1. MODULATION OF INTERLEUKIN-1, TUMOR NECROSIS FACTOR-\( \alpha \), INTERLEUKIN-4, INTERLEUKIN-6, INTERLEUKIN-10, AND INTERFERON-\( \gamma \) BY AQUEOUS EXTRACTS OF SWERTIA CHIRAYITA

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Objectives: Swertia chirayita (Gentianaceae), is a herb used in Indian system of medicine as remedy for chronic fever, liver disorder and for curing different diseases. We studied the effect of aqueous extract of Swertia chirayita on cytokines that are Pro-inflammatory [(IL-\( \beta \)], interleukin-6 (IL-6) and tumor necrosis factor-\( \alpha \); (TNF-\( \alpha \)], anti-inflammatory [interleukin-4 (IL-4)], interleukin-10 (IL-10) and immunoregulatory [Interferon-\( \gamma \) (IFN-\( \gamma \))] in nature in Adjuvant Induced Arthritis (AIA) mouse, a chronic model of inflammation.

Methods: Aqueous extract of Swertia chirayita (11.86 mg/kg, body weight/day) was orally administered to adult female AIA mice for a period of 10 days and the levels of TNF-\( \alpha \), IL-\( \beta \), IL-4, IL-6, IL-10 and IFN-\( \gamma \) were estimated using solid phase sandwich ELISA method in the frozen hind paw homogenates. Joint distortion and joint swellings were estimated at the end of the course of the disease. Attempts to identify chemical constituents of Swertia chirayita responsible for cytokine-modulating activity was also undertaken by HPTLC and reverse phase TLC.

Results: We observed significant depletion in the levels of TNF-\( \alpha \), IL-\( \beta \), IL-4 and IL-6 and elevation in the levels of IL-10 in AIA mice treated with aqueous extract of Swertia chirayita in comparison to control. A significant reduction in joint circumference was also observed in AIA mice treated with the aqueous extract of Swertia chirayita. HPTLC fingerprint revealed the absence of all the non-polar constituents like swerchirin, methyl-swertianin, swertanone and chiratol in the aqueous extracts. Reverse phase TLC chromatogram revealed the presence of amarogentin (a known major bitter principle) and mangiferin (a xanthone derivative) in nature in Adjuvant Induced Arthritis (AIA).

Conclusion: Aqueous extract of Swertia chirayita is effective in controlling the initial arthritic reaction in AIA mice in the light of joint inflammation, joint distortion and pro- and anti-inflammatory cytokine profiles. It appears that amarogentin and mangiferin are responsible for the modulation of the pro- and anti-inflammatory and immuno-regulatory cytokines.

2. COMPARISON OF DOUBLE-STRENGTH AMPILOX (AMPICILLIN 500 mg + CLOxacillin 500 mg) AND ERYTHROMYCIN IN LOWER RESPIRATORY TRACT INFECTIONS

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Objectives: Lower Respiratory Tract Infection’s which include pneumonia, acute bronchitis, acute exacerbations of chronic bronchitis and chronic obstructive pulmonary disease, contribute a major proportion of patients attending a general OPD. Community Acquired Pneumonia remains a common and potentially serious illness representing one of the most common causes of infection related mortality worldwide, and especially in India. Since, Ampicillin, Cloxacillin, and Erythromycin are scheduled drugs in our hospital, this comparative trial was undertaken to determine the safety and efficacy of double strength doses of these drugs for the treatment of Lower Respiratory Tract Infections.

Methods: Patients of either sex, diagnosed by signs and symptoms to be suffering from Lower Respiratory Tract Infections, and not on any concurrent antimicrobial medication were included in this ethically approved study. Patients received Ampilox (Ampicillin 500 mg + Cloxacillin 500 mg) four times a day for 7 days and Erythromycin 500 mg four times a day for 7 days. On enrolment, baseline signs and symptoms were recorded on the basis of cough, breathlessness, chest pain, rales and rhonchi. In addition, laboratory investigations, sputum smear and culture, X-ray chest were done. Patients were required to follow up on day 3 and day 7. On each follow-up visit, signs and symptoms, tolerability and adverse events if any were recorded. At the end of the treatment (day 10), laboratory investigations, X-ray chest were repeated. On day 14 global assessment was carried out with respect to safety, efficacy and tolerability.

Results: Treatment by Ampilox (Ampicillin 500 mg + Cloxacillin 500 mg) produced significant improvement in clinical and laboratory variables. Both cough and breathlessness reduced significantly from 2.10±0.56 to 0.93±0.57 and 0.75±0.67 to 0.08±0.27 respectively at day 10. The severity of rales was reduced from 0.79±0.49 to 0.15±0.36. Significant reduction in chest pain, wheezing and rhonchi were seen. Statistically significant reductions were seen in WBC counts.

Conclusion: Ampilox (Ampicillin 500 mg + Cloxacillin 500 mg) used for 7 days was equally efficacious as Erythromycin in a dose of 500 mg four times a day for 7 days in the treatment of LRTI. Besides, these drugs are scheduled drugs in the hospitals, a cheaper option for the patients. Thus, these drugs may be considered as drugs of first choice in the treatment of Lower Respiratory Tract Infections.
EVALUATION OF MECHANISM OF ANTI-DIABETIC ACTION OF CHROMIUM

SHINDE UA, GOYAL RK

Earlier findings from our laboratory have revealed insulin sensitizing action of chromium compounds [chromium chloride and chromium picolinate] in experimental rodent models of both type I and type II diabetes mellitus. However, the mechanism of these effects remains to be explored.

Objective: The present study was undertaken to probe cellular action mechanisms underlying the anti-diabetic action of chromium using 3T3-L1 adipocytes and C2C12 myoblasts.

Methods: Confluent 3T3-L1 preadipocyte cultures were incubated with chromium compounds (0-10 μM) alone and in combination with insulin (1 μg/ml) at 37°C in an atmosphere of 5% CO₂, 95% air. Intracellular triglyceride content and cellular membrane protein was measured colorimetrically. Confluent C2C12 cultures were incubated with chromium compounds (10 mM) alone and in the presence of insulin (6 μM). The glucose uptake in the cells was studied using radiolabeled glucose in liquid scintillation counter.

Results: Chromium chloride alone did not produce any effect, however, in the presence of insulin significantly increased triglyceride synthesis in the 3T3-L1 cells. Chromium picolinate failed to produce any effect alone or in the presence of insulin. Treatment of C2C12 cells with chromium chloride significantly enhanced uptake of radioactive glucose into the cells only in the presence of insulin. Chromium chloride alone and chromium picolinate alone or in the presence of insulin failed to produce any significant effect on glucose uptake. However, in our earlier findings chromium picolinate was found to produce greater effect on glucose uptake. However, in our earlier findings chromium picolinate was found to produce greater effect on glucose uptake.

Conclusion: Our data suggest that anti-diabetic activity of chromium observed in vivo could be attributed to its insulin sensitizing action at the two major target sites, adipocytes and skeletal muscles. Though chromium picolinate failed to produce any significant effect in vitro, its higher potency in the in vivo models could be attributed to better absorption at the gastrointestinal level.
Conclusion: Medical officers should keep pace with the fast evolving knowledge of medicine and physicians of tertiary care hospitals must analyze rationally the hard facts of clinical data and select the P-drug carefully, so as to provide maximally beneficial treatment to the patient in the long run.

6. COMPARATIVE BIOEQUIVALENCE STUDY OF RIFAMPICIN GIVEN WITH AND WITHOUT PIPERINE IN FIXED-DOSE -COMBINATION

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Tuberculosis occurs throughout the world and remains an important cause of morbidity in developing countries. New advances in formulation technology have increased patient compliance. Bioequivalence of rifampicin has been reported to be significantly more in combination with piperine. In the present study of bioavailability of rifampicin with and without piperine, blood samples collected at various intervals were assessed by standard HPLC technique. Area under curves (AUC), Cmax and Tmax were calculated for each volunteer. Concentration of rifampicin with piperine in FDC was increased at different intervals, which was statistically not significant in comparison with concentration of rifampicin alone in Fixed Dose Combination.

7. LOW DOSE Vs HIGH DOSE DISULFIRAM IN ALCOHOLISM

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Objective: To find suitability of high dose versus low dose of Disulfiram for alcohol challenge, to study side effect profile of Disulfiram in Ethanol Reaction (DER).

Methods: Male alcoholics aged between 18-50 years were selected for the study from a general hospital psychiatric service. 67 cases were randomly allocated into high and low dose groups. High dose group were given 5 gm and low dose group were given 2.5 gm of disulfiram totally over a period of 4 days and 7 days respectively. The ethanol challenge was carried out the fourth day in high and seventh day in low dose patients. DER were recorded every 15 minutes on a checklist, Severity was measured on a severity scale.

Results: Socio-demographic characteristics in the sample were homogenous. Duration of dependence and quantity of ethanol consumed did not vary statistically in both groups. There was statistically significant difference in systolic and diastolic blood pressure, ESR and leucocytes in both groups. Clinically patients had more gastrointestinal and neuropathic symptoms in high dose group prior to challenge. Headache, restlessness and weakness were reported more in high dose group after challenge. Severity of DER did not vary statistically in relation to dose of disulfiram, duration of alcohol use and BMI, though clinically high dose group had more severe reaction.

Conclusion: High dose of disulfiram is as safe as low dose but has slightly more adverse effect before and after challenge which is statistically not significant. DER is more convincing to patients and their family members as an effective treatment and reduces hospital stay in selected patients.

8. INTENSIVE ADVERSE DRUG REACTION MONITORING IN VARIOUS SPECIALITY CLINICS OF ALL INDIA INSTITUTE OF MEDICAL SCIENCES

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Objective: Adverse drug reactions are a major cause of morbidity and mortality. Indian studies in this regard are few and bulk of information comes from the developed countries. A study was therefore carried out by National Pharmacovigilance Centre, All India Institute of Medical Sciences to know the incidence of adverse drug reactions in various departments of the institute.

Methods: Intensive bedside monitoring under a prospective adverse drug reaction surveillance program in various clinical departments like internal medicine, orthopaedics, psychiatry, hematology and institute rotary cancer hospital (IRCH) was carried out. The study included both in-hospital patients and patients from outpatient department from June 1999 to August 2000. Patients were studied prospectively.

Results: A total of 804 (M=452, F=352) patients were studied and out of these 180 (22.38%) were found to have adverse drug reactions. The incidence in individual department were as follows: Internal Medicine-26 (20.8%), Orthopaedics-42 (19.3%), Psychiatry-53 (24.7%), Hematology-31 (14.2%) and Institute Rotary Cancer Hospital-28 (100%).

Conclusion: The incidence of adverse drug reactions in various clinical specialties of All India Institute of Medical Science was found to be 22.38%. This calls for the urgent need to reinforce the pharmacovigilance in the country.

9. INVESTIGATION OF ANTIMICROBIAL USE PATTERN IN THE INTENSIVE CARE UNIT OF A TEACHING HOSPITAL IN WESTERN NEPAL

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Objective: An antimicrobial utilisation review was carried out in the intensive care unit of the Manipal teaching hospital, a tertiary care hospital in Pokhara, western Nepal to determine the prescribing frequency and rationality of use of antimicrobials.

Methods: The patient outcome, the duration of stay in the intensive care unit and the age and sex distribution of the patients were also studied. 297 inpatient records of admitted patients were studied.

Results: Mean ± SD drugs per patient was 3.45 ± 1.78. The mean ± SD age of patients was 53.9 ± 19.92 years. 50.17% of the patients received an antimicrobial. 70.47% of the antimicrobials were used therapeutically and 29.53% were used for prophylaxis. 84.56% of the antimicrobials were used without obtaining bacteriological evidence of infection. The commonest organisms isolated on culture were Pseudomonas aeruginosa, Klebsiella pneumoniae, Streptococcus pneumoniae and Staphylococcus aureus. 28.86% of the antimicrobials were prescribed for lower respiratory tract infections based on the putative site of infection. 61.86% of the antimicrobials were prescribed by the parenteral route and mainly the older generation of antimicrobials were used. In 39 out of the 149 patients prescribed an antimicrobial the use was irrational.
**Conclusions:** This study reveals a lot of scope for prescriber education to improve prescribing patterns. This study also emphasises the need for regular auditing of antimicrobial prescriptions to prevent their irrational use as well as unnecessary cost to the patients.

**GUFIC PRIZE AND INDIGENOUS PHARMACOLOGY PAPERS**

10. QUALITY ASSURANCE OF HERBAL HEPATO-PROTECTIVE FORMULATIONS THROUGH ITS FREE RADICAL SCAVENGING ACTIVITY

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**Objective:** Attempts has been made to develop quality control standards for efficacy of polyherbal hepatoprotective formulations.

**Methods:** Three different marketed hepatoprotective formulations of mostly common ingredients has been selected for present study. Liver homogenates were incubated with different concentration (100, 200 and 400 μl) of hepatoprotective syrups an fixed concentration of ferric ammonium sulphate (100 μl). The protective effects of hepatoprotective syrups against ferric ammonium sulphate induced lipid peroxidation were assessed by TBARS. (Thiobarbituric Acid Reactive Substance) method.

**Results:** The results indicated that the different syrups has a variable extent of free radical scavenging activity at same concentration. The concentration dependent variations in prevention of lipid peroxidation were also observed.

**Conclusion:** The study reveals that the hepatoprotective quality of hepatoprotective syrups can be ascertained by assessing the free radical scavenging efficacy of the formulation.

11. ANTIULCER ACTIVITY OF TEPHROSIA PURPUREA IN RATS

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**Objective:** In the present investigation the antiulcer activity of aqueous extract of roots of Tephrosia purpurea (AETP) was studied using various ulcer models in albino rats.

**Methods:** Antiulcer activity of AETP was studied in rats in whom ulcers were induced by per oral administration of absolute alcohol (1 ml) or 0.6 M HCl (1 ml) or by pyloric ligation. AETP was administered in the dose of 1 to 20 mg/kg, p.o. 30 minutes prior to ulcer induction. The antiulcer activity was assessed by determining and comparing the ulcer index of the test drug group animals with vehicle control group animals. Parameters consisting of gastric acidity, pepsin, total carbohydrates (TC) and protein concentration (PC) were estimated in the pyloric ligated rats.

**Results:** The ulcer index in the AETP treated animals was found to be significantly less in all the three models than that observed in the vehicle control animals. This antiulcer property was more prominent in animals in whom ulcers were induced by 0.6 M HCl and pyloric ligation than in whom ulcers were induced by absolute alcohol. AETP treatment decreased the gastric acidity, pepsin, protein concentration (PC) and increased the total carbohydrates concentration (TC), TC/PC ratio as compared to vehicle control in the pyloric ligated rats.

**Conclusion:** Our results suggest that AETP possesses significant antiulcer property which could be by either cytoprotective action of the drug or by inhibition of acid secretion. Further studies are in progress to elucidate the exact mechanism of action and the active principles responsible for its antiulcer potential.

12. EFFECT OF BLACK TEA EXTRACT ON GASTRO-INTESTINAL SYSTEM

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**Objectives:** To study the effect of black tea extract (BTE) and its constituents on gastrointestinal system in rodents.

**Methods:** The in vivo methods used were gastric transit by charcoal meal test, castor oil induced diarrhea and normal defaecation in mice and fluid accumulation in rat. The in vitro preparations used were isolated rat fundal strip, myenteric plexus of guinea-pig ileum and peristalsis of guinea pig ileum by Trendelenberg’s method.

**Results:** BTE increased gastric transit at low concentrations and possessed anti-diarrhoeal activity at higher concentrations. The increase in gastric transit produced by low concentrations of BTE was reduced after pretreatment with atropine, morphone, MCN-A-343 and L-arginine. BTE facilitated the peristaltic reflex and markedly enhanced the 'tonic hump' response to transmural stimulation of longitudinal muscle of guinea-pig ileum. BTE and L-NMMA also significantly reduced the field stimulated NANC relaxation of isolated rat fundal strips. Naloxone significantly inhibited the anti-diarrhoeal activity of BTE and loperamide.

**Conclusion:** A cholinergic involvement and a partial role of prostaglandin and nitric oxide are responsible for the effect of BTE on gastrointestinal motility. Opioid system plays a role in the anti-diarrhoeal effect of BTE.

13. LOCAL ANAESTHETIC EFFECT OF SPILANTHES ACRELLA IN EXPERIMENTAL ANIMAL MODELS

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**Objective:** Spilanthes acmella is an indigenous herb from the family Asteraceae. It grows throughout the tropics. The whole plant has been described to possess medicinal properties. The leaves produce a tingling, numbing effect when chewed. The flowers are used to relieve toothache. The present study was undertaken to evaluate the local anaesthetic (LA) action of Spilanthes acmella in experimental animal models.

**Methods:** Aqueous extract of Spilanthes acmella (ASA) was tested for LA action by (i) intracutaneous wheal in guinea pigs at doses of 10 mg, 20 mg from 20% w/v in 0.9% saline solution (Inj. 0.2ml), (ii) plexus anesthesia in frogs with drug solution sufficient to dip the lumbar plexus from 20% w/v in 0.7% saline solution.
Normal saline and 2% xylocaine were used as control and standard respectively.

**Result**: The values of negative responses with standard, test and control drugs (mean±SEM) were 35±0.51, 25.33±3.27 (10 mg), 31.33±1.08 (20 mg) and 1.5±0.76 with a 'p' value of <0.001 with control in all the cases. The time of onset of LA activity (plexus anaesthesia in frogs using 0.1 (N) Hcl as stimulus for foot withdrawal reflex) of ASA and xylocaine 2% were 5.33±0.57 and 2.75±0.31 respectively. The foot withdrawal reflex was positive till 24.16±1.54 mins in control group.

**Conclusion**: The present study indicates that ASA has highly significant local anaesthetic action.

14. **ANTI-HYPERGLYCEMIC AND ANTI-OXIDANT ROLE OF MULBERRY (M.INDICA L.) LEAVES**

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**Objective**: To investigate the anti-hyperglycemic and anti-oxidant role of mulberry (M.indica L.) leaves in diabetic rats and to compare with that of standard anti-diabetic drug, glibenclamide.

**Methods**: Streptozotocin induced (55 mg/kg) diabetic male wistar albino rats were used as experimental models; one group was given standard diet containing 25% (as per dose response) dry mulberry leaf powder, another group was given glibenclamide (0.5 mg/kg) for a period of 8 weeks. The anti-hyperglycemic and anti-oxidant role was assessed by determining their effect on blood glucose, lipid peroxidation in erythrocytes and on the activity of various antioxidant enzymes in erythrocytes and compared with that of controls.

**Results**: Mulberry treated diabetic animals showed a good glycemic control vs glibenclamide. Increased lipid peroxidation (123%) in erythrocytes observed in diabetic controls was significantly reduced by mulberry leaves (41%) in a better way than the drug. Decreased activities of antioxidant enzymes viz., glutathione peroxidase, glutathione reductase, glutathione-s-transferase and increased activity of catalase observed in uncontrolled diabetes were reverted to normal by mulberry treatment more efficiently than the drug. This indicates controlled generation of free radicals as evidenced by decreased lipid peroxidation in RBC, resulted due to a good glycemic control achieved by mulberry leaves.

**Conclusion**: Mulberry leaves possess anti-hyperglycemic and anti-oxidant properties.

15. **THE ANTIULCER EFFECTS OF AZADIRACHTA INDICA IN PYLORIC-LIGATED RATS**

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**Objective**: To study the antiulcer effect of Azadirachta indica (Neem) on gastric ulcers induced by pyloric ligation method in albino rats.

**Methods**: Albino rats of either sex weighing between 150-250 g were divided into six groups of six in each. The animals were fasted for 24 h. Gastric ulcer was induced by Shay’s method of pyloric ligation. Neem leaf extract (NLE) was administered in doses of 10, 20, 40, 80 and 160 mg/kg to groups I to VI respectively. The animals were sacrificed after 19 h of pyloric ligation and their stomachs were examined for ulcers. The gastric contents were subjected to analysis of free and total acidity and volume of gastric secretion was also noted.

**Results**: NLE was found to reduce the ulcer index, free and total acidity as well as the volume of gastric secretion significantly at 80 and 160 mg/kg does.

**Conclusion**: NLE possesses significant antiulcer and antisecretory effect in pyloric ligated rats.

16. **ANTICONVULSANT EFFECT OF LORAZEPAM IN COMBINATION WITH CALCIUM CHANNEL BLOCKERS**

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**Objectives**: To study the anticonvulsant activity of lorazepam (LZM) a Benzodiazepine, on various (acute and chronic) models of convulsions in rats and also to study its effect in combination with various, Calcium Channel Blockers(CCBs) viz., nimodipine, nimodipine and verapamil.

**Methods**: The anticonvulsant profile of LZM and its combination with CCBs was evaluated in two acute experimental models of epilepsy viz. (i) MES seizure test and (ii) PTZ-induced convulsions as well as on a chronic model of epilepsy viz. PTZ-induced kindling.

**Results**: In acute studies LZM (0.1-5 mg/kg, i.p.) significantly decreased the duration of tonic hind limb extensor phase (THE) in a dose-dependant manner and also reduced the incidence of convulsions in MES. PTZ (50 mg/kg) treated animals, LZM (0.01-5mg /kg) significantly delayed the onset and decreased the duration of clonic convulsions. LZM (1mg/kg) protected the kindled animals, significantly (PTZ 30 mg/kg twice weekly for 8-9 weeks). In combination studies, LZM (1 mg/kg) was combined with sub-threshold doses of nifedipine (2 mg/kg), Nimodipine (1 mg/kg) and verapamil (10 mg/kg). Anticonvulsant effect of LZM was potentiated by nifedipine only in MES model.

**Conclusion**: The results with acute and chronic studies suggest that LZM possesses significant anticonvulsant activity and also improves the anticonvulsant profile in its combination with nifedipine.

17. **BLOCKADE OF LPS - MEDIATED HYPERALGESIA BY L-NAME, A NITRIC OXIDE SYNTHASE INHIBITOR: MODULATORY ROLE OF NO AND CYCLOOXYGENASE ENZYME**

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**Objectives:** To investigate the role of iNOS in LPS - mediated hyperalgesia in mice and the regulatory role between prostanoids in vivo using L-NAME, a non - specific nitric oxide synthase inhibitor, and spirulina purified protein (SPP) containing G-phyocyanin, NS-398 and rofecoxib, COX-2 selective inhibitor in various nociceptive assays.

**Methods:** LPS (50 μg/mouse, i.p. or 10 μg/paw, i.pl.) mediated hyperalgesia was assessed via chemical, thermal and mechanical nociceptive tests in mice.

**Results:** Treatments of mice with L-NAME (5-20 mg/kg, i.p. or 10-40 mcg/paw, i.pl.) significantly reversed the LPS-mediated hyperalgesia in peripheral or central nociception in mice. Treatment with SPP (50 and 100 mg/kg, p.o.), NS-398 (10 mg/kg, p.o.) and rofecoxib (10 mg/kg, p.o.), significantly exhibited antihyperalgesic effect in chemical hyperalgesia. These COX-2 inhibitors significantly potentiated the L-NAME reversal of LPS-mediated hyperalgesia.

**Conclusion:** These results suggest that iNOS plays a significant role in LPS - mediated hyperalgesia and simultaneous inhibition of COX-2 enzyme leads to modulatory effect between NO and prostanoids.

18. **REVERSAL OF LIPOPOLYSACCHARIDE-INDUCED BEHAVIORAL AND THERMAL HYPERALGESIA BY QUERCETIN**

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**Objectives:** To investigate the modulatory role of quercetin on Lipopolysaccharide (LPS) induced hyperalgesia in mice.

**Methods:** Laka mice (20-30 g) of either sex bred in Central Animal House facility of Panjab University were used in the present study. Central nociception was assessed with paw flick and hot plate methods and behavioural hyperalgesia was assessed by paw licking, rearing and redness after the intra-plantar injection of LPS (10 μg/kg).

**Results:** LPS induced a significant decrease in nociceptive threshold in hot plate and tail flick tests at 6, 10, 18 and 24 h after intraplantar LPS injection. LPS also led to a marked increase in redness and licking of the injected paw and decrease in rearing behaviour. Quercetin (50 and 100 mg/kg, i.p.), like dexamethasone (0.5 mg/kg, i.p.) and rofecoxib (5 mg/kg, i.p.) given 30 min before and 8, 19 h after LPS challenge attenuated central as well as behavioral hyperalgesia. The attenuation on LPS-induced hyperalgesia by quercetin was significantly reversed by naloxone (2 mg/kg) whereas yohimbine (5 mg/kg) had no effect on alteration of pain response by quercetin.

**Conclusion:** The results of the present study demonstrated that quercetin suppresses endotoxin-induced behavioral and thermal hyperalgesia through opioidergic mechanisms.

19. **EVALUATION OF THE ROLE OF NITRIC OXIDE IN IMMUNE RESPONSIVENESS IN STRESSED AND NON-STRESSED ANIMALS**

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**Objective:** Stress reportedly affects various facets of the immune system. CNS besides being crucial for stress also regulates immune function. Common neural substrates like limbic-hypothalamic-pituitary-adrenal (LHPA) axis are involved in such CNS-immune system interaction. Current data indicate a role for nitric oxide (NO) in the regulation of LHPA axis. The present study investigates the role of NO in immune modulation in both stressed and non-stressed animals.

**Methods:** The study was carried out in male Wistar rats and Swiss albino mice. For measuring humoral immune responses, haemagglutination titre to sheep red blood cells (SRBC) and for cell-mediated immune responses foot pad thickness test and % leucocyte migration inhibition (% LMI) test were performed.

**Results:** Administration of L-arginine (1 g/kg, i.p.) before subjecting the animals or restraint stress (RS) antagonized the immunosuppressive effect of RS on both humoral and cell-mediated immune responses. Pretreating the animals with 7-nitroindazole (7-NI) (50 mg/kg, i.p.), a brain NO synthase inhibitor further enhanced the RS-induced immunosuppression. L-arginine (500 mg-1 g/kg, i.p.) when administered to naive non-stressed animals produced a significant reduction in antiSRBC antibody titre, foot-pad thickness and % LMI. However, unlike its effect on RS-induced immunomodulation 7-NI failed to modulate immune responsiveness in non-stressed animals, although it significantly blocked the immune suppressive effects of L-arginine.

**Conclusion:** NO appears to play an important role in immune responsiveness especially during stress-induced immuno-modulation.

20. **SILDENAFIL, A PHOSPHODIESTERASE 5 INHIBITOR ENHANCES THE ANTINOCICEPTIVE EFFECT OF MORPHINE**

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**Objective:** To investigate the peripheral effect of sildenafil (a specific inhibitor of PDE5) on morphine - induced antinociception.

**Methods:** The antinociceptive activity of an inhibitor of phosphodiesterase 5 alone or combined with morphine was assessed using paw pressure behavioural test (Randall - Selitto test) and acetic acid - induced writhing assay in experimental animals.

**Results:** Local administration of sildenafil (phosphodiesterase 5 inhibitor) exhibited a dose - dependent (50-200 mcg/paw, i.pl) antinociceptive effect against paw pressure test. Sildenafil also demonstrated antinociceptive effect (1-10 mg/kg, i.p.) against writhing assay. Co-administration of sildenafil (100 mcg/paw, i.pl and 2 mg/kg, i.p.) significantly enhanced the antinociceptive effect of morphine (2 mcg/paw, i.pl and 2 mg/kg, i.p respectively). The antinociception produced by the drugs alone or combined was due to a local action, as its administration in the contralateral paws was ineffective. Pretreatment with L-NAME (nitric oxide synthesis inhibitor), methylene blue (guyanlyl cyclase inhibitor) or naloxone (opioid receptor antagonist) blocked the effect of sildenafil - morphine combination in both the tests.
**Conclusion:** These results suggest that opioid receptors, NO and cyclic GMP mechanisms are involved in the combined antinociceptive effect. Further, sildenafil produced antinociception per se and increased the response of morphine, probably through the inhibition of cyclic GMP degradation.

**21. EFFECT OF 5-HT \(_3\) ANTAGONIST-ONDANSETRON ON NOCICEPTION**

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**Objective:** 5-HT\(_3\), receptors present at peripheral nerve endings mediate nociception and in the descending fibers from Nucleus Raphe Magnus (NRM) in spinal cord, they have inhibitory action on nociception path. So this study was taken up to find the effect of 5-HT\(_3\) antagonist-ondansetron on nociception.

**Methods:** 12 groups of albino rats, six in each group were utilized for this study. Both Tail Flick Latency (TFL) & Acetic acid-induced writhing were observed for nociceptive study. Normal saline was used as negative and morphine as positive control drugs. Normal saline 1 ml, Ondansetron 1, 2 and 4 mg/kg and Morphine 1 and 2 mg/kg were administered intraperitoneally to separate groups of rats for recording the TFL and perform the Writhing test.

**Results:** Ondansetron in the dose of 2 and 4 mg/kg significantly increased the TFL and decreased the Acetic-acid Writhing, indicating significant anti-nociceptive action. In comparison to morphine-the antinociceptive action of ondansetron was slow in onset but of prolonged duration.

**Conclusion:** Ondansetron possess significant ‘anti-nociceptive’ action in addition to its anti-emetic action.

**22. EFFECT OF HONEY ON PHENYTOIN KINETICS IN RABBITS**

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**Objective:** To evaluate the effect of honey on phenytoin kinetics in rabbits.

**Methods:** Single dose of phenytoin (10 mg/kg, p.o.) along with saline was administered to New Zealand white rabbits (n=8). Blood samples were collected at 0, 0.5, 1, 1.5, 2, 4, 6, 8, 10, 12, 14, 16 and 24 hrs after drug administration from marginal ear vein. After a washout period of seven days phenytoin (10 mg/kg, p.o.) was administered with honey (2.34 ml/kg, p.o.) and the blood samples were collected as above. To the same animal honey (2.34 ml/kg, p.o. single dose) was continued for seven days. On 8th day a combination dose of honey and phenytoin (3 ml) alongwith phenytoin (28 mg/kg) was administered and blood samples were drawn from 0-48 h. Plasma was separated and assayed for phenytoin by HPLC technique and various pharmacokinetic parameters were calculated.

**Results:** In single dose, as well as multiple dose honey, there was significant increase in C\(_{\text{max}}\), T\(_{\text{max}}\), t\(_{1/2}\) a, t\(_{1/2}\)e and AUC (0-\(\infty\)) of phenytoin.

**Conclusion:** Honey increases the rate and extent of absorption of phenytoin. The result warrants the reduction of phenytoin dose when administered with honey, to avoid any toxicity.

**23. INFLUENCE OF HONEY ON THE PHARMACOKINETICS OF PHENYTOIN IN RABBITS**

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Department of Pharmacology, PGIMER, Chandigarh.

**Objective:** To find out the effect of honey on the pharmacokinetics of phenytoin in rabbits.

**Methods:** In a cross-over study, phenytoin was given orally in a dose of 28 mg/kg and blood samples were drawn at different time intervals from 0-24 h. After a washout period of 7 days, honey in a dose of (3 ml) was administered alongwith phenytoin (28 mg/kg) and blood samples were drawn from 0-48 h. After this 3 ml honey was given everyday for another 7 days. On 8th day honey (3 ml) alongwith phenytoin (28 mg/kg) was administered and blood samples were drawn from 0-48 h. Plasma was separated and assayed for phenytoin by HPLC technique and various pharmacokinetic parameters were calculated.

**Results:** In the dose of honey, there was significant increase in C\(_{\text{max}}\), T\(_{\text{max}}\), t\(_{1/2}\) a, t\(_{1/2}\)e and AUC (0-\(\infty\)) of phenytoin.

**Conclusion:** Honey increases the rate and extent of absorption of phenytoin. The result warrants the reduction of phenytoin dose when administered with honey, to avoid any toxicity.

**24. EFFECT OF TRIMETAZIDINE AND DESFERRIOXAMINE ON GLYCEROL INDUCED ACUTE RENAL FAILURE**

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**Objective:** Rhabdomyolysis, non-traumatic and traumatic, may account for approximately 10-15% of all cases of acute renal failure (ARF). Ischemia, vascular congestion, and reactive oxygen species (ROS) seems to play the causative role in ARF. The aim of this study was to evaluate the effects of trimetazidine, an antiischemic drug having antioxidative property, and desferrioxamine, an iron chelator on the experimental ARF induced by glycerol.

**Methods:** Thirty male wistar rats weighing 150-250 g were included in the study. The rats were randomly divided into five groups; group 1 served as control; group 2 was given 50% glycerol (8 ml/kg, i.m.); group 3 was given glycerol plus trimetazidine (3 mg/kg, i.p. 30 min before glycerol and repeated after 12 h); group 4 was given glycerol plus desferrioxamine (50 mg/kg & 100 mg/kg respectively, s.c. 30 min before glycerol and repeated after 12 h). The renal injury was assessed by measuring serum creatinine, BUN, creatinine and urea clearance. The oxidative stress was measured by renal MDA levels, reduced glutathione and by enzymatic activity of catalase, glutathione reductase and superoxide dismutase.

**Results:** BUN and serum creatinine were increased significantly in glycerol treated group and there was a significant decrease in urea and creatinine clearance. This deterioration in renal function tests was improved significantly in desferrioxamine treated animals, however, this was not the case in trimetazidine treated animals.

**Conclusion:** Desferrioxamine, by interacting with Fenton reaction chemistry, and Trimetazidine, by its antiischemic and antioxidative
property protected the kidney against the oxidative stress produced by glycerol induced ARF. Based on these results this study points towards iron as a potential mediator in glycerol induced ARF.

25. EFFECT OF THE ANTI-OXIDANTS ALPHA-TOCOPHEROL ACETATE AND SODIUM SELENITE ON HEPATOTOXICITY INDUCED BY ANTI-TUBERCULAR DRUGS IN RATS.

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Objective: To assess the hepatoprotective effects of alpha-tocopherol acetate, sodium selenite and their combination on anti-tubercular drugs induced hepatotoxicity in albino rats.

Methods: Hepatotoxicity was produced in rats by combination of anti-tubercular drugs namely INH, rifampicin and pyrazinamide given orally as suspension for 30 days. Treatment groups received alpha-tocopherol acetate, sodium selenite and their combination respectively orally also for 30 days along with the anti-tubercular drugs. Liver damage was assessed by biochemical and histological parameters at the end of 30 days period.

Results: Alpha-tocopherol acetate, sodium selenite and their combination significantly reduced the levels of serum bilirubin, serum alanine aminotransferase, serum aspartate aminotransferase and serum alkaline phosphatase and increased the levels of serum protein as compared to the control group receiving anti-tubercular drug. Anti-oxidants when used in combination in this study also significantly prevented the histological changes in livers as compared to rats that received antitubercular drugs.

Conclusion: Alpha-tocopherol acetate and sodium selenite show hepatoprotective action against anti-tubercular drugs induced hepatic damage in rats.

26. RELATIONSHIP BETWEEN CHANGES IN THE GLYCAEMIC STATE AND PAIN THRESHOLD INDUCED BY PROKINETIC DRUGS.

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Objective: To study the effect of prokinetic drugs on glycaemic state and to correlate, if any, with their anti-nociceptive responses.

Methods: Adult male Swiss Albino mice were used. The anti-nociceptive effect of the prokinetic drugs, domperidone (0.05-5 mg/kg, p.o./i.p.) and cisapride (0.05-5 mg/kg, p.o./i.p.) was assessed using acetic acid induced abdominal constriction assay. The drugs were administered 30 minutes prior to anti-nociceptive assay. In the same animals the blood glucose was measured using Advantage glucometer using appropriate glucose sticks. This was done just prior to the administration of the prokinetic drugs and acetic acid challenge. The results were subjected to ANOVA followed by Dunnett's test.

Results: Domperidone when given orally produced a dose-related inhibition of abdominal constriction from 0% to a maximum of 60.1%. A similar effect was recorded after intraperitoneal administration. Cisapride also inhibited constrictions almost to the similar degree in the dose ranges used. However, the lowest dose (0.05 mg/kg, i.p.) produced 15.9% inhibition in contrast to 0% after domperidone. The blood glucose levels in normal mice ranged between 113 to 137 mg/dl. Neither domperidone nor cisapride significantly altered blood glucose in drug treated mice.

Conclusion: The results indicate that prokinetic drugs possessing anti-nociceptive response per se did not significantly alter the glycaemic state of the mice. This indicates that changes in the glycaemic and the algesic states are dissociated.

27. GASTRIC ANTIULCER ACTIVITY OF CALCIUM CHANNEL BLOCKERS (CCBS) IN RATS.

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Objective: 1) To evaluate the antiulcer effects of CCBS in an experimental model of gastric ulceration. 2) To compare these effects with ranitidine.

Methods: 80 albino rats were divided randomly into 8 groups i.e. 1 - 8. All the rats received aspirin in the dose of 40 mg/100 gm on the first 3 days of the study. Rats of groups 2, 3 & 4 received low doses of Nifedipine (0.25 mg/100 gm), Verapamil (1 mg/100 gm) and Diltiazem (1.5 mg/100 gm) respectively while rats of groups 5, 6 & 7 received the same drugs in high doses that were twice the low doses i.e. 0.5 mg, 2 mg and 3 mg/100 gm body weight respectively. Rats of group 8 were administered ranitidine in the dose of 2.7 mg/100 gm.

Results: Rats from groups 2-8 showed a significant reduction in the ulcer index and the histopathology scores. The CCBS showed significant anti ulcer activity in both the doses. Verapamil and Diltiazem in high doses were as effective as Ranitidine in reducing the ulcer index scores. All the CCBS were comparable to ranitidine in their ability to reduce the histopathology scores in both the doses.

Conclusion: All the CCBS showed excellent anti-ulcer activity in aspirin-induced gastric ulceration. This anti-ulcer activity was comparable to that of Ranitidine.

28. STUDY OF PRESCRIBING PATTERN OF ANTIMICROBIAL AND OTHER AGENTS IN INPATIENTS OF IGMC, NAGPUR.

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Objective: Evaluation of prescribing pattern of all drugs in inpatients with a special emphasis on antimicrobial agent prescribing in major clinical departments.

Methods: A prospective cross sectional study was conducted in inpatients of IGMC, over a six months period. The data was collected randomly from case records of 190 inpatients admitted in medicine, surgery, gynecology and obstetrics department. Parameters included were demographic data of patients, drugs given and laboratory investigations. Analysis of rationality of administration of antimicrobials was done as per modified Kunin's criteria.

Results: Number of drugs prescribed in 190 patients was 1105 with mean number of drugs per patients 6. Average duration of
The most frequently prescribed group of drugs were antimicrobial agents (34.57%) followed by vitamins (19.18%). Amoxicillin was most commonly prescribed antimicrobial agent which constitutes 27.74% of all antimicrobials followed by gentamicin (21.20%). Drugs prescribed by brand name were 46.15%, in fixed dose combinations were 25.6% and those administered by parenteral route were 43.16%. In 23.13% patients more than three antimicrobial agents were prescribed and only 16 patients were treated according to the culture sensitivity report. According to modified Kunin’s criteria, use of antimicrobial agent was inappropriate in 49.7% patients.

Conclusion: The results indicate a considerable scope for improving the prescribing pattern of drugs and minimizing the use of antimicrobial agents, thus helping the clinician to achieve the goal of rational use of drugs.

29. CISAPRIDE AND METOCLOPRAMIDE ON GL INERTIA IN MORPHINE TREATED MICE

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Objective: Opioids are effective analgesics for moderate to severe pain such as post surgical/cancer-associated pain. Opioids often produce undesirable effects on gastrointestinal tract such as constipation, bloating and abdominal distension. Various prokinetics are used for reversing GI inertia, but it is not known which prokinetic is better in such situations. The objective was to study the relative efficacy of cisapride and metoclopramide on GI inertia in morphine treated mice.

Methods: Male albino mice weighing between 25-30 g, fasted for 24 h with access to water ad libitum were used. Each experimental group consisted of six animals. Methyl cellulose (1.5%) with Phenol red (0.4%) in water was used as test meal to measure small intestinal transit (SIT). Cisapride (10 mg/kg) and metoclopramide (10 mg/kg) alone or along with morphine (1 mg/kg, s.c.) was given p.o. to mice 45 min before the test meal. Morphine was given s.c. 15 min before the test meal. Animals were killed 15 min after the test meal to measure SIT.

Results: Morphine significantly reduced the SIT compared to the controls (19.8±1.25 vs 51.11±3.6). Cisapride did not show any prokinetic effect compared to the controls however it antagonized the inhibitory effect of morphine by 66.7%. In contrast to this metoclopramide (74.05±3.97) increased SIT but when combined with morphine this effect was reduced by 59%.

Conclusion: Cisapride is a better prokinetic agent in antagonizing morphine induced GI inertia.

30. EFFECT OF THEOPHYLLINE ON DURATION OF HOSPITAL STAY IN ASTHMA

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Objective: To observe the effect of theophylline on the duration of hospital stay in hospitalized adult asthma patients.

Methods: Thirty six asthma patients (Age 42.1±16 years; 17 males, 19 females) were admitted in medical ward of hospital. They were treated with β2 agonist (inhalation and nebulization) corticosteroids (inhalation and oral) and broad spectrum antibiotics when required. Twelve patients were not treated with theophylline. Twelve other patients were treated with theophylline tablet 300 mg orally 12 h. 12 other patients were treated with injection aminophylline 500 mg intravenously slowly 12 h. All the patients were discharged when their general physical condition had improved and remained stable for next 12 h. Data collected were analysed by statistical function of MS Excel by using MS-Win 98.

Results: 12 Asthma patients who were not treated with theophylline had average duration of hospital stay of 14.2±12.1 days. 12 other patients who were treated with theophylline tablet 300 mg orally had average duration of hospital stay of 6.8±4.06 days. 12 other patients treated with injection aminophylline 500 mg intravenously slowly, had average duration of hospital stay of 5.3±2.2 days. There was negative correlation (r=0.45; P<0.01) between theophylline dose and duration of hospital stay.

Conclusion: Theophylline used for treatment of hospitalised adult asthma patients significantly (tablet P<0.07 and injection P<0.05) reduced the duration of hospital stay in asthma patients. This may reduce the cost of treatment and cost of hospital stay in asthma patients.
Conclusion: Though the selection of antimicrobial drugs used in dermatology were rational to a large extent, on the basis of WHO model prescribing information, some lacunae were observed and these issues were discussed with clinicians in relation to various aspects of drug use. The results indicate that there is a scope for improving prescribing habits and such periodic audit of drug prescribing is desirable in rationalizing the prescribing practices.

32. EVALUATION OF A HERBOMINERAL PREPARATION IN POSTMENOPAUSAL OSTEOPOROSIS

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Objective: Osteoporosis is common in postmenopausal women, resulting in progressive decrease in bone mineral density, which lead to increased susceptibility to fractures and serious morbidity. Hormone replacement therapy is recommended for prevention and treatment of postmenopausal osteoporosis. However many postmenopausal women decline HRT or discontinue it because of side effects. Hence there is a need to explore clinical benefits of herbal medicines in improving bone mineral density. This study was performed as an early exploratory short term study to determine the benefits of a herbomineral preparation.

Methods: After obtaining Institutional Ethics Committee permission and written informed consent, 50 postmenopausal women were randomized into two groups and received either drug or placebo, in a dose of two tablets twice daily for six months. Clinical assessment of back pain and bone density measurements by Dual Energy X ray Absorptiometry - DEXA scan were carried out at baseline and at the end of six months of treatment.

Results: There was a significant improvement in the T score and BMD at the level of Lumbar spine (p<0.05) and femur neck (p>0.05) as compared to the basal scores in patients receiving the drug, while a slight reduction was noted in the T score and BMD in patients receiving placebo therapy as compared to their basal scores. There was significant improvement in the clinical symptoms of back pain in both the drug and placebo groups.

Conclusion: It is evident from this study that the herbomineral agent exerts beneficial effects. It is important to note that although the clinical symptoms improved equally in placebo and drug treated group, bone mineral density improvements were seen in the drug treated group only. Hence in clinical studies evaluating newer agents for osteoporosis, it is necessary to include bone mineral density studies in addition to clinical symptomatology to confirm efficacy. Further, long term studies with the herbomineral preparation must be conducted for confirmation of efficacy.

33. PRESCRIBING TRENDS IN ESSENTIAL HYPERTENSION

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Objective: To compare the Antihypertensive prescribing trends in a teaching hospital in Mumbai with the guidelines laid down in the 6th Report of Joint National Committee (JNC) on Detection, Evaluation and Treatment of Hypertension.

Methods: Patients with Essential hypertension attending the Medicine and Hypertension OPDs of B.Y.L. Nair Hospital from July 10 to September 10, 2001 were interviewed. Relevant information was obtained from these interviews and from the patients' OPD papers. Antihypertensive prescribing trends were analysed, and compared with JNC-6 recommendations.

Results: 62.09% of patients were on monotherapy and 37.54% were on combination therapy. In monotherapy, Calcium channel blockers (62.79%) were the most frequently prescribed class in all patient profiles. Immediate release Nifedipine was the most frequently prescribed drug. This was in variance with JNC recommendations. Drug combinations used were rational in all patients. Beta blocker + CCB was the most frequently prescribed two-drug combination. Prescription audit revealed ADRs in 8.3% patients. ADRs were most commonly associated with the use of Nifedipine.

Conclusion: Antihypertensive prescribing pattern in Nair Hospital is governed by the availability of the drugs in hospital pharmacy, rather than the JNC recommendations. Nifedipine, Propranolol and Atenolol are the only antihypertensive drugs on hospital schedule. It is desirable to have at least one more antihypertensive drug on the hospital schedule-either Amlodipine, Enalapril or Hydrochlorothiazide. There is a need to strike a balance between the limited choice of drugs available and the JNC recommendations.

34. SURVEILLANCE OF DRUG PRESCRIBING TRENDS IN SKIN OPD OF IGMCH

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Introduction: A prospective study of prescription pattern of dermatological drugs in O.P.D. patients was carried out to provide feedback to clinicians, policymakers and research workers of IGMC Nagpur.

Objective: Surveillance of drug prescribing trends in skin O.P.D. of IGMCH, Nagpur.

Methods: Data was collected from records of patients attending skin O.P.D. of IGMCH, Nagpur; for period of 1st Feb. to 15th Feb 2001. A total No. 336 records of skin O.P.D. patients were studied regarding corticosteroids, antimicrobial and antifungal prescribing. The details studied were name of drug, dose, route frequency and number of drugs per prescription.

Results: The total No. of drugs prescribed in 336 patients was 900. i.e. on average 2.67 drug were prescribed per patient. Out of this average 34.44% drugs were topical and 65.56% were oral.

The most commonly used drugs were antihistaminics 64% (chlorpheniramine maleate), antibiotics 62.5% (Septiran, Doxycycline) Corticosteroids 37% (Topical betamethasone in combination with gentamicin, miconazole and salicylic acid). Other drugs used were keratolytics, emollients, antiseptics, ectoparasiticides, vitamins ranging from 18 to 21%.

Conclusion: Periodic therapeutic audit is necessary to rationalise the use of drugs.
35. **PATTERN OF USE OF ALTERNATIVE MEDICINE IN EPILLEPTIC PATIENTS IN A TERTIARY CARE HOSPITAL**

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**Objective:** Many patients use alternative medicine for their health problems especially where long-term treatment is required. Epilepsy is the most prevalent neurological disorder requiring long term treatment and compliance. The objective of the study was to see the pattern of use of alternative medicine in epileptic patients.

**Methods:** We interviewed 1000 patients with seizure disorder visiting the Neurology Outpatient department regarding use of alternative medicine in the past. The pattern of use, the education status and the cause for deviating towards these therapies was noted in these patients.

**Results:** Overall 32% of patients had used alternative medicines in the past out of which ayurvedic medicines were the most frequently used (81%). Use of such therapies was more frequent in the uneducated rural population (67%). Influence of society and family was the most common cause for deviating towards these therapies. All the patients who took these therapies visited the provider of such therapies.

**Conclusion:** As more patients use alternative medicines, physicians should ask their patients regarding use of these therapies and should discuss these practices with their patients in order to safeguard their health.

36. **POST MARKETING SURVEILLANCE STUDY OF PANTOPRAZOLE IN INDIAN PATIENTS**

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**Introduction:** Proton pump Inhibitors are drugs of choice for suppressing gastric acid production. They provide the most rapid relief of gastro esophageal reflux disease symptoms as well as esophageal healing when compared with H$_2$ receptor blockers or prokinetic agents.

Their superiority over H$_2$ receptor blockers has also been demonstrated when used in maintaining esophageal healing and symptom relief.

Pantoprazole is a new PPI, which was launched in 1999. This study was conducted to determine its safety and tolerability in a cross section of the Indian population.

**Methods:** This was a open study in 390 patients involving 39 physicians at various centers throughout India. Details as to the diagnosis of the patient, the dose and duration of therapy, predominant symptom observed, the degree and day of relief as observed by the patient and reported by the doctor, concomitant medication and details of adverse events were documented.

**Results:** Complete relief was observed in 285 patients (73%), partial relief in 81 patients (20.76%) and none in 24 patients (6.15%). Average symptom relief on day 8 of starting therapy was observed. Adverse drug reactions were observed in 11% of patients.

**Conclusion:** In conclusion pantoprazole demonstrated good efficacy in the various indications in which it was used. The efficacy of pantoprazole was found to be comparable to that in published literature, it is well tolerated, with there being no serious adverse events observed during the course of the study.

**INDIGENOUS PHARMACOLOGY**

37. **INFLUENCE OF BRYOPHYLLUM PINNATUM (LAM.) LEAF EXTRACT ON WOUND HEALING IN ALBINO RATS**

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**Objective:** To study the effect of Bryophyllum Pinnatum (Lam.) leaf extracts viz., petrol ether (P.E), alcohol (A.L.E) and water (W.E) on healing of excision, incision and dead space wounds in albino rats.

**Methods:** Excision, resutured incision and dead space wounds were induced in Wistar rats of either sex under light ether anaesthesia, taking aseptic precautions control animals received normal saline and other groups received P.E., W.E. and A.L.E. for a period of 10 days. On eleventh day after estimating the breaking strength of resutured incision wounds (under anaesthesia) animals were sacrificed and the granulomas were removed for estimating the breaking strength, quantification of granuloma tissue and their biochemical and histological studies in control and various treated groups were done, whereas only W.E was used for excision wounds in order to mimic the traditional use of the drug in folk medicine, epithelisation time was measured from day-0 (wounding day) till the day of scar totally falling of with no raw wound left behind. The shape and size of the scars were noted on the day of complete epithelisation and were followed up to the 21st post wounding day.

**Results:** All the three extracts viz P.E, W.E and AL. E showed significant increase in the Breaking strength of Incision wound, cotton pellet dry weight and hydroxyproline content of granulation tissue (p<0.001) when compared to control group and W.E showed significant increase in wound contraction and formation of scars on 17th post wounding day.

**Conclusion:** The results of the present study indicate that not only locally applied water extract hastened the healing process in open wounds but all the extracts administered systemically promoted the healing of resutured incision wounds and dead space wounds, as indicated by increased breaking strength and hydroxyproline content of the tissue.

38. **PARTICIPATION OF $\alpha$-RECEPTORS IN ANTI-NOCICEPTIVE ACTIVITY OF QUERCETIN, A DIETARY FLAVONOL**

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**Introduction:** Central noradrenergic system appears to play a modulatory role in the transmission of pain impulses. Electrical
stimulation of brain stem noradrenergic nuclei is reported to produce analgesia. Clonidine, a central α₂-receptor agonist possess profound analgesic property. Quercetin, a flavonol isolated from querciton bark (Quercus discolor) is reported to competitively inhibit the binding of [³H] clonidine to α₂-receptors. There are sporadic reports on the significant analgesic activity for certain flavonoids such as hydroxyethyl rutoside and gossypin but the underlying mechanisms have not been studied as yet.

**Objective:** The present study was aimed to explore the antinociceptive potential of quercetin, a bioflavonoid and to have an insight into the possible mechanism.

**Methods:** Swiss albino mice (20-30 g) of either sex were used. The nociceptive threshold was measured by tail flick latency to radiant heat. Baseline latency to tail withdraw to the radiant heat source (3-5 sec) was established. A cut off time of 10 sec was used to prevent any injury to the tail. In hot plate test mice were individually placed on a Eddy’s hot plate maintained at a constant temperature (55±0.3°C). The latency to first signs of paw licking or jump response to avoid heat nociception was taken as an index of nociceptive threshold with cut off time of 15 seconds.

**Results:**
1. Quercetin (25-100 mg/kg, i.p., suspended in 0.5% CMC in normal saline) showed a dose dependent increase in nociception threshold against tail flick and hot plate assay.
2. Quercetin induced antinociception could be attenuated by pretreatment with yohimbine, a selective alpha 2 blocker.
3. A significant analgesic response was demonstrated when subeffective dose of quercetin (25 mg/kg) was combined with a subeffective dose of clonidine (0.25 mg/kg) and this response was also sensitive and reversed by yohimbine.

**Conclusion:** On the basis of this data we put forward the hypothesis that α₂-receptors participate in mediation of antinociceptive activity of quercetin.

39. **ANTIPYRETIC EFFECT OF NEEM SEED OIL ON ALBINO RATS**

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**Objective:** Azadirachta Indica (Neem), an indigenous plant is reported to have several medicinal properties. The present work is undertaken to study the antipyretic activity of Neem Seed Oil (NSO) on Albino rats.

**Methods:** NSO was obtained in pure form from the Indian Herbs research supply Company Limited, Saharanpur, (U.P.). The antipyretic activity of NSO was studied in Brewer’s yeast induced pyrexia in rats. Fever was induced by injecting 20 ml/kg of 20% Brewer’s yeast suspension in normal saline in inguinal region and rectal temperature was recorded by clinical thermometer. NSO in the doses of 1/4 ml, ½ ml, 1 ml/kg body weight were injected intraperitoneally to different group of rats 10 h after the yeast injection and the temperature was recorded at intervals and the results were statistically analyzed.

**Result:** NSO in the dose of ⅔ and 1ml/kg showed significant antipyretic effect in Brewer’s yeast - induced pyrexia.

**Conclusion:** NSO has dose- dependent antipyretic activity.

40. **FURTHER STUDIES ON ADAPTOGENIC ACTIVITY OF WITHANOLIDE-FREE HYDROSOULBEL FRACTION FROM THE ROOTS OF WITHTANIA SOMNIFERA DUN**

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**Objective:** To develop chemically and biologically standardized safe and efficacious herbal therapy as an adaptogen. The plant based drug have emanated on the basis of therapeutic activity and standardized herbal preparations have better therapeutic potential, efficacy, less toxic and inexpensive than the pure isolated compounds for the various ailments.

**Methods:** The present study pertains to the pharmacological evaluation of plant Withania somnifera DUN. with special emphasis on the adaptogenic activity (in vivo) in animals. A new withanolide-free hydrosoluble fraction isolated from the plant Withania somnifera DUN. was evaluated for its adaptogenic potential against the chemical and physical induced stress in rats and mice. The parameters studied to assess the anti-stress activity viz. Carrageenan induced trauma in rats; Antigen (SRBC) induced humoral Immuno response in mice; Chemical (CCl₄) stress and physical (swimming) stress induced hepatic function in rats.

**Results:** Bioassay guided fractionation of the 70% alcoholic extract led us to identify a withanolide-free hydrosoluble fraction (12.5-100 mg/kg, p.o.) showed promising anti-stress activity in dose dependent manner in all the parameters studied. Percent inhibition observed - in carrageenan induced trauma 22.33-66.66%; Humoral antibody increase in primary antibody synthesis 70.0-71.18%, secondary antibody synthesis 23.33-66.66%. In chemical (CCl₄) induced stress hepatic function it significantly revert the elevated levels of various parameters i.e. serum - GPT 44.52-69.72, GOT 22.14-52.26, ALP 47.96-59.34, TG 32.21-59.73, and hepatic glycogen (depletion) 22.21-63.53% and lipid peroxidation 31.74-65.23%. Swimming stress causes a significant alteration in hepatic function and increase in normal value were significantly inhibited by it - serum GPT 44.65-79.16, GOT 19.15-66.03, ALP 26.65-62.35, TG 21.10-52.11 and hepatic glycogen (depletion) 23.95-51.85 & Lipid peroxidation 69.15-76.38% respectively. It did not show any obvious manifestation of acute toxicity observed for 72 hours and appeared safe up to 3g/kg, p.o. administered in mice, it also did not cause any behavioural changes and adverse effect on autonomic and central nervous system when given 100 mg/kg, p.o. for 15 days in experimental study.

**Conclusion:** The studies reveal that withanolide-free hydrosoluble fraction is capable to increase the capacity to tolerate non-specific stress in experimental animals as evident from the results and it does not interfere with the normal physiological functions of the body, this fraction validate the use of Withania somnifera DUN. as Rasayanay in Indian system of medicine, for the remedies of various ailments. Further studies are needed to explore its mechanism of action and possible therapeutic use in modern clinical practice.

41. **HEPATOCURATIVE AND ANTI-OXIDANT PROFILE OF HP - 1, A POLYHERBAL PHYTOMEDICINE**

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Objective: The hepatoprotective profile and mode of action of HP-1, a polyherbal formulation was determined. HP-1 is comprised of Phyllanthus niruri and extracts of Terminalia belerica, Terminalia Chebula, Phyllanthus emblica and Tinospora cordifolia and is prescribed for treatment of liver dysfunction.

Methods: In vitro hepatotoxic activity was determined on primary monolayer cultures of rat hepatocytes as percentage protection against CCl₄-induced leakage of lactate dehydrogenase (LDH) and glutamate pyruvate transaminase (GPT) and alteration in cellular glutathione (GSH). In vivo hepatoprotective profile was determined prophylactically by measuring reversal of toxicity due to CCl₄. The biochemical parameters monitored were serum glutamate oxaloacetate transaminase (GOT) and GPT. Liver parameters determined were: lipid peroxidation (LPO), catalase and superoxide dismutase (SOD) activities. The effect of HP-1 was compared with ascorbic acid, β-carotene and α-tocopherol. In vitro antioxidant activity was measured by the ability of HP-1 to quench enzymatically and non-enzymatically produced superoxide radical anions.

Results: HP-1 showed a high anti-hepatotoxic activity as evidenced by a significant restoration of GSH levels in cells and reversal of leakage of LDH and GPT. It inhibited CCl₄-induced enhancement of serum transaminases, and LPO levels in liver. HP-1 prevented in a very significant manner the depletion of catalase and SOD as a result of CCl₄ challenge. This effect was more pronounced compared to the any of the known anti-oxidants tested. HP-1 produced concentration dependent scavenging of superoxide anions produced both in enzymic and non-enzymic reactions in vitro.

Conclusion: Results from this study showed that HP-1 is a potential hepatoprotective formulation. Generation of lipid peroxides accompanied by a substantial loss of GSH and enzymatic antioxidants are significantly attenuated by HP-1. This herbal formulation with its potential ROS quenching activity could contribute significantly in the recovery of biological defense mechanisms of liver damage under oxidative stress.

42. ANTIINFLAMMATORY AND ANTI NEOPLASTIC ACTIVITIES OF TEA ROOT EXTRACT

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Objective: To study the antiinflammatory and antineoplastic effects of the saponin rich methanol-water extract of tea root.

Methods: Antiinflammatory studies were carried out employing carrageenan-induced oedema, cotton pellet induced granuloma and Freund's adjuvant induced polyarthritis in rats and croton oil induced ear inflammation in mice. The anticancer effect was investigated on Ehrlich ascites carcinoma (EAC) in mice by taking intraperitoneal EAC cell count after fourteen days treatment. SOD level in serum was measured by xanthine-xanthine oxidase system, MTT assay was done to evaluate the metabolic activities of cells and precursor incorporation study was done to examine DNA-synthesis rate.

Results: At a dose of 10 mg/kg TRE reduced the carrageenan-induced oedema in rat by 52% and significantly inhibited cotton pellet induced granuloma in rat. TRE reduced EAC cell count by 83% and reduced the cell size. SOD level in serum was changed by TRE significantly. Metabolically active EAC cells was reduced in TRE treated animals as revealed by MTT assay. The rate of DNA synthesis was also reduced after TRE as indicated by reduced ³H-deoxy-thymidine incorporation.

Conclusion: The study reveals that tea root extract possesses significant antiinflammatory and anticancer effects and that the saponins are probably responsible for these activities.

43. EFFECT OF NEEM LEAF EXTRACT ON HEPATOTOXICITY INDUCED BY ANTI-TUBERCULAR DRUGS IN RATS.

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Objective: To assess the hepatoprotective activity of neem leaf extract on anti-tubercular drugs induced hepatotoxicity in albino rats.

Methods: Hepatotoxicity was produced in rats by combination of anti-tubercular drugs namely INH, rifampicin and pyrazinamide given orally as suspension for 30 days. Treatment groups received neem leaf extract in the dose of 1 ml/100 gm daily orally along with anti-tubercular drugs for 30 days.

In the second phase of study the effect of neem leaf extract on established hepatotoxicity induced by anti-tubercular drugs was studied by giving neem leaf extract for 20 days after withdrawal of anti-tubercular drugs.

Liver damage was assessed by biochemical and histological parameters.

Results: Neem leaf extract significantly prevented rise in the levels of serum bilirubin, serum alanine aminotransferase, serum aspartate aminotransferase and serum alkaline phosphatase and fall in the levels of serum protein. Similarly it significantly prevented the histological changes as compared to the control group receiving anti-tubercular drugs. Neem leaf extract also significantly reversed the biochemical and histological changes when administered after withdrawal of anti-tubercular drugs.

Conclusion: Neem leaf extract significantly prevented as well as reversed the hepatotoxic damage induced by antitubercular drugs in rats.

CVS, ENDOCRINOLOGY, TOXICOLOGY & NEROPHARMACOLOGY

44. ANGIOTENSIN AT RECEPTORS IN REMOTE RENAL PRECONDITIONING OF MYOCARDIUM

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Introduction: The underlying mechanism of myocardial preconditioning after brief period of renal ischaemia-reperfusion are unknown.

Objective: The present study was aimed to investigate this
phenomenon of renal preconditioning of the myocardium and to characterize the participation of angiotensin II (AngII) receptors, using an in vivo rat model of acute myocardial infarction.

**Methods:** Wistar rats of either sex were used in this study. Rats were anaesthetized via intraperitoneal administration of thiopental sodium (40 mg/kg). Anaesthetized rats underwent a left thoracotomy and pericardiotomy. A laparotomy was performed to expose the left renal artery. Animals were then preconditioned with four episodes, each consisting of 5 min of renal artery occlusion followed by 10 min of reperfusion, or underwent a 60min sham period of anaesthesia. Subsequently, the left coronary artery was then occluded for 30 min and reperfused for 24 h.

**Conclusion:** Based on the data in hand we can infer that angiotensinAT1 receptors participate in renal preconditioning of the myocardium in in vivo rat hearts.

**45. THE EFFECT OF EXOGENOUS PHOSPHATIDIC ACID IN VASCULAR SMOOTH MUSCLE CELLS**

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**Objective:** Exogenous phosphatidic acid (PA) has been shown to regulate Ca$^{2+}$ transport in a number of cells; however, the effect and mechanism of action of PA evoked changes in [Ca$^{2+}$]i in vascular smooth muscle cells (VSMCs) are not clear.

**Methods:** We employed the A-10 VSMC preparation and Fura-2 technique to study the effect of exogenous PA.

**Results:** We observed a dose dependent increase in [Ca$^{2+}$]i. Preincubation of cells with an extra cellular Ca$^{2+}$ chelator, EGTA (1 mM); sarcoplasmic reticulum (SR) Ca$^{2+}$-ATPase inhibitors, [cyclosporin acid (25 µM; n = 6) and thapsigargin (10 µM; n = 6)]; inositol(1,4,5)P3 (InsP$_3$) inhibitor, [2-nitro-4-carboxyphenyl N. N-diphenyl carbamate (12.5 µM; n = 6)]; a potent membrane permeable blocker of InsP$_3$ mediated Ca$^{2+}$ release [xestospongin C (7.5 µM n = 6)] or an activator of protein kinase C (PKC), [phorbol 12-myristate 13-acetate (100 nM to 100 µM; n = 6)] depressed the PA (10 µM) - evoked increase in [Ca$^{2+}$]i.

**Conclusion:** These results suggest that the PA - induced increase in [Ca$^{2+}$]i in VSMCs may occur secondary to the release of Ca$^{2+}$ from the SR stores, rather than the opening of the sarcolemmal Ca$^{2+}$ channels. Secondly, PA evoked Ca$^{2+}$ mobilization is regulated by PKC activity in VSMCs. Thirdly, the PA-induced increase in [Ca$^{2+}$]i may be due to the activation of PLC through the involvement of G protein - dependent pathway.

**46. COMPARISON OF ATENOLOL AND AMLODIPINE ON SERUM LIPIDS AND ATHEROSCLEROSIS**

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**Objective:** To study the effect of atenolol and amlodipine on lipid profile and atherosclerosis.

**Methods:** Forty male rabbits were divided into four groups of ten animals each. These groups received plain diet, atenolol diet, atenolol diet plus atenolol and atenolol diet plus amlodipine respectively. Atherogenic diet consisted of pork fat oil (5 ml/ rabbit + 5% cholesterol in deoiled rice and wheat bran). Lipid profile (serum cholesterol, serum triglyceride and serum HDL-cholesterol) were estimated at 15 days interval for a period of 10 weeks. At the end of the study, the animals were sacrificed, thoracic aorta was removed and calculation of atherosclerotic plaque area was done using planimetry. The drugs were given in the following dosages atenolol 25 mg/kg/day and amiodipine 2.5 mg/kg/day. The data was analyzed using student ' t ' test for paired and unpaired groups.

**Results:** There was significant rise in lipid levels in the group given atherogenic diet alone (72% rise in serum cholesterol), in the atenolol group there was an increase of 68% in serum cholesterol levels, in the amlodipine group the rise was 66%. The area of plaque formation was 4.6 cm$^2$ in the atherogenic diet group, it was 4.8 cm$^2$ in the atenolol group and 3.5 cm$^2$ in amiodipine group.

**Conclusion:** Atenolol exhibited a greater atherogenic activity as compared to amiodipine in rabbits given concurrent therapy with atherogenic diet and these drugs.