an epidemiologic questionnaire and measure CYP1A activity as a putative biomarker of chronic exposure to dioxins.

Patients (or Materials) and Methods: Volunteers living in Melun area for at least 5 years (between 1974 and 2002) were included in the study. A questionnaire was designed to assess source and length of exposure, risk and confounding factors, and environmental sources of variability in CYP1A activity. The following items were systematically assessed: place of habitation, place and type of work, other sources of pollution, food questionnaire, smoking, caffeinated drinks and alcohol consumption, and medications (CYP1A inhibitors/inducers). They had a full medical history and physical examination with a special focus on skin lesions. CYP1A activity was assessed 2 hours after the ingestion of a drink containing caffeine through measurement of the ratio (MR) of 17X/137X by liquid chromatography mass spectrometry. CYP1A activities were compared with the phenotypes of healthy volunteers and to the acute dioxin intoxication of Victor Yushchenko described by Sorg et al. (Lancet 2009; 374:1179-85.)

Results: Forty-eight volunteers (age, 11–78) were included in the study (25 men, 23 women). A high frequency of dysthyroidism and cancer was noticed in the population. Eleven had a history of thyroid disease (23%) and 7 (14.5%) had cancer. Skin lesions were described in 13 patients (27%). Mean CYP1A activity of the exposed population was comparable to the healthy volunteers (17X/137X MR of 0.250 SD 0.08 and 0.273 SD 0.12, respectively). However, 8 exposed volunteers (16%) had a 17X/137X MR above 0.4, indicating that CYP1A is induced (maximal 17X/137X MR of 0.649). CYP1A activity was not correlated with the presence of thyroid disease, cancer, or skin lesions. After acute dioxin intoxication, CYP1A was more strongly induced (maximal 17X/137X MR of 1.9). Induction was still persistent 2 years after acute exposure.

Conclusion: A high frequency of dysthyroidism (23%) and cancer (14.5%) was noticed in a sample population of Melun area exposed chronically to dioxins from a waste incinerator. CYP1A was induced in 16% of the population but without significant association with thyroid disease, cancer, or skin lesions. After acute dioxin intoxication, the magnitude of CYP1A induction was 3- to 6-fold higher.

Disclosure of Interest: None declared.

PP234—INTOXICATION WITH ATYPICAL ANTIPSYCHOTICS IN YOUNG CHILDREN: A MULTICENTRE ANALYSIS OF POISONS CENTRES DATA

M. Meli1; C. Rauber-Lüthy1; P. Hoffmann-Walbeck2; H.-J. Reinecke1; D. Prasa4; U. Stedtler5; E. Färber6; G. Dieter7; M. Meli1; C. Rauber-Lüthy1; P. Hoffmann-Walbeck2; H.-J. Reinecke1; D. Prasa4; U. Stedtler5; E. Färber6; G. Dieter7; M. Meli1*; C. Rauber-Lüthy1; P. Hoffmann-Walbeck2; H.-J. Reinecke1; D. Prasa4; U. Stedtler5; E. Färber6; G. Dieter7

1Division of Science, Swiss Toxicological Information Centre, Associated Institute of the University of Zurich, Zurich, Switzerland; 2Poison Information Centre Berlin, Berlin; 3Poison Control Centre Mainz, Mainz; 4Poison Information Centre Erfurt, Erfurt; 5Poison Information Centre Freiburg, Freiburg; 6Poison Information Centre North, Göttingen, Germany; 7Poison Information Centre Wien, Vienna, Austria; and 8Department of Clinical Pharmacology and Toxicology, University Hospital Zurich, Zurich, Switzerland

Introduction: Although accidental poisoning with atypical antipsychotics in children is 1 of the most important causes of morbidity after accidental ingestion of medications, the number of studies that have assessed the effects of acute exposure to this class of drugs is very limited. The aim of this study was to achieve a better characterization of the acute toxicity profile in young children of the common atypical antipsychotics clozapine, olanzapine, quetiapine, and risperidone.

Patients (or Materials) and Methods: Multicenter retrospective analysis of cases with atypical antipsychotics intoxication in children <6 years, reported by physicians to German, Austrian, and Swiss Poisons Centres between January 1, 2001, and December 31, 2009.

Results: A total of 106 cases of intoxication (31 clozapine, 29 olanzapine, 12 quetiapine, and 34 risperidone) were analyzed. Mean age was 2.6 years (range, 0.8-5.5). There were 52 (49%) females, 43 (40.6%) males, and in 11 (10.4%) cases gender was not reported. No correlation between age and number of ingested pills was found (Spearman correlation coefficient, 0.16). Concerning the number of ingested pills, there was no significant difference between males and females (Wilcoxon test, P = 0.39). Overall toxicity was rated as severe in 2 (19%), moderate in 28 (26.4%), and minor in 47 (44.3%) cases according to the Poisoning Severity Score. Twenty-eight (26.4%) cases were asymptomatic. No fatalities were recorded. Neurological and cardiovascular symptoms were predominating. Minor reduction in vigilance (Glasgow Coma Scale score >9) (62.3%) was the most frequently reported symptom, followed by miosis (12.3%) and mild tachycardia (10.4%). Extrapyramidal motor symptoms were observed in 1 case (0.9%) after ingestion of 2 mg (0.1 mg/kg) of risperidone. Electrocardiography was performed in 32 (30.2%) children: 3 (2.8%) showed extrasystoles, and in 1 (0.9%) case a prolonged QTc interval (468 ms) was recorded after the ingestion of 150 mg (13.6 mg/kg) of quetiapine. For clozapine, the lowest dose causing objective symptoms or signs was 0.8 mg/kg, resulting in aggressiveness, ataxia, dysarthria, and somnolence; for olanzapine, 0.4 mg/kg resulting in ataxia and somnolence; for quetiapine, 3.1 mg/kg resulting in ataxia and somnolence; and for risperidone, 0.05 mg/kg resulting in somnolence and mild tachycardia. In most cases, surveillance and supportive care were sufficient to achieve a good outcome, and all children made a full recovery.

Conclusion: Most children poisoned with the atypical antipsychotics clozapine, olanzapine, quetiapine, and risperidone had a benign clinical course without sequelae. Extrapyramidal side effects were rare, and the only case reported was caused by risperidone. Symptomatic patients should be monitored for central nervous system depression, and an electrocardiogram should be obtained.

Disclosure of Interest: None declared.

PP237—EVALUATION OF THE EFFECT OF DIMETHOATE INTOXICATION ON MALE RAT REPRODUCTIVE PERFORMANCES

J.M. El-Medany1; A.M. El-Medany2; A.A. Guemere2; and Y.A. Bassioni2

1Anatomy; and 2Pharmacology, Alexandria University College of Medicine, Alexandria, Egypt

Introduction: Ormonophorpus compounds are widely used in industry, agriculture, and for public health purposes. The aim of this work was to study the effect of dimethoate on fertility in adult male rats and the possible underlying mechanism of action.

Patients (or Materials) and Methods: The study was conducted on healthy, sexually mature male Wistar albino rats weighing between 250 and 300 g. Animals were assigned randomly into 4 groups, each of 6 rats as follows: Group 1, control, orally administered with 1 mL of corn oil. Groups 2, 3, and 4 received dimethoate at a dose equivalent to 7, 10.5, and 21 mg/kg body weight, respectively. Commercially available kit was used. Fertility test: Each male was allowed to undergo mating with 2 females (3–4 months old) of proven fertility during the last 10 days of the experiment. Serum and organ collections for determination of acetylcholinesterase activity and for histopathologic evaluations using light and electron microscopic study.
Results: A significant increase (P < 0.05) in feed consumption, body weight gain, relative weights of testis and epididymis and intratesticular cholesterol level, follicle stimulating hormone (FSH), lutetinizing hormone (LH), and prolactin was found in rats received dimethoate. On the other side, a significant decrease (P < 0.05) in absolute weight of testes and epididymis, serum cholesterol and testosterone levels, serum acetylcholine esterase (AChE) activity, total sperm count, motility and fertility index was observed compared with the control group. Histopathologic results also indicated enlargement of interstitial space, inhibition of spermatogenesis, and variable degrees of degenerative changes in the seminiferous tubules up to total cellular destruction.

Conclusion: Our results proved that dimethoate, could act as neuroendocrine disruptor via inhibition of AChE activity and increase of acetylcholine level in brain. This effect might be linked to the suppression of the brain’s release of hormones that stimulate the gonadotrophic hormones (LH and FSH). So we have to be aware that dimethoate has detrimental effects on the male rat reproductive system.

Disclosure of Interest: None declared.

PP239—SYNTHESIS OF THE FIVE BANGLADESHI UNANI MEDICINES DERIVATIVES: IN VITRO STUDIES OF THEIR PHARMACOLOGICAL ACTIVITIES
M.A.H. Mollik
Biological Sciences, Peoples Integrated Alliance, Bogra, Bangladesh

Introduction: The art of herbal healing has very deep roots in Bangladeshi culture and folklore. Unani medicines serve as a major source of primary health care for Bangladeshi people. The reasons for their use range from easy access, affordability, beliefs in traditional systems, and long-term safety. Unani medicines have been used to treat individuals infected with human immunodeficiency virus (HIV) and therefore need scientific validation, a view supported by the herbalists.

Patients (or Materials) and Methods: The studies aimed to evaluate the in vitro cytotoxicity, immune-modulatory, and anti-HIV activities of traditional multiple herbal preparations from the herbalists. Triphola, Mohasudarshan, Dhoshomula, Sarasvati, and Hingoshtak medicines were supplied by the herbalists.

Results: Changes in adenosine triphosphate and glutathione over 36 hours were measured using luminometry. Changes in 13 cytokines were assayed using an enzyme-linked immunosorbent assay–based absorbance assay. Protective effects against HIV killing of metallohydroxothioxanthone, and 1,3-dihydroxythioxanthone, showed the highest antileptospiral activities with the MIC varying from 100 to ≥800 µg/mL. Combinations of γ-mangostin with penicillin G and 1,3,8-trihydroxyxanthone with ampicillin generated synergistic effects at the FIC index of 0.05 to 0.75 and 0.51 to 0.75, respectively. However, antagonistic activity against L. interrogans serovar Saigon was observed when combining γ-mangostin with penicillin G.

Conclusion: The results demonstrated that the xanthones from G mangostana and hydroxyxanthone analog inhibited growth of leptospires and there were synergistic effects between these xanthones and antibiotics, which could enhance the efficacy of both drugs for the treatment of leptospirosis.

Disclosure of Interest: None declared.

PP240—PHARMACEUTICAL QUALITY OF GENERIC LEVODOPA/BENSERAZIDE PRODUCTS
G.L. Vital-Durand1; L. Arnet2; U.E. Gasser1; and A. Fischer4
1Mature Products, Hoffmann–La Roche; 2PHARMAZEUTISCHE WISSENSCHAFTEN, Pharmazentrum, Basle; 3ClinResearch, Aesch; and 4Quality Control, Hoffmann–La Roche, Basle, Switzerland

Introduction: Objective: To compare the pharmaceutical quality of 7 generic levodopa/benserazide combination products marketed in Germany with the original product (Madopar® / Prolopa®). Madopar® / Prolopa® is a combination of levodopa (L-Dopa), the precursor of dopamine (DA), and benserazide, a dopamine decarboxylase inhibitor (DDCI). It is indicated in the treatment of Parkinson’s disease, dopamine-responsive dystonia, and restless legs syndrome.

Patients (or Materials) and Methods: Madopar®/Prolopa® tablets and capsules were used as reference materials. The generic products tested (all 100 mg/25 mg formulations) included 4 tablet formulations (ie, Levodopa/Benserazid beta [Betapharm], Levodopa/ Benserazid-CT [CT Arzneimittel], dopadura B [Mylan dura], and Levodopa/Benserazid ratiopharm [ratiopharm]) and 3 capsules (ie, Levodopa/Benserazid beta [Betapharm], Levodopa/ Benserazid-CT [CT Arzneimittel], dopadura B [Mylan dura], and Levodopa/Benserazid ratiopharm [ratiopharm]) and 3 capsules

Disclosure of Interest: None declared.