), low-density lipoprotein (LDL), tHcy, MDA and GH levels, , were significantly higher in PTZ group than control group. A decrease in high-density lipoprotein (HDL) with high atherosclerotic index was demonstrated. The administration of LTG in PTZ treated rats improved the PTZ-kindled seizures with a significant decrease in TC, TG and LDL-C, MDA and increase in HDL–C and GH level. Contrarily, no beneficial effect of LTG on tHcy levels was found. LTG improved endothelium dysfunction. LTG alone decrease all serum lipid profile, MDA, and GH but increase MDA, serum tHcy and decrease GH in the tissues. Histopathologic examination revealed that LTG has a neuro and cardiovascular protective effects as indicated by decreased neurodegeneration and atherosclerosis of aorta and coronaries.

Conclusion: LTG produces a significant improvement in vascular risk markers with better seizures control in this rat model of kindling seizures.

Keywords: Antiepileptic drugs, lamotrigine, markers of vascular risk, kindling seizures, homocysteine.

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P 11. Fenofibrate a Peroxisome Proliferator Activated Receptor - α Agonist Pretreatment Ameliorates Concanavalin A-Induced hepatitis in Rats

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Background: Peroxisome Proliferator Activated Receptor α (PPAR- α) are physiologically highly expressed by hepatocytes, where they play a pivotal anti-inflammatory and metabolic role. The decreased expression and functional activity of PPARα in hepatocytes during hepatitis C virus infection may contribute to the pathogenesis of the disease in humans.

Aim of the study: Evaluating the effects of PPARα activation with fenofibrate (FF) on liver inflammation, fibrosis and portal pressure (PP) in concanavalin A (conA)-induced hepatitis in rats.

Methods: The rats were randomly assigned to 3 groups; control group (received 1ml saline iv/wk), con A group (received 20mg/kg iv/wk) and Con A with FF (100 mg/kg/day p.o) group. The study was performed in 8 weeks. Measurement of PP was performed by the end of the 8th week. Blood samples and livers were collected by the end of the 1st , 2nd , 4th and 8th injections of Con A for biochemical, histopathological and immunohistochemistry studies for α-smooth muscle actin (α SMA).

Results: FF group had a significantly lower PP (-88%) than con A group. In addition there is a significant decrease of serum ALT and AST with significant reduction of hepatic, TNF-α and MDA compared to con A group. Histopathological examination revealed that pretreatment with FF significantly suppresses early inflammation, reduced αSMA, and hepatocytes apoptosis induced by Con A, thereby preventing the progression of chronic liver injury.

Conclusions: PPARα activation significantly reduced PP, liver inflammation and fibrosis, suggesting that it may represent a new therapeutic strategy for hepatitis and its complications.

Key words: PPARα; fenofibrate; concanavalin A; portal pressure; Malondialdehyde; tumor necrosis factor alpha.

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P 12. Amelioration of high fat diet induced Non-alcoholic steatohepattis and insulin resistance by bupropion in rats via reduction of TNF-alpha

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Background: Depression has long been recognized to be associated with a number of chronic medical conditions; liver disease is one of them. At the same time, depression can influence the progression of nonalcoholic fatty liver disease (NAFLD).
Aim of the study: The present study aimed to investigate the effect of bupropion to ameliorate the hepatic changes, insulin resistance and some cardiovascular changes induced by the HFD and its possible underlying mechanism
Methods: The rats were divided at random into three groups: the Normal group was fed standard laboratory chow diet, the HFD group was fed HFD only for 15 weeks, and the bupropion treated group was fed HF diet for 15 weeks followed by oral bupropion 50mg/kg for 4 weeks.
Results: Bupropion treatment significantly improved serum lipid, liver enzyme, and HOMA-IR. Although it has significant effect on the intima/ media ratio, there was no significant effect on endothelial dysfunction on isolated aortic ring. Histopathological examination supported the role of buporopion in alleviating diet induced NASH. Additionally, bupropion significantly decreased liver TNF-α.
Conclusion: The findings of the present study highlighted the role played by the proinflammatory cytokine TNF-α in the pathophysiology of NASH and the associated insulin resistance and endothelial dysfunctions. Bupropion has potential role in improving steatohepatitis, hyperlipidemia, insulin resistance effect that could be through TNF-α inhibition. Since bupropion is well known antidepressant, it will be a candidate drug in treatment of depression in hepatic diseased or metabolic disturbed patients.

P 13. Effect of Ginkgo biloba extract on corticosteroid-induced ocular hypertension in rabbits

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Background: Ginkgo biloba extract (EGb) has attracted interest due to its neuroprotective, potent antioxidant and blood flow regulatory activities. Recently, it has shown possible benefits in normal tension glaucoma.

Aim of the study: To assess the potential effect of standardized extract of EGb (EGb 761) on ocular hypertension induced in rabbits by a single subconjunctival administration of betamethasone (3.5 mg).

Methods: Animals were randomly allocated into 6 groups in which group I served as normal. After ocular hypertension has been established (7 days post induction), rabbits of group II were left untreated while those of groups III and IV were topically treated, once daily, for 7 days with timolol (0.5 %) and EGb 761 (0.05 %), respectively. Groups V and VI received EGb 761 (20 mg/kg; p.o.) and a combination of EGb 761 (20 mg/kg; p.o.) and timolol (0.5 %; topically), once daily for 7 days, respectively. Another group (VII) was also included where EGb 761 (20 mg/kg; p.o.) was prophylactically given for the 2 weeks. Intra-ocular pressure (IOP) was measured throughout the experiment using Schiotz tonometer. Levels of whole blood reduced glutathione (GSH), plasma malondialdehyde (MDA), and aqueous humor total antioxidant capacity (TAC) were estimated. Corneal histopathological changes were also examined.

Results: Levels of IOP and MDA were increased by betamethasone while those of TAC and GSH were decreased, as compared to normal group. Topical EGb 761 and timolol showed similar suppression of the elevated IOP as compared to betamethasone group. EGb 761 improved MDA and TAC levels as compared to betamethasone and timolol groups. Results of oral and topical EGb 761 administration were comparable to each other. EGb 761 improved also the histopathological features of corneal tissue. Prophylactic EGb 761 prevented the elevation of IOP and improved TAC, MDA, GSH levels as compared to betamethasone group. It merits mention that the group that received combined treatment showed the best results.

Conclusion: EGb 761 might represent a potential avenue of therapy for ocular hypertension and adjunctive dietary supplement might be advocated to halt the progress of the disease.

Key words: Ginkgo biloba, betamethasone, timolol, ocular hypertension, antioxidant.

P 14. The Effect of Ibuprofen on Depressive like Behavior Induced by BCG Inoculation in mice: Role of Prostaglandins and Nitric Oxide

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Background: Prostaglandins (PGs) and nitric oxide (NO) may be involved in the pathophysiology of depression. Since NSAIDs decrease PG and NO production, they may have an antidepressant effect.

Aim of the study: Is to explore a possible antidepressant action of ibuprofen in an inflammatory model of depression.

Methods: Depressive like behavior was induced by inoculation of Bacillus Calmette-Guerin (BCG) to mice (10^8 CFU/mouse intraperitoneally) and evaluated using the forced swim test (FST) and the tail suspension test (TST). PGE_2 and NO levels were estimated in the brain.

Results: Mice injected with BCG showed a significant increase in the duration of immobility during FST and the TST and a significant increase in cerebral PGE_2 and NO levels. Fluoxetine administered in drinking water at a dose of (80 mg/l) 5 days before BCG and for 14 more days, resulted in significant decrease in the duration of immobility during FST and TST and in cerebral PGE_2 and NO levels. Both ibuprofen (200 mg/l) and L-NAME (1 gm/l) administered in drinking water 24 hours before BCG and for 14 more days, resulted in significant decrease in the duration of immobility during FST and TST and in cerebral PGE_2 and NO levels, that was comparable to fluoxetine's effect. On the other hand, L-arginine administered at a dose of 1 gm/l in drinking water together with ibuprofen reversed its effect on FST and TST.

Conclusion: These results suggest that NO and PGE_2 play an important role in the depressive like behavior induced by BCG in mice. Ibuprofen may have an antidepressant effect through inhibition of PG and NO production, especially in depression secondary to chronic inflammation.

P 15. Nitric oxide and alpha-2 adrenoceptors are involved in ibuprofen preemptive analgesic effect in postsurgical pain in mice

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Background: Control of post-operative pain is far from satisfactory, though it is a primary concern due to its close ties with clinical outcome. Non-steroidal anti-inflammatory drugs (NSAIDs) remain an important choice. Nitric oxide (NO) plays an important role in the development and maintenance of inflammatory hyperalgesia. NSAIDs were shown to inhibit NO production in different clinical and experimental studies. Monoamines also play a key role in the modulation of nociception at all levels of the neuroaxis

Aim of the study: The aim of the present work is to study the involvement of adrenergic system and NO in the antinociceptive mechanism of ibuprofen in postsurgical pain in mice.

Methods: Postsurgical pain was induced by unilateral surgical incision in the mouse hind paw. Mechanical allodynia was tested by von-Frey filaments. NO levels were estimated in the thoracolumber segment of the spinal cord.

Results: Surgical incision resulted in mechanical allodynia and increased spinal NO levels. Ibuprofen (30 - 300 mg/kg) administered intraperitoneally (i.p.), 30 minutes before the incision, dose-dependently decreased the development of mechanical allodynia and at a dose of 100 mg/kg, it reduced spinal NO level. Administration of ibuprofen (100 mg/kg i.p.) 30 min following surgery, did not significantly reduce mechanical allodynia. While L-NAME (50 mg/kg i.p.) also decreased the development of postsurgical mechanical allodynia, L-Arginine (600 mg/kg i.p.) restored mechanical allodynia in ibuprofen-treated mice. The selective alpha-2 adrenoceptor blocker, yohimbine (4 mg/kg i.p.), administered 30 min before ibuprofen also blocked ibuprofen effect on mechanical allodynia.

Conclusion: These results suggest that both the inhibition of NO synthesis and alpha-2 adrenoceptors are involved in the analgesic activity of ibuprofen in post-surgical pain.

P 16. Estrogens improve the vascular and metabolic alterations in fructose-induced insulin resistant ovariectomized rats

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Background: Insulin resistance is a metabolic disorder that is increasing worldwide and plays a major role in the pathophysiology of the most common human diseases including type 2 DM, hypertension, dyslipidemia and coronary heart disease.

Aim of the study: The present study aimed to test the effects of 17-β estradiol (EST) and genstein (GEN) on some cardiovascular, metabolic, and biochemical changes that associate insulin resistance induced in rats.

Methods: Insulin resistance was induced in both sham-operated and ovariectomized mature female rats by receiving fructose (21% in drinking water for 8 weeks). Ovariectomized insulin-resistant animals were treated subcutaneously with EST (100 µg/kg) or GEN (1 mg/kg) on daily basis for a total period of 3 weeks.

Results: The current study revealed that fructose-induced insulin resistance in both sham-operated and ovariectomized rats decreased the vascular responsiveness of isolated rat aortic rings towards the vasoconstrictor norepinephrine and impaired the vascular responsiveness towards the vasodilator acetylcholine (Ach) without affecting that towards sodium nitroprusside. Induction of insulin resistance was also associated with elevated blood pressure (BP), hyperinsulinaemia, hypertriglyceridaemia, hypercholesterolaemia, increased oxidative stress, and decreased serum level of nitric oxide (NO). Treatment of insulin-resistant ovariectomized rats with either EST or GEN improved the vascular responsiveness of isolated aortic rings towards Ach and succeeded to decrease the elevated BP. Moreover, both EST and GEN decreased the oxidative stress, hypertriglyceridaemia, insulin resistance/compensatory hyperinsulinaemia, and serum low density lipoprotein level. Treatment with EST was found to increase the reduced serum level of NO.

Conclusions: Both EST and GEN showed protective and beneficial effects in insulin-resistant ovariectomized rats as they improve the studied cardiovascular, metabolic and biochemical alterations.

P 17. Gastro-protection of Atorvastatin in Indomethacin-induced Ulcer: Role of Tumor Necrosis Factor-alpha and Prostaglandins

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Background: Using non-steroidal anti-inflammatory drugs as over-the-counter pain-killers may predispose to gastric ulcer as a side effect.
Aim of the study: The objective of this study is to investigate the possible benefit of a common statin used in hyperlipedemic patients; atorvastatin, in ameliorating the ulcerogenic effect of indomethacin, and to explore the possible mechanisms involved.
Methods: Atorvastatin (10 mg/kg/day) was administered orally for 7 days. At day 7, gastric ulcer was induced by a single dose of indomethacin (40 mg/kg i.p.), with or without atorvastatin pre-treatment.
Results: Indomethacin induced gastric ulcer as evident by notable gastric ulceration in histopathological sections compared to normal control. Gastric tissue in rats receiving indomethacin showed significantly higher oxidative stress markers as lipid peroxidation represented by increased malondialdehyde (MDA) content, with significant decrease in gastric tissue nitric oxide (NO) and prostaglandin E2 (PGE2) levels, as well as reduction in catalase and superoxide dismutase antioxidant enzymatic activities. In addition, indomethacin induced inflammatory signs as shown by the significant increase in tumor necrosis factor-alpha (TNF-α) level assessed via ELISA. Pre-administration of atorvastatin significantly decreased ulcer index (16±1) compared to that of indomethacin alone (34±2). In addition, atorvastatin restored normal gastric histological structure and reverted oxidative and inflammatory markers tested.
Conclusion: Atorvastatin confers gastro-protection against indomethacin-induced ulceration via reducing gastric oxidative stress and increasing gastric NO and PGE2 levels, as well as decreasing the inflammatory marker; TNF-α.

P 18. Effect of Nigella sativa and wheat germ oils on scopolamine-induced memory impairment in rats

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Background: Dementia is characterized by a loss of or decline in memory and other cognitive abilities. The most common form of dementia is demonstrated in Alzheimer's disease.

Aim of the study: To investigate the potential effects of Nigella sativa oil (NSO) and wheat germ oil (WGO) on memory impairment induced in rats by a single intraperitoneal injection of scopolamine (16 mg/kg).

Design and methods: Animals were randomly allocated into 5 groups where group I served as normal and group II served as scopolamine-untreated group. The other 3 groups were orally pretreated with NSO (1 ml/kg), WGO (170 mg/kg), and the reference drug, donepezil (10 mg/kg), respectively for 14 consecutive days before scopolamine injection. Cognitive (spatial and non-spatial working memories in the T maze alternation task and object recognition test, respectively) and certain brain biochemical parameters (malondialdehyde (MDA), tumor necrosis factor-alpha (TNF-α), and reduced glutathione (GSH) contents as well as cholinesterase activity) were assessed.

Results: Scopolamine-untreated group showed deficits of spatial and non-spatial working memories in the T maze alternation task and object recognition test, respectively. In addition, scopolamine increased brain MDA and TNF-α contents as well as cholinesterase activity while decreased its GSH content. Prior treatment with either NSO or WGO reversed scopolamine-induced memory impairment in both T maze alternation task and object recognition test. NSO succeeded to decrease the elevated MDA and TNF-α brain contents and increased its GSH content. NSO did not affect the elevated brain cholinesterase activity. WGO, on the other hand, did not affect elevated MDA and TNF-α brain contents while increased its content of GSH. WGO was found to decrease the elevated brain cholinesterase activity.

Conclusions: Memory enhancing effect of NSO might be related to its anti-oxidant and anti-inflammatory activities, while that of WGO might be via its anti-oxidant and anti-cholinesterase properties.

Key words: Nigella sativa oil, wheat germ oil, scopolamine, memory impairment, rats.

P 19. Protective mechanisms of atorvastatin in ameliorating doxorubicin-induced hepato-renal toxicity

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Aim of the study: This study is to investigate the mechanisms by which the anticancer drug doxorubicin (Dox)-induced hepato-renal damage could be prevented by Atorvastatin (Ator), a cholesterol-lowering statin.

Methods: Ator (10 mg/kg for 10 days) was administered orally, and, in independent rat groups, Dox hepato-renal toxicity was induced via a single i.p. dose (15 mg/kg at day 5 of experiment), with or without Ator. Dox caused deterioration in hepato-renal function, as it increased BUN, creatinine, ALT and AST levels compared to control**.**

Results: Dox also caused distortion in normal renal and hepatic histology, with significant oxidative stress, as it decreased GSH concentration and catalase activity and increased malondialdehyde level. In addition, Dox caused nitrosative stress, as it increased nitric oxide level, with down-regulation of eNOS. Furthermore, Dox caused inflammatory effects as shown by up-regulation of hepato-renal NF-κB expression and increment of TNF-α concentration. Dox also caused apoptotic effect, as it up-regulated Bax expression in liver and kidney. Using Ator with Dox restored hepato-renal functions and normal histological structure, as well as reversed oxidative/nitrosative stress markers, inflammatory signs and apoptosis.

Conclusions: These findings suggest Ator as a protective adjuvant against Dox toxicity, via antioxidant, anti-nitrosative, anti-inflammatory and anti-apoptotic mechanisms.

P 20. The Hepatoprotective effect of vanillic acid in thioacetamide induced hepatotoxicity in rats.

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Background: Thioacetamide (TAA) is a hepatotoxin frequently used for experimental purposes which produces centrilobular necrosis after a single dose administration. In spite of the fact that oxidative stress seems to play a very important role in the mechanism of TAA-induced injury,
Aim of the study: The present study was conducted to evaluate the hepatoprotective effect of vanillic acid (VA) one of the major phenolic constituents of vanilla on thioacetamide (TA) induced acute hepatotoxicity in rats in comparison with silymarin.
Methods: group I normal control group **Group 2:** rats were given vanillic acid (200mg/kg, p.o) for 15 days. **Group 3:** rats were given TAA (200 mg/kg/day, i.p) for two consecutive days **Group 4, 5:** rats were given vanillic acid (100mg/kg) and (200mg/kg) p.o. for 15days; and TAA was given in the last 2 days (14^{th}, 15th day). **Group 5:** rats were given silymarin (50 mg/kg p.o.) for 15days; and TAA was given in the last 2 days (14^{th}, 15th day). All rats were sacrificed on the 16th day. The following parameters were estimated: transaminase enzymes ALT, AST, and bilirubin, as liver function tests were estimated in serum. Moreover in the liver homogenate the following parameters were evaluated: Nuclear factor-kappaB, tumor necrosis factor α and nitric oxide as inflammatory markers as well as oxidative stress markers: Malondialdehyde (MDA), reduced glutathione (GSH) content and catalase (CAT) activity. In addition the histopathological examination was evaluated for the degree of hepatic injury.
Results: Rats exposed to TAA showed a significant increase in the activities of hepatocellular enzymes in serum, lipid peroxidation, inflammatory markers and a significant decrease in antioxidant status in liver. These alterations were reversed by VA pretreatment.
Conclusion: VA significantly improved the toxic effects of TAA compared with silymarin the standard hepatoprotectant. The powerful antioxidant together with the anti-inflammatory activities of VA could explain its hepatoprotectant action in the current model. It's greatly recommended to use VA as a natural hepatoprotectant against chemically-induced hepatotoxicities.
Key words: Vanillic acid, thioacetamide, liver function test, anti-inflammatory markers, oxidative stress markers.

P 21. Immunomodulatory Effect of Triton, Simvastatin and Fenofibrate on the Innate Immune Response

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Background: The engulfing capacity of human phagocytes plays an important role in the immune defense of the organism (innate immune response). In the past few years it was noticed that patients receiving simvastatin or fenofibrate therapy may experience reduced infection-associated mortality and morbidity.
Aim of the study: the effect of simvastatin as well as fenofibrate in hyperlipidemia induced by triton WR1339 (in 2 dose levels) on the innate immune response, in presence and absence of infection was evaluated.
Methods: Male Swiss albino mice were treated with either heat killed E. coli or saline. They were then classified into 14 groups. 2 groups were used as control groups (non-infected and infected control). All other mice were injected I.P. by triton in a low or high dose (200 and 400 mg/kg, respectively, 3 times weekly for three weeks) to induce hyperlipidemia. The effect of treatments with either simvastatin (100 mg/kg daily) or fenofibrate (100 mg/kg daily) in hyperlipidemic mice on the phagocytic activity of peritoneal macrophages (as an indicator of the innate immune response) in both normal and immunized mice were investigated.
Results: simvastatin or fenofibrate treatment improved significantly both the elevated lipid profile and the innate immune response even in the presence of infection in triton-induced hyperlipidemia.
Conclusion: this study revealed that triton in low or high dose and treatment of hyperlipidemia with either simvastatin or fenofibrate increased the synthesis and activity of peritoneal macrophages in infected and non-infected mice.

P 22. Thymoquinone blocks lung injury and fibrosis by attenuating bleomycin-induced oxidative stress and activation of nuclear factor Kappa-B in rats.

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Background: Pulmonary fibrosis is one of the most common chronic interstitial lung diseases with high mortality rate after diagnosis and limited successful treatment**.**
Aim of the study: The present study was designed to assess the potential antifibrotic effect of thymoquinone (TQ) and whether TQ can attenuate the severity of oxidative stress and inflammatory response during bleomycin (BLM) induced pulmonary fibrosis.
Methods: Male albino rats were treated intraperitoneal with either BLM (15 mg/kg, 3 times a week for 4 weeks) and/or TQ (5 mg/kg/day, one week before and until the end of the experiment).
Results: BLM significantly increased lung weight and the levels of lactate dehydrogenase, total leucocytic count, total protein and mucin in bronchoalveolar lavage and these effects were significantly ameliorated by TQ treatment. As markers of oxidative stress, BLM caused a significant increase in the levels of lipid peroxides and nitric oxide accompanied with a significant decrease in the antioxidant enzyme activity of superoxide dismutase and glutathione-S-transferase. TQ treatment restored these markers toward normal values. TQ also counteracted the over expression of activated form of nuclear factor kappa-B (NF-κB) in lung tissue that was induced by BLM. Fibrosis was assessed by measuring hydroxyproline content, which increased markedly in the BLM group and significantly reduced by concurrent treatment with TQ. Furthermore, histopathological examination confirmed the antifibrotic effect of TQ.
Conclusions: Collectively these findings indicate that TQ has potential antifibrotic effect beside its antioxidant activity that could be through NF-κB inhibition. Accordingly, TQ might be employed as a therapeutic agent for attenuating pulmonary fibrosis.

P 23. Therapeutic Trial of Intralesional Injection of Mycophenolate Mofetil in Psoriasis Vulgaris: Clinical, Histopathological and Immunohistochemical Evaluation

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Background: Systemically administered mycophenolate mofetil (MMF) has a beneficial effect in psoriasis patients.

Aim of the study: Our purpose was to investigate the efficacy and safety of intralesional MMF in ordinary psoriasis vulgaris and to find out the best regimen of treatment.

Methods: In twelve plaque psoriasis patients, response to different concentrations (3.125, 6.25, 12.5 and 25 mg/ml) of MMF have been objectively evaluated and compared to control (5% dextrose). Patients were divided into two groups, group (A): patients who were injected once every two weeks for six weeks and group (B): patients who were injected once every week. Group B was divided into two subgroups; subgroup (B1): patients who were injected three times at one week interval and subgroup (B2): patients who were injected two times at one week interval. Patients were followed up clinically, histopathologically, and immunohisto-chemically for CD3.

Results: Maximum response to MMF was achieved 8 weeks after initiation of therapy. There was significant reduction of erythema, thickness, scaliness ($P \leq 0.01$) but not surface area ($P = 0.152$) compared to control. Histopathologically, there was significant reduction in scores of parakeratosis, acanthosis, dilatation of papillary vessels and density of dermal mononuclear infiltrate. Immunohistochemical semi-quantitative analysis revealed variable, but in general, obvious degree of reduction in the density of CD3+ cellular infiltrate (i.e. T-cells) at the eighth visit compared to the first visit in all specimens examined. No significant difference could be seen in the efficacy of different concentrations with different regimens. No systemic or local adverse effects were noted apart from mild and transient burning sensation especially with higher concentrations.

Conclusions: Intralesional MMF could be adopted as a safe and effective adjunctive line of treatment especially in localized plaque psoriasis.

P 24. Quercetin attenuates di (2-ethylhexyl) phthalate (DEHP) - Induced reproductive toxicity in male rats

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Background: Di (2-ethylhexyl) phthalate (DEHP) is a phthalic acid ester used as a plasticizer in industry, and known as reproductive toxicant. Quercetin (QU) is natural flavonoid has powerful antioxidant properties.

Aim of the study: This study was planned to demonstrate the testicular toxicity of DEHP in the adult rats and evaluate the potential protective effects of QU against such DEHP–induced testicular toxicity.

Methods: Fifty rats were equally divided into five groups; 1st group was kept as control and given corn oil as a vehicle. In 2nd group, DEHP was orally administered at a dose of 900 mg/kg for 15 consecutive days. In the 3rd group, QU was orally administered at a dose of 90 mg /kg/day as in the 2nd group, while in the 4th group; rats were treated with QU (90mg/kg) 24 hrs before and along with DEHP treatments as in group 2. Rats in the 5th group were treated with QU (30mg/kg) adapting the same pattern of treatment as in the 4th group. Relative testes weight, sperm characteristics, and testicular histological changes were determined. Use ELISA method to measure serum testosterone level. Also, serum total acid phosphatase (TACP) and prostatic acid phosphatase (PACP) activities were determined by colorimetric method. Testicular tissues were used to measure the activities of lactate dehydrogenase isoenzyme C4 (LDH-X), Superoxide Dismutase (SOD) and Catalase (CAT) as well as the contents of Glutathione (GSH) and Malondialdehyde (MDA).

Results: Relative testes weight, sperm motility and count were significantly decreased associated with marked increase in the abnormal sperm head and tail with obvious testicular damage post DEHP treatment. In addition, DEHP intake significantly increased MDA content accompanied with significant decline in the level of (GSH) as well as (CAT), (SOD) and (LDH-X) activities in the testicular tissues. Also, DEHP administration markedly decreased serum testosterone level and (TACP) activity associated with significant increase in the activity of (PACP). These effects of DEHP on sperm parameters, histological changes, hormone levels and biochemical parameters were mitigated by QU treatment.

Conclusion: QU as a nutraceutical may be useful for modulation of DEHP-induced testicular damage.

Keywords: di (2-ethylhexyl) phthalate, Quercetin, sperm parameters and ELISA.

P 25. Appropriateness of antibiotic use at two university hospitals in Egypt

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Background: Many infectious diseases have been brought under control in the 20th century, by improved living conditions, public health measures, vaccinations and antimicrobial agents. Early optimism about the approaching end of all bacterial infections was premature, and in the last two decades there has been an increase in infectious disease morbidity and mortality. In addition, many organisms have developed resistance to antibiotics to which they used to be susceptible, prompting the development of more broad-spectrum—and expensive—agents. With the growing need for broad-spectrum agents, have come reports of inappropriate antimicrobial drug use, which contributes to the development of resistance and wastes resources.

Aim of the study: To evaluate the appropriateness of antibiotic use in patients hospitalized in two University hospitals

Methods: A survey study about antibiotic use at two University Hospitals: Ain Shams a governmental University Hospital and Misr University for Science and Technology (MUST) a private hospital. Ten departments were included in the study from Ain Shams University hospital. All departments in MUST hospital were included in the study. A pre-structured and coded check list was used to collect data about antibiotic therapy of inpatient cases.

Results: Number of patients receiving antibiotics was 348 out of 848 admitted cases. Out of which 145 (42%) prescriptions were appropriate and the remaining 203 (58 %) were inappropriate. Prescriptions were considered inappropriate because of inadequate choice of the drug (53%); errors in doses, intervals or duration (30%); choice of combined drugs (28%). Treatment of community-acquired infections was more inappropriate than nosocomial infections (23% versus 11%; $P < 0.05$). Inappropriate prescription was higher in those with system affected not renal nor hepatic (78%) than those with renal or hepatic disease (22%).

Conclusion: Inappropriateness of antibiotic prescription is still high even in university hospitals and so important issue that need close adherence to guidelines for each situation necessitating prescribing antibiotics not only therapeutic but also prophylactic prescription. Attention should be given to cases with special illnesses needing dose adjustment as hepatic and renal cases.

Key words: Appropriateness, antibiotics use, University Hospitals

P 26. Culture of medication use and drug prescription among medical students

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Background: Drugs have benefits and side effects so it is necessary to be taken in a specific regimen in accurately measured dose otherwise it is toxic and causes more harm.

People may disuse drugs in the form of getting medications of others who told them that they have improved when they had taken those medications. They also may repeat a previous prescription. It is common in some countries to get pharmacist consultation but the case might be worsened because mostly it is a symptomatic treatment without history taking or clinical examination. There are many drugs which may be commonly taken without doctor consultation e.g. analgesics for headache and other minor painful conditions which causes gastritis and may be peptic ulcer on the long run, antibiotic abuse with resultant resistant organisms etc.

Aim of the study: Study aimed to determine practice and attitude towards self medication by medical students and assess their knowledge and practice of drug prescription.

Methods: A cross-sectional study was conducted on a sample of randomly selected medical students from Ain Shams University. A self administered questionnaire was used to collect data about self medication practicing and for each drug category namely antibiotics, analgesics, vitamins, sedatives and herbals. Assessing students experience about the rules to be followed by physicians in writing prescriptions. Also rules of drug supply by the pharmacist. The third item was about prescription of medication by the students, circumstances associated with and their attitude towards prescribing medication before graduation. Ethical requirements in the form of verbal consent were ensured and data was collected using self administered questionnaires. The Chi square tests for qualitative data and t student test and ANOVA test for quantitative data and logistic regression analyses were performed using SPSS V15 to identify associations and differences.

Results: The sample consisted of 66.4% females and 33.6% male medical students. Out of which 58.8% 54.4%, 87.2%, 12%, 28% took antibiotic, vitamins, analgesics, sedatives, herbal products respectively without prescription. Only 1.6% agree with buying drugs via the internet compared to 79.8 said that the internet was not a good source for drugs. As regards the personal behavior towards following any prescription 14.4% always followed properly the prescription compared to 63.3% stated that they always discontinued the drug on improvement 13.6% reported that they always repeated the prescription without medical advice. Also 60% said that they increased the dose without medical advice. As regards the reported side effects 4.8%, 1.6%, 12% as a result of interaction between drugs, increase dose without medical advice and early stopping of treatment respectively.

Conclusion: Self medication and drug prescription are practiced by some undergraduate medical students. Raising the issue of more orientation, and stressing upon those topics in their curriculum is required.

Key words: Culture medication use drug prescription medical students.

P 27. Tamgermanitin, A unique isoferulic acidamide isolated from Myricaria germanica (Tamaricaceae) with potent cytotoxic and apoptotic activity against three different solid tumor cell lines

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Background: Natural products, including plant phenolics provide a major source of chemical diversity that has consistently proven its value for the development of novel drugs for more effective antineoplastic agents.

Aim of the study: Assessment of the cytotoxicity of phenolic components isolated from Myricaria germanica against three different solid tumor cell lines, namely liver (Huh-7), breast (MCF-7), and prostate (PC-3).

Methods: Following column chromatographic fractionation of the leaves extract of M. germanica, 20 compounds (1–20) were isolated. Cytotoxicity assays and viability analysis of the extract, column fractions and isolated phenolics were tested by SRB-U assay. DNA flow-cytometry was used to assess the cell cycle distribution of Huh-7 and MCF-7cell lines. In addition, the determination of caspase-3 and Poly (ADP-ribose) polymerase (PARP) enzyme activities in Huh-7 cell line were estimated using cell free system enzyme assay.

Results: Phytochemical investigation of the extract lead to the isolation and structural elucidation of Tamgermanitin, a unique N-trans-Isoferuloyltyramine, together with the hitherto unknown polyphenolics, 2,4-di-O-galloyl-(α/β)-glucopyranose and kaempferide 3,7-disulphate. In addition, 18 known phenolics were also separated and characterized. The extract, its chromatographic column fractions and the isolated isoferuloyltyramine, Tamgermanetin demonstrated potential cytotoxic effect against Huh-7, MCF-7, and PC-3 cell lines. The IC50's were found to be substantially low with low resistance possibility. Tamgermanitin induced death signal as evidenced by the significant increase in the pre-G apoptotic cell fraction and the elevated caspase-3 activity in Huh-7 cell line. It is noteworthy that it increased the accumulation of cells at G2/M phase. This suggests that Tamgermanitin-induced apoptosis involves interaction with microtubules. In addition to, inhibition of PARP enzyme activity by Tamgermanitin might, at least partly, sensitize tumor cells to death signal. This assumption is supported by the low R-fraction in all tested cell lines.

Conclusion: we report on the isolation and identification of a novel compound; Tamgermanitin from the aqueous alcohol extract of Myricaria germanica leaves. Further, different fractions of the extract and Tamgermanitin exhibit potent cytotoxic activities which warrant further investigations.

P 28. Pharmacological effects of 20-hydroxy-ecdysone (20-HE) of Atriplex lindleyi subspecies inflata and Atriplex leucoclada grown in Egypt

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Background: Phytoecdysteroids are plant steroidal analogues of invertebrate steroid hormones (ecdysteroids). They have a wide range of pharmaceutical uses as anabolic, adaptogenic, anti-diabetic, hypocholestrolaemic, anti-osteoporosis, hepato-nephroprotective, anti-tumor and immunoprotective agents. Also ecdysteroids have been tested for toxicity and it was proved to be safe.

Isolation of 20-hydroxy ecdysone (20-HE) from the ethyl acetate fraction of A. lindleyi subsp. inflata which is detected in A. leucoclada by TLC. Quantification of 20 hydroxy ecdysone (20-HE) in A. lindleyi subsp. inflata and A. leucoclada carried out by EIA technique proved the concentration of 20-HE to be 9.15 and 7.3 µg/g dried aerial parts of the two species, respectively (El-Sakhawy, et al., 2012)*

Aim of the study: Estimation of anabolic and androgenic effects obtained from total alcoholic extracts, ethyl acetate fractions of both Atriplex species under investigation as well as pure isolated 20-HE compound in comparison with testosterone hormone.

Methods: The anabolic activity was proved by the increase in the ratio of weights of levator ani muscle to prostate gland in castrated male albino rats while the androgenic activity was verified by the increase in weights recorded in genital organs viz. prostate gland, seminal vesicles, epididimis and vas difference also in castrated male albino rats.

Results: The anabolic effect of the ethyl acetate fraction of A. lindleyi subsp. inflata demonstrated a higher activity than the alcohol extract of the same species. In the contrary, the alcohol extract of A. leucoclada showed a higher anabolic activity than its ethyl acetate fraction, while the androgenic activity of alcohol extract of A. lindleyi subsp. inflata, was greater than its ethyl acetate fraction, while in A. leucoclada, the ethyl acetate fraction was more effective than the alcohol extract.

Conclusion: 20-HE was detected mainly in the ethyl acetate fractions of both Atriplex species; we assume that these activities are attributed to its content in the tested fractions. The total alcohol extract and the ethyl acetate fraction of A. lindleyi subsp. inflata showed greater anabolic and androgenic activities than their analogues in A. leucoclada. The higher amount of 20-HE in the aerial parts of A. lindleyi subsp. inflata may give explanation to these biological findings.

*El-Sakhawy, F.S., Abou-Hussein, D.R., El-Kersh, D. M. and Sleem A. A. (2012) Egypt. J. Biomed. Sci.:40, 97-113.

P 29. Diazepam Aggravates Mucosal Damage in Rat Model of Colitis in A Dose Dependent Way

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Background: Anxiety is a frequent symptom in gut disorders and among the available pharmacological options, anxiolytics are considered to be effective drugs that are easily administered and show excellent safety and tolerability. However, in 2012 there is a real world study of Colitis ulcerative (Ulcerative colitis) among people who take Diazepam.
Aim of the study: In our study, we will try to confirm if the use of benzodiazepines may enhance the inflammatory bowel disease or not.
Methods: Three doses of diazepam were assessed comparatively in an experimental model of colitis. Thirty male albino rats were divided into 5 groups (n=6 each); Group I: Sham group, Group II: colitis was induced with 1 ml 5% acetic acid transrectal (TR) without medication. Groups III, IV, V: Intra-peritoneal (IP) diazepam was administered for two days with and after inducing colitis 1, 3, 6mg/kg respectively. All subjects were sacrificed 48 hours after colitis induction and a distal colon segment was assessed macroscopically and microscopically for degree of damage. The inflammatory response was assessed by measurement of colonic myeloperoxidase activity (MPO), serum tumor necrosis factor α (TNFα), fecal lactoferrin and calprotectin.
Results: Data from group II were significantly higher compared to the sham group ($P<0.05$). Groups III, IV and V showed significant exacerbation ($P<0.05$) in a dose dependent manner.
Conclusion: Accordingly, diazepam may have a deleterious effect when administrated in this rat model of colitis
Keywords: colitis, rats, acetic acid, diazepam, TNF α, MPO, Lactoferrin, calprotecin
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P 30. Assessment of Hen's Egg Test-Chorioallantoic Membrane (HET-CAM) for Screening of Anti-Cancer Activities of Drugs

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Background: The chick embryo (Hen's egg) test (**HET**) is one of the alternative methods for animal testing. It is essentially an in vivo test, but has also several advantages of in vitro tests. Blood vessels of fertilized eggs are formed in a membrane called chorioallantoic membrane (**CAM**). The latter is considered as one of the ideal models to study angiogenesis, pro- and anti-angiogenesis factors. Transplantation of heterogonous cells and tissues to the **CAM** is also an established model to evaluate many parameters of tumor growth.

Aim: The present study was designed to assess the use of **HET-CAM** for measuring angiogenesis and thus its value for screening of anti-cancer activities of drugs.

Methods: To provide the suitable environment for chick embryo growth, an electronically-controlled fertilized egg incubator was first build-up, and then some factors for **CAM** visualization, blood vessels formation, and angiogenesis were studied. As pro- and anti-angiogenesis agents, cupper sulphate and dexamethasone were respectively used. Local applications of various concentrations of either agent were assessed. Moreover, Ehrlich ascites tumor growth was also evaluated.

Results: Our results demonstrated that factors needed for proper studying of angiogenesis and tumor growth include: incubation conditions, position of placing the egg inside the incubator, location of the observatory window, observatory window opening date. As ideal positive controls for pro- and anti-angiogenesis agents, concentrations of copper sulphate (50 μg/0.02 ml) and dexamethasone (0.02 μg/0.02 ml) were selected. A new imaging method for **HET-CAM** was developed. Results of the present study revealed also the success of digital image analysis of blood vessels and tumor transplanted on the CAM.

Conclusions: Ideal methodology for using **HET-CAM** model to study angiogenesis and tumor growth was established. Additionally, a new accurate angiography quantitative procedure for **HET-CAM** was provided with less variability.

P 31. Niosomal vesicles of Ketotifen Fumarate As targeting delivery system

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Background: Ketotifen Fumarate (KF) has been widely used as an anti-allergic and anti-anaphylactic agent in adult and children in the treatment of bronchial asthma. A systematic review found that KF was of benefit in improving control of asthma and wheezing in children with mild to moderate symptoms. Many studies in children found that long-term therapy with Kf decreased the risk of asthma onset and frequency. Niosome-mediated pulmonary drug delivery may increase drug retention-time in the lungs, and more importantly, reduction in extrapulmonary side-effects which invariably results in enhanced therapeutic efficacies.

Aim of work: The aim of the work is to formulate KF in niosomal vesicles loaded in MDIs in order to improve its bioavailability and pharmacokinetics profile compared to KF alone.

Methods: Niosomal vesicles entrapping Ketotifen Fumarate has been prepared of mixtures containing span 60 and cholesterol in molar ratios of 3:1, 3:3 and 3:5, using hydration method. Niosomal morphology, particles size, and the entrapment efficiency EE % were investigated using SEM. DSC and X-ray diffraction of the formulated niosomes has been performed. In-vitro release pattern of KF from formulated niosomes was also estimated. The metered dose inhalers containing selected niosomes (3:3) were given in a dose of 400 µg of KF (F2) to human volunteers. Blood samples were collected at different time interval, Kf was measured using HPLC method and compared with those volunteers given drug loaded alone in MDI.

Results: The obtained results revealed that niosomes were spherical in shape with particle size ranged from 2.3-5.7µm. Niosomes entrapping not more than 73% of KF. The KF release percent after 8h from 3:1, 3:3 and 3:5 molar ratios were 70%, 65% and 55% respectively. Intra-day precision results showed that; the average recovery percent of the drug was found to be 98.99%. Moreover, Pharmacokinetic and the bioavailability parameters of KF and niosomal KF MDIs revealed that; AUC and C_{max} of KF from F1( ) and F2( ) were 13.49±0.1935 mg.min./ml, 0.2659±0.0017 mg/ml versus 16.99±0.3052 mg.min./ml, 0.1417±0.0017 mg/ml respectively. In addition, T_{max} of KF from F1 and F2 was attainted after 15 and 60 min. Furthermore, niosomal KF showed plasma concentrations 0.11020 mg/ml and 0.11020 mg/ml which are higher than those delivered via KF 0.0305 mg/ml and 0.0173 mg/ml at 120 and 180 minutes after administration, respectively.

Conclusion: From the previous results, it can be concluded that, KF MDIs achieved targeting effect at the site of action, in addition to KF loaded niosomes MDIs which accomplished not only targeting, but also controlled effect at the site of action.

P 32. Evaluation of the possible modulatory effects of Cinnamic acid and Cinnamaldehyde on Cisplatin-induced nephrotoxicity in rats

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Background: Cinnamic acid (CA) and Cinnamaldehyde (CD) are the major constituents of cinnamon species. They possess various pharmacological properties of which their antioxidant activity is a prime one. Therefore, it is rational to hypothesize that they may ameliorate oxidative stress induced by cisplatin (Cisp.), a widely used chemotherapeutic agent.

Aim of the study: The present study was designed to assess the possible protective and modulatory effects of CA and CD against cisp-induced nephrotoxicity in rats.

Methods: Nine groups of male rats were used; groups 1 (control) and 2, received saline and DMSO, respectively; groups 3 & 4 received CA (50 mg/kg, p.o.) or CD (40 mg/kg, p.o.), respectively; group 5 received cisp in a single dose of 5 mg/kg, i.p.; group 6 and 7 were pretreated with CA (50 mg/kg, p.o. for 7 days) or CD (40 mg/kg, p.o. for 7 days), followed by a single dose of cisp (5 mg/kg, i.p.); groups 8 & 9 received cisp (5 mg/kg, i.p.), followed by CA (50 mg/kg, p.o., for 7 days) or CD (40 mg/kg, p.o., for 7 days), respectively.

Results: A single dose of cisp caused a significant increase in blood urea nitrogen (BUN) and creatinine levels with a significant decrease in serum albumin as well as marked elevation in lipid peroxides measured as malondialdehyde (MDA) content of kidney tissue, accompanied with a significant decrease in reduced glutathione (GSH) content of kidney and antioxidant enzymes (SOD, CAT & GPX) activity as compared to control group. On the other hand, pre- or post-treatment with CA or CD ameliorated cisp-induced nephrotoxicity as indicated by restoration of BUN, creatinine, albumin and kidney contents of MDA, GSH, CAT, SOD & GPX. CA and CD counteracted the deleterious effects of cisp and reduced the histopathological changes.

Conclusion: These results revealed the protective and therapeutic beneficial effects of CA and CD in cisp-induced nephrotoxicity rat model.

Keywords: Cinnamic acid, Cinnamaldehyde, Antioxidant, Cisplatin and Nephrotoxicity.

P 33. Evaluation of the Possible Modulatory Effects of Captopril on Cisplatin-Induced Nephrotoxicity in Rats: A Dose Dependent Study

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Background: Captopril (Cap) is a specific competitive inhibitor of angiotensin I-converting enzyme. It is a popular anti-hypertensive agent. It has been reported to possess various pharmacological properties as free radical scavenger.

Aim of the study: the present study is rational to hypothesize that captopril may ameliorate oxidative stress induced by cisplatin (CIS), a widely used chemotherapeutic agent.

Methods: Rats were randomized into 4 treatment groups, as follows: (1) saline solution (NaCl 0.9%); (2) cisplatin (CIS); (3) Cap (60 mg/kg/) + CIS; (4) Cap (100 mg/kg/) + CIS.

Results: A single dose of cisplatin (5mg/kg), caused a marked increase in blood urea nitrogen (BUN), creatinine, gamma glutamyle transferase (GGT) levels with a significant decrease in serum albumin, protein and heme oxygenase 1 (HO-1) as well as marked elevation of renal malondialdehyde (MDA), accompanied with a significant decrease in reduced glutathione (GSH), catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPX), a significant elevation of endotheline-1 (ET-1), tumor necrosis factor alpha (TNFα), rat monocyte chemoattractant protein-1 (RMCP-1) and nitric oxide (NO). However, administration of Cap (60 mg/kg) or Cap (100 mg/kg) ameliorated cisplatin nephrotoxicity by restoration of kidney functions, HO-1, NO, kidney contents of MDA, GSH, CAT, SOD & GPX, hampering the inflammatory mediators and cytokines (TNFα, ET-1 and RMCP-1). Cap 60 and Cap 100 counteracted the deleterious effects of cisplatin and improved the histopathological changes.

Conclusion: These results revealed the protective effects of captopril in cisplatin-induced nephrotoxicity rat model in a dose dependent manner.

Key words: Cisplatin- Captopril-Nephrotoxicity- HO1- ET1- TNFα- RMCP1.

P 34. Potential effect of the medicinal plants; Calotropis procera, Ficus elastica and Zingiber officinale against Schistosoma mansoni in mice

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Background: although no clinically relevant resistance to the only schistosomicidal drug praziquantel (PZQ) has been described to date, development of drug-resistance remains a growing threat. Calotropis (C.) procera, Ficus (F.) elastica and Zingiber (Z.) officinale are well known medicinal plants and have been traditionally used for many diseases.

Aim of the study: the present work aimed to evaluate the antischistosomal activity of these plant extracts against Schistosoma (S.) mansoni.

Methods: male mice exposed to 80±10 cercariae/mouse were divided into two batches. The first was divided into 5 groups; (I) infected untreated, while groups from (II–V) were treated orally (500 mg/kg for 3 consecutive days) by aqueous stem latex and flowers of C. procera, latex of F. elastica and ether extract of Z. officinale respectively. The second batch was divided into four comparable groups (except Z. officinale-treated group) similarly treated as the first batch in addition to the antacid ranitidine (30 mg/kg) 1 h before extracts administration. Safety, worm recovery, tissues egg load and oogram pattern were assessed.

Results: results indicate that C. procera latex and flower extracts are toxic even in small doses before washing off toxic rubber. Z. officinale extract produced numerical insignificant decrease (7.26%) in S. mansoni worms. When toxic rubber was washed off and the antacid ranitidine used, C. procera (stem latex and flowers) and F. elastica latex extracts revealed significant antischistosomal worm reductions by 45.31, 53.7 and 16.71% respectively. Moreover, C. procera extracts produced significant reductions in tissue egg load (≈ 34–38.5%) and positively affect the oogram pattern.

Conclusion: the present study may be useful to supplement information with regard to C. procera and F. elastica antischistosomal activity and provided a basis for subsequent experimental and clinical trials.

Keywords: Schistosoma mansoni - medicinal plants - Calotropis procera - Ficus elastica - Zingiber officinale

P 35. The possible protective effect of naringenin against gentamicin-induced nephrotoxicity in rats

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Background: The use of gentamicin as aminoglycoside antibiotic is limited by its nephrotoxicity. Naringenin a citrus fruits bioflavonoid has already been pharmacologically evaluated as a potential antioxidant and anti-inflammatory.

Aim of the study: The present study was designed to evaluate the possible protective effect of naringenin on gentamicin-induced nephrotoxicity in rats compared with N-acetylcysteine.

Methods: 7 groups of rats (n=10) were used: 1st group: normal control (vehicle), 2nd group: gentamicin (100 mg/kg, i.p), 3rd: N-acetylcysteine (40 mg/kg, i.p.) with gentamicin, 4th and 5th groups: naringenin (50, 100 mg/kg, p.o., respectively) alone, 6th and 7th groups: naringenin (50,100 mg/kg, p.o., respectively) with gentamicin. At the last day of treatment (8 days), the 24 hr urine volume was collected for assessment of urine volume and blood samples were taken for determination of serum creatinine, blood urea nitrogen (BUN), creatinine clearance (Ccr). Then rats were scarified, their kidneys were excised, one portion was used for determination of reduced glutathione (GSH), malondialdehyde (MDA), nitric oxide (NO) contents, in addition to total antioxidant capacity, superoxide dismutase (SOD), myeloperoxidase (MPO) activities, other portion was used for histopathology study.

Results: Gentamicin injected rats showed a significant increase in urine volume, serum creatinine, BUN, NO, MDA contents and MPO activity accompanied with a significant decrease in Ccr, GSH content, total antioxidant capacity and SOD activity as compared with normal group. N-acetylcysteine normalized all the mentioned parameters except urine volume (significantly decreased), Ccr and total antioxidant capacity (increased) with no effect on MPO activity as compared to the gentamicin group. Naringenin ameliorated the nephrotoxicity in a dose dependent manner; naringenin 100 mg/kg normalized all mentioned parameters. These results were confirmed by the histopathological results.

Conclusion: naringenin significantly ameliorated gentamicin-induced nephrotoxicity and these results recommend its use as natural nephroprotective agent.

Key words: Gentamicin, naringenin, N-acetylcysteine, nephrotoxicity, oxidative stress.

P 36. The combination of α-Tocopheryl succinate and sodium selenite on breast cancer cells in vitro and in vivo: A merit or a demerit?

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Background: α-Tocopheryl succinate (α-TOS) is a pro-vitamin that induces apoptosis in malignant cells in vitro and in vivo with no toxic effects in normal cells. Selenium is an essential trace element and is recently reported to be a strong inducer of apoptosis in cancer.

Aim of the study: This study was designed to investigate the modulatory effect of sodium selenite (SSe) on α-TOS-induced apoptosis in breast cancer cells.

Methods: An in vitro study was carried out on breast cancer cell line (MCF7) to determine the I.C.50 of α-TOS, SSe and their combination. Type of interaction between SSe and α-TOS was evaluated using isobologram and combination index equations, in addition, oxidative, apoptotic and autophagic markers were assessed. An in vivo study on mice bearing Ehrlich tumor to study the survival and the anti-tumor effect of α-TOS, SSe and their combination was carried out.

Results: Our data showed an antagonistic effect between SSe and α-TOS, an increase in survival of breast cancer cell line treated with α-TOS in presence of (2 μM) SSe. SSe decreased α-TOS-induced increase in lipid peroxidation and activation of caspase-3 with no changes in Bcl-2 and Mcl-1 protein levels. Moreover, SSe increased autophagy markers (Beclin-1 and LC3B protein levels) of MCF7 cells treated with the α-TOS. A significant increase in the tumor volume of mice treated with the combined treatment compared with α-TOS was found. However, there was insignificant difference in the mean survival time of all the treated groups.

Conclusion: SSe antagonizes the cytotoxicity of α-TOS via inhibiting the apoptosis and increasing autophagy.

Key words: α-Tocopheryl succinate, sodium selenite, breast cancer, cytotoxicity, autophagy

P 37. Involvement of serotonergic and dopaminergic transmission in the antidepressant effects of malt extract

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Background: The beneficial effect of malt extract in clonidine-induced depression was previously reported; however its mechanism of action remains unclear.

Aim of the study: The present study aimed to investigate the role of different neurotransmitters, oxidative stress biomarkers and inflammatory cytokines on the action of malt extract.

Methods: Animals were classified into normal (n= 8) and depressed rats (n=48). Induction of depression was done by i.p. injection of clonidine (0.8 mg/kg) daily for 7 successive days. Depressed rats were sub-classified into 6 groups (n=8) treated for one week as follows: Group I received 1% tween 80 p.o. (control group); whereas the remaining 5 groups received malt extract (1250 mg/kg; p.o.) alone or preceded (30 min) by i.p. injection of spiperone (0.03mg/kg), sulpiride (7.5 mg/kg), phentolamine (5 mg/kg) or propranolol (7.5 mg/kg), respectively. Forced swimming test (FST) was carried out 24 h after the last administered dose, then animals were sacrificed and brains were isolated to be used for estimation of serotonin, dopamine and norepinephrine contents as well as inflammatory and oxidative stress biomarkers.

Results: Clonidine increased total immobility time and decreased struggling time in FST parallel to alterations in brain neurotransmitters, inflammatory and oxidative stress markers. Treatment of depressed rats with malt extract reversed clonidine-induced behavioral and biochemical changes. Moreover, the actions of malt extract were partly antagonized in groups pre-treated with spiperone or sulpiride.

Conclusion: Serotoninergic and dopaminergic transmission are involved in the antidepressant effects of malt extract in addition to its antioxidant and anti-inflammatory effects.

Key words: Depression, Malt extract, Spiperone, Sulpiride, Neurotransmitters, Cytokines.

P 38. Curcumin enhances the antifibrotic effect of perindopril on CCL4 induced hepatic fibrosis in rats

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Background: Liver cirrhosis shows a worldwide distribution and affects all races, ages and both sexes; it is among the top ten causes of death in the world. In the last decade, there have been major advances in the knowledge of liver fibrosis pathogenesis. Liver fibrosis may regress following treatment with anti- fibrotic drugs. This hope has been an active area for research. Recent studies have revealed that both curcumin (CUR) and angiotensin-converting enzyme inhibitor (ACE-I) exert an anti-fibrotic effect.
Aim of the study: The aim of this study was to examine the combined effect of the ACE-I, perindopril (PE), and CUR on CCL4 induced hepatic fibrosis in rats.
Methods: Fibrosis was induced in rats by carbon tetrachloride (CCL4) administration in a dose of (0.3mg/kg subcutaneously) twice weekly for 6 weeks. Fibrotic rats were randomly assigned to one of three groups. PE (8mg/kg/day), CUR (200mg/kg/day) and PE (8mg/kg/day) + CUR (200mg/kg/day), each given orally for 4 weeks starting 2 weeks after CCL4 injection. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total proteins, serum albumin and albumin globulin (A/G) ratio were performed by colorimetric methods. Hepatic tissue specimens were histopathologically evaluated by hematoxylin & eosin staining.
Results: Single treatment of CCL4 induced hepatic fibrosed rats with either PE or CUR significantly attenuated liver fibrogenesis as evidenced by significant improvement in biochemical measurements and confirmed by histopathological examination. The anti-fibrotic effect of PE was more potent than CUR. The combination treatment with PE and CUR had markedly improved the liver biochemistry and histopathology and highly significant protective effect was observed in this group more than any of these drugs when used alone.
Conclusion: The results showed that curcumin enhanced the anti-fibrotic effect of perindopril as well as the improvement of hepatic steatosis in rats with CCL4 induced liver fibrosis, this combination may provide a new strategy for anti-liver fibrosis therapy

P 39. Protective effect of curcumin against cadmium toxicity on pregnant rats and their fetuses at morphological, physiological and molecular level

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Background: Cadmium (Cd) is one of the most toxic heavy metals .This metal is a serious environmental and occupational contaminant and may represent a serious health hazards to humans and other animals. Curcumin, the yellow bioactive component of turmeric has established its antioxidant activities.

Aim of the study: This work studies the effect of curcumin (50 mg/Kg/day) against the toxic effect of cadmium (18.4mg/kg) in pregnant rats dams and their fetuses**.**

Methods: Fourty pregnant rats are divided into four groups, the 1st group is control receiving distilled water, the second group received cadmium from 7th to 16th day of gestation, third and fourth groups treated with curcumin from 1st to 20th day of gestation. Group 4 received also cadmium from 7th to 16th day of gestation.

Results: The results showed decrease in maternal body weight gain, increase in the rate of abortion, resorption and growth retardation of fetuses and malformations in their skeleton in group received cadmium. Also there were decrease in RBCs, and hemoglobin concentration while increase in the WBCs count. Cadmium increased serum level of AST, ALT, LDH, urea and creatinine comparing to the control group. Cadmium caused DNA fragmentation in the liver of fetuses. However curcumin decreased the toxic effects of cadmium on dams and their fetuses.

Conclusion: This study demonstrates that oral pretreatment with curcumin at dose of (50 mg/Kg/day) could decrease the toxic effect of cadmium on dams and their fetuses.

Key words: Cadmium, Curcumin, liver, kidney function and DNA fragmentation.

P 40. Quercetin and its metabolites potentiate Doxorubicin-induced apoptosis and augment its cytotoxicity in HepG2 cells

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Background: The efficacy of Doxorubicin (DOX) in treatment of hepatocellular carcinoma (HCC) is directly related to its dose. Quercetin and its metabolites (Tamarixetin and Kaempferol) showed promising data against some types of malignant cell lines at high doses.
Aim of the work: This work aims to study the ability of Quercetin (Quer), Tamarixetin (Tam) or Kaempferol (Kaemp) to potentiate the cytotoxic effect of DOX and the underlying mechanism(s) in HepG2 cells.
Methods: The lowest cytotoxic concentration of DOX and the safe concentrations of the tested flavonoids have been used. The cells were classified into 8 groups. The first served as control group exposed to 0.1% Dimethyl sulphoxide (DMSO) for three consecutive days. The second group exposed to the lowest cytotoxic concentration of DOX (0.62μM) for three consecutive days. Cells in the third, fourth and fifth groups were exposed to a safe concentration (5μM) of either Quer or Tam or Kaemp respectively. Sixth, seventh and eighth groups were exposed to DOX (0.62μM) combined with 5μM of either Quer or Tam or Kaemp respectively for 72 hours. At the end of exposure period, intact cells were used for assessment of cell viability and apoptotic cell. Cell lysates were prepared to determine Bcl2 gene expression and caspase-9 content as well as levels of reduced glutathione (GSH) and malondialdehyde (MDA).
Results: Doxorubicin resulted in significant increases in cytotoxicity, apoptotic cell death, caspase–9 content and MDA level but suppression of Bcl-2 gene expression and marked depletion of GSH content in comparison to the control values. Combination of DOX with either Quer or Tam or Kaemp caused further increases in cytotoxity, apoptotic cell death, Caspase-9 content, and MDA level along with extensive decreases in Bcl-2 gene expression and GSH compared to corresponding control group.
Conclusion: From the previous data it could be concluded that exposure of HepG2 cells to Quer or its metabolites can improve the therapeutic outcome from DOX and potentiate its cytotoxic effect. This may be at least in part through induction of oxidative stress- mediated apoptosis or suppression of anti-apoptotic gene, Bcl-2. These data may shed attention for further studies to open a new therapeutic window during the treatment of HCC by the use of natural flavonoid as adjuvant therapy.
Keywords: Hepatocellular carcinoma, Doxorubicin, Flavonoids, Oxidative stress, Apoptosis and Cytotoxicity.

P 41. Sodium Selenite Improves Folliculogenesis in Radiation-Induced Ovarian Failure: A Mechanistic Approach

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Background: Radiotherapy is a major factor contributing to female infertility by inducing premature ovarian failure (POF). Therefore, the need for an effective radioprotective agent is evident.

Aim of the study: The present study investigated the mechanism of potential radioprotective effect of sodium selenite on radiation-induced ovarian failure and whether sodium selenite can stimulate in-vivo follicular development in experimental rats.

Methods: Immature female Sprague-Dawely rats were either exposed to gamma-radiation (3.2 Gy, LD20), once and/or treated with sodium selenite (0.5 mg/kg), once daily for one week before irradiation. Follicular and oocyte development, apoptotic markers, proliferation marker as well as oxidative stress markers were assessed 24-h after irradiation. In addition, fertility assessment was performed after female rats became completely mature at two months of age.

Results: Sodium selenite significantly enhanced follicular development as compared to the irradiated group. Sodium selenite significantly reversed the oxidative stress effects of radiation that was evidenced by increasing in lipid peroxide level and decreasing in glutathione level, and glutathione peroxidase (GPx) activity. Assessment of apoptosis and cell proliferation markers revealed that caspase 3 and cytochrome c expressions markedly-increased, whereas, PCNA expression markedly-decreased in the irradiated group; in contrast, sodium selenite treatment prevented these alterations. Histopathological examination further confirmed the radioprotective efficacy of sodium selenite and its in-vivo effect on ovarian follicles' maturation.

Conclusion: Sodium selenite showed a radioprotective effect and improved folliculogenesis through increasing ovarian granulosa cells proliferation, estradiol and FSH secretion, and GPx activity, whilst decreasing lipid peroxidation and oxidative stress, leading to inhibition of the apoptosis pathway through decreasing the expressions of caspase 3 and cytochrome c.

P 42. A study on the amoebicidal effect of Nigella sativa seeds (aqueous and alcoholic extracts) and wheat germ agglutinin on pathogenic Acanthamoeba

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Background: Acanthamoeba keratitis is a corneal disease, the occurrence of which has been rising in correlation to the increasing number of contact lens wearers. Treatment of Acanthamoeba keratitis has been fairly successful using a variety of drugs.although their use has shown several side effects. Medicinal plants can be an alternative resource of novel anti-protozoal drugs with high effectiveness and low toxicity.
Methods: The in vitro effect of different concentrations of Nigella sativa seeds aqueous and alcoholic extracts as well as wheat germ agglutinin was studied on pathogenic Acanthamoeba, isolated from Acanthamoeba keratitis patients, in comparison to chlorhexidine 0.02% as a drug control.
Results: Chlorhexidine (0.02%) gave 100% inhibition percentage of Acanthamoeba trophozoites after 24, 48 and 72 hrs incubation. The minimal lethal concentration (MLC) of N. sativa aqueous extract on Acanthamoeba trophozoites was 5 mg/ml and that of the alcoholic extract was 10 mg/ml after 24 hrs incubation. A MLC of 500 ug/ml was recorded for both extracts after 48 hrs.
The MLC of N. sativa aqueous and alcoholic extracts on Acanthamoeba cysts was 30 mg/ml after 24 hrs with a highly significant ($p<0.001$) difference compared to the drug control which had an inhibition percentage of 56% after 24 hrs, 64% after 48 hrs and 80% after 72 hrs incubation. A MLC of 25 mg/ml of N. sativa aqueous extract was obtained after 48 hrs with a significant difference ($p<0.05$) compared to the drug control.
The MLC of WGA on Acanthamoeba trophozoites was 50 µg /ml after 24, 48 and 72 hrs incubation which was similar to the effect of the drug control. Nearly similar inhibition percentages of Acanthamoeba cysts were obtained by WGA (1 mg/ml) and chlorhexidine (0.02%) after 24 hrs (60% vs. 56%) and after 48 hrs (68% vs. 64%) respectively. Inhibition percentage of 80% was obtained by WGA (2 mg/ml) after 48 hrs incubation which was significantly higher ($p<0.05$) than the drug control (64%) and by both medications after 72 hrs.
Conclusions: So, N. sativa aqueous and alcoholic extracts as well as WGA showed considerable lethal effects on Acanthamoeba trophozoites and cysts. These effects were dose and time dependent and were comparable to or even superior than the effect of the commonly used chlorhexidine (0.02%).
Key Words: Acanthamoeba spp. Nigella sativa, Wheat germ agglutinin.

P 43. Modulating effect of tulathromycin (Draxxin®) on rats with ulcerative colitis

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Background: Tulathromycin is a new semi-synthetic macrolide antibiotic of the triamilide subclass. It used for the treatment of bovine respiratory disease. The direct antimicrobial effects of the drug alone do not fully justify its superior clinical efficacy. It is hypothesize that it may have immunomodulating and anti-inflammatory properties.
Aim of the study: The present study was conducted to evaluate the effects of Draxxin on acetic induced-ulcerative colitis using rats as an experimental model.
Methods: Forty male rats were randomly assigned into 5 groups; each of eight. The 1st group served as a sham group which injected with saline. Rats in other groups were transrectally administered 1 ml of 4% acetic acid solution for induction of ulcerative colitis. The 2nd group acts as ulcerative colitis group and received saline. The 3rd group received sulfasalazine at a dose of 500 mg/kg daily and acts as a standard control group. The 4th and 5th groups subcutaneously injected with Draxxin at doses of 2.5 and 5 mg/kg b.wt. for 5 days after induction of colitis. At the 6th day, colon tissue weight and length were examined and the colonic mucosal injury was assessed by macroscopic scoring, and histological examination. Furthermore, the colonic tissue content of myeloperoxidase (MPO), tumor necrosis factor (TNF-α), interleukin-1β, interleukin-6, and prostaglandin E_2 (PGE_2) were evaluated.
Results: All parameters were altered in ulcerated rats, and improved in rats receiving Draxxin; an effect that was comparable to that of the standard sulfasalazine especially at the highest dose level. Colonic mucosal injury was parallel with the biochemical evaluations and cytokines analysis as well as histopathological examination.
Conclusion: These data indicate a protective effect of tylathromycin against colitis, suggesting a major role for bacteria, anaerobes in particular, in the development of acetic acid-induced damage. It could also be concluded that tulathromycin is an effective anti-inflammatory and may be a promising therapeutic option for ulcerative colitis.
Key words: tulathromycin, ulcerative colitis, anti-inflammatory

P 44. Pyrolidine Dithiocarbamate Plays a Modulatory Role against Scopolamine-Induced Cognitive Impairment in Rats

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Background: Alzheimer's disease (AD), the most common cause of progressive dementia in the elderly population, is a chronic neurodegenerative disorder that leads to disturbances of cognitive functions. Although the primary cause of AD remains unclear, brain acetylcholine deficiency, oxidative stress and neuroinflammation may be considered the principal pathogenic factors.
Aim of the study: The present study was constructed to investigate the anti-amnestic effect of pyrolidine dithiocarbamate (PDTC) on scopolamine-induced behavioral and neurochemical changes in rats.
Methods: PDTC (50 and 100 mg/kg) and donepezil (2.5 mg/kg) were orally administered for 14 successive days. Dementia was induced at the end of the treatment period by a single injection of scopolamine (20 mg/kg; i.p.), and Y-maze test was conducted 30 min thereafter. Rats were then sacrificed and homogenates of cortical and hippocampal tissues were used for the estimation of noradrenaline, dopamine and serotonin contents along with acetylcholinesterase activity. In addition, certain oxidative stress biomarkers such as thiobarbituric acid reactive substances and reduced glutathione were assessed.
Results: Histological examination of cortical and hippocampal tissues was also performed. Scopolamine resulted in memory impairment that was coupled by alterations in the estimated neurotransmitters, acetylcholinesterase activity and oxidative stress biomarkers. Histological analysis revealed serious damaging effects of scopolamine on the structure of cerebral cortex and hippocampus. Pretreatment of rats with PDTC in both doses mitigated scopolamine-induced behavioral, neurochemical and histological changes in a manner comparable to donepezil.
Conclusion: The observed antiamnestic effect of PDTC makes it a promising candidate for clinical trials in patients with cognitive impairment.

P 45. Breast cancer promoting potential of the water disinfection byproduct acrylonitrile

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Background: Acrylonitrile (ACN) is a widely used intermediate in the manufacture of plastics, acrylic fibers, synthetic rubbers and resins that are used in a variety of products including food containers and medical devices. It was also found in chlorinated drinking water. Experimental evidence indicated that ACN is a mutagenic, carcinogenic, and neurotoxic chemical. Inhalation or ingestion of ACN was associated with the development of astrocytomas, forestomach squamous cell papillomas, mammary gland tumors in rats, alveolar and bronchial carcinomas in B6C3F1 mice. There is inadequate evidence in humans, however, for the carcinogenicity of ACN in breast cancer and its putative underlying mechanisms.

Aim: The specific aims for this study are: i) Identification of the carcinogenic effect of ACN in breast cancer cell model, ii) Characterization of the underlying molecular mechanisms of the carcinogenic potential of ACN.

Methods: SRB-cytotoxicity assay was used to determine the subcytotoxic concentration range of ACN to be used in the subsequent proliferation assay studies and in order to further elucidate the molecular mechanisms involved in ACN-induced carcinogenesis in MCF-7 breast cancer cells.

Results: The preliminary results of the present study indicated that the subcytotoxic concentrations (<100 µM) of ACN significantly enhanced the proliferation of MCF-7 breast cancer cells after 1, 4, 5 and 6 days of exposure. Concentrations above 100 µM of ACN however, showed prominent cytotoxicity.

Conclusion: Lower concentrations <100 µM will be used to identify the basic molecular mechanisms of the proliferating effect of ACN in MCF-7 cells.

Keywords: Acrylonitrile, Breast cancer, MCF-7, SRB-assay.

P 46. Nephroprotection of Lacidipine against Gentamycin-Induced Nephrotoxicity in Albino Rats

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Background: Gentamycin, a widely-used aminoglycoside antibiotic, is recognized as possessing significant nephrotoxic potential in human beings. Gentamycin-induced nephrotoxicity is suggested to be mediated via reactive oxygen species.
Aim of the Study: The present study investigated the possible antioxidant nephroprotective effect of lacidipine as a calcium-channel blocker in a gentamycin-induced nephrotoxicity model in albino rats.
Methods: Albino rats were divided into 3 groups. Group 1 received normal saline. Group 2 received gentamycin 80 mg/kg intraperitoneally for 14 days. Group 3 received lacidipine 1 mg/kg intraperitoneally 3 days before and 14 days concurrently with gentamycin. This dose does not affect the blood pressure of rats, as evidenced in the pilot study.
Results: Gentamycin-induced nephrotoxicity was evidenced by a marked reduction in creatinine clearance.
Treatment with lacidipine improved creatinine clearance compared to the gentamycin-treated group. In addition, it reduced thiobarbituric acid reactive substance, as an index of lipid peroxidation, with significant increases in superoxide dismutase enzyme in erythrocyte lysates and kidney catalase enzyme activities.
Conclusion: This study recommends the use of lacidipine in prophylaxis against gentamycin-induced nephrotoxicity.
Keywords: lacidipine, gentamycin, nephrotoxicity, antioxidant, albino rats

P 47. Combination of Simvastatin and Aliskiren Reduces Hyperlipidemia and Some Oxidative Markers in cholesterol-Fed Rabbits

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Background: One of the important therapeutic problems is the association of atherosclerosis in the majority of hypertesnsive patients. Many studies are directed towards reporting any possible anti-hyperlipidemic effect of antihypertensive drugs so as to reduce the number of drugs used to treat those patients.
Aim of the Study: The present study aims to determine the effects of aliskiren, as a renin inhibitor, on serum cholesterol & triglycerides and some oxidative markers, either alone or in combination with simvastatin as an HMG-CoA reductase inhibitor], in cholesterol-fed rabbits.
Methods: The study was performed for 12 weeks on 5 groups of Newzealand rabbits. They were divided into control groups (1&2) and treated group (3,4&5). Serum cholesterol & triglycerides, superoxide dismutase (SOD) enzyme in erythrocyte lysates, TBARS content, activities of catalase and glutathione enzymes in liver homogenates of tested rabbits were measured.
Results: All treated groups [3,4,5] showed a significant improvement of all the measured lipid and antioxidant markers in comparison with non-treated cholesterol-fed rabbits.
Conclusion: A significant reduction of hyperlipidemia and some oxidative markers in cholesterol-fed rabbits were observed by a combination of simvastatin and aliskiren.
Key words: simvastatin, aliskiren, lipids, antioxidant, cholesterol-fed rabbits.

P 48. Effect of green tea extract on experimentally induced Parkinson's disease in rats

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Background: Parkinson's disease (PD) is a neurodegenerative movement disorder that associated with selective degeneration of nigrostriatal dopamine neurons. PD is characterized by its cardinal motor symptoms of muscle rigidity, bradykinesia, resting tremors, and postural instability. Treatment of PD aims to provide symptomatic relief, reduce disability, and maintain independent functioning and consequently improving the quality of life of the patient. There are many plants, which were claimed to have anti parkinsonian activities.

Aim of the study: The aim of the study is to explore the effect of green tea extract on experimentally- induced PD in rats.

Methods: Animals were divided into 3 groups (n= 10). The first group received vehicles only. Group2, received rotenone (1.5mg/kg; S.C.) every other day for 12 days. Group3, received rotenone (1.5mg/kg; S.C.) every other day for 12 days and green tea (10mg/kg; P.O.) daily for 12 days. Behavioral examinations (catalepsy and locomotor activity) were conducted in all groups at the end of the treatment period. Biochemical parameters; malondialdehyde (MDA), total anti-oxidant capacity (TAC) and tumor necrosis factor-alpha (TNF-α) were determined in the brain homogenate. In addition, expression of caspase-3 in the midbrain was carried out.

Results: Our results showed that green tea significantly improved the catalepsy and the locomotor activity of the parkinsonian rats. The brain contents of MDA and TNF-α and TAC were significantly improved after treatment with green tea extract. Furthermore, green tea resulted in marked decrease in the caspase-3 expression in the midbrain of the parkinsonian rats.

Conclusion: It can be concluded that green tea has beneficial effects in PD based on its antioxidant, anti-inflammatory and neuroprotective effects