alone was without effect but in combination with IFN-gamma markedly impaired the ability of the long-acting beta-agonist to phosphorylate CREB. This suggests a novel mechanism whereby IFN-gamma interferes with beta-agonist signaling by impairing phosphorylation of CREB. This may be important in reducing the responses to beta-agonists in refractory asthma.
Conclusion: IFN-gamma interferes with beta-2 agonist signaling by impairing phosphorylation of CREB. This may be important in reducing the responses to beta-agonists in refractory asthma.
Disclosure of Interest: None declared.

PP256—COMPARATIVE STUDY BETWEEN ANGIOTENSIN INHIBITORS & THEIR RECEPTOR BLOCKERS ON ULCERATIVE COLITIS IN RATS

J.H. Elmedany[1*]; A.H. El-Medany[2]; and H.I. Hagar[2]
[1]Anatomy, King Saud University, College of Medicine, Anatomy Department; and [2]Pharmacology, King Saud University, College of Medicine, Pharmacolgoy Department, Riyadh, Saudi Arabia
Introduction: Ulcerative colitis is an inflammatory chronic disease primarily affecting the colonic mucosa; the extent and severity of colon involvement are variable. The cause of UC remains unknown. However, some findings recently point to an overstimulation or inadequate regulation of the mucosal immune system as a major pathophysiologic pathway. The role of angiotensin-converting enzyme blockers or angiotensin receptor blockers in the possible modulation of colon inflammation had not been verified. This prompted us to assess and compare the possible protective and therapeutic effects of captopril and valsartan on the extent and severity of ulcerative colitis induced by acetic acid in rats and to study the possible underlying mechanism of action of these drugs.
Patients (or Materials) and Methods: Seventy male Wistar albino rats were used. The animals were randomly divided into 7 groups each of 10 rats. Group 1: Normal control group, received Arabic gum PO 0.5 mlkg–1 (using gavage for all groups). Group 2: Acetic acid control group given 2 mL/rat 3% acetic acid rectally and Arabic gum PO for 2 weeks before induction of colitis. Group 3: Acetic acid control group 2 mL/rat 3% acetic acid rectally and Arabic gum PO for 2 weeks after induction of colitis. Group 4: Taken captopril HCl dissolved in Arabic gum at a dose of 30 mgkg-1 PO daily for 2 weeks before induction of ulcerative colitis. Group 5: Taken valsartan dissolved in Arabic gum at a dose of 30 mgkg-1 PO daily for 2 weeks before induction of ulcerative colitis. Group 6: Taken captopril HCl at a doses of 30 mgkg-1 PO once daily for 2 weeks after induction of UC. Group 7: Taken valsartan in a doses of 30 mgkg-1 PO once daily for 2 weeks after induction of ulcerative colitis.
Results: The results were assessed by histologic assessment of colonic tissues and measurement of malondialdehyde (MDA), tumor necrosis factor (TNF-α), transforming growth factor (TGF-1b), angiotensin-converting enzyme (ACE), reduced glutathione (GSH), and platelet activating factor (PAF) levels in colonic tissues. Oral pretreatment with captopril or valsartan in a dose of 30 mgkg-1 body weight (prophylactic groups) and continuously for 2 weeks after induction (therapeutic groups) significantly reduce MDA, TNF-α, PAF, TGF-1b, and ACE levels in colonic tissues as compared with acetic acid control group. Also, a significant increase in GSH level was observed in colonic tissues. Captopril and valsartan attenuated the macroscopic and microscopic colonic damage induced by acetic acid.
Conclusion: These results suggest that either captopril or valsartan may be effective as prophylactic or treatment of UC through inhibition of ACE and scavenging effect on oxygen-derived free radicals.
Disclosure of Interest: None declared.

PP257—CHLOROGENIC ACID AS POTENTIAL ANTI-INFLAMMATORY ANALGESIC AGENT

A.M. El-Medany[1*]; Y.A. Bassiouni[1]; M.M. Khattab[1]; and A.A. Mahesar[2]
[1]Clinical Pharmacolgoy, Alexandria University College of Medicin, Alexandria, Egypt; and [2]Clinical Pharmacolgoy, king Saud University College of Medicin, Riyadh, Saudi Arabia
Introduction: Nonsteroidal anti-inflammatory drugs represent 1 of the most widely prescribed drugs used for treatment of pain and inflammation. The prescription of current existing anti-inflammatory drugs is hampered by their adverse effects over time. In the recent years, there is an upsurge in the areas related to newer developments in the prevention of disease especially the role of free radicals and antioxidants. Phenolic compounds are receiving increased attention as epidemiologic studies have highlighted the association between the consumption of polyphenolic–rich food and beverages and the prevention of various human diseases. The present study investigated the analgesic and anti-inflammatory effects of chlorogenic acid (CGA), a polyphenolic compound present in many foods and beverages using carrageenan (Carr)-induced paw edema in rats and formalin – induce analgesia in mice.
Patients (or Materials) and Methods: Swiss mice (25–35 g) and Wistar rats (180–220 g), were used, chemicals and drugs (Formalin, Carrageenan, Indomethacin, CGA). Elisa Kits were used to study the effect of CGA on Carr-induced paw edema, 0.1 mL of 1% suspension of Carr in 0.9% Nacl solution was injected. The antinociceptive effects of CGA were tested by the formalin- induced hindpaw licking procedure in the day light. Elisa Kits were used to study the effects of CGA on some indices of oxidative stress. Reduced Glutathione and Malondialdehyde in paw tissues.
Results: Treatment of rats with CGA (50, 100, 150 mg/kg) significantly reduced the rats paw edema induced by Carr and the formalin-induced pain in mice ($P < 0.05$) as compared with control groups. A significant reduction in rat paw volume in nitric oxide induced edema was observed ($P < 0.05$).CGA produced a significant reduction in malondialdehyde and significant increase in reduced glutathione in paw tissues ($P < 0.05$).
Conclusion: These results confirm that CGA has both analgesic and anti-inflammatory properties that may be related to the ability of this polyphenol to reduce the levels of superoxide and peroxynitrite anion radicals. CGA showed a promising potential drug of natural anti-inflammatory property to control oxidative stress.
Disclosure of Interest: None declared.

PP259—THE ABILITY OF ANTI-S100 ANTIBODIES TO AMELIORATE THE SEVERITY OF EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS IN WISTAR RATS

J.L. Dugina[1*]; I.N. Abdurasulova[2]; I.A. Ertuzun[1]; and O.I. Epstein[1]
[1]Materia Medica Holding Company, Moscow; and [2]Research Institute of Experimental Medicine RAMS, Saint-Petersburg, Russian Federation
Introduction: The pharmacologic profile of antibodies to S100 protein (anti-S100) in release-active form has been studied since 1998. Animal studies revealed that they possess anxiolytic-like, antidepressant-like, and neuroprotective activity. GABA-ergic system as well as sigma1 receptor are involved in the realization of their effects. The aim of the present study is to assess the influence of anti-S100 treatment on the course of experimental allergic encephalomyelitis (EAE).
Patients (or Materials) and Methods: EAE was induced female Wistar rats (200–220 g) by a single subcutaneous inoculation of a spinal cord homogenate emulsified in complete Freund's adjuvant (100 mg of homogenate of homologous spinal cord, 0.2 mL CFA,

and 0.2 ml of saline). The following substances were administered intragastrically 2 times a day at 7-hour intervals for 30 days starting from the 1st day of EAE induction: anti-S100 (n = 20, 2.5 mL/kg/d); distilled water (control; n = 20, 5 mL/kg/d). Reference drug (Glatiramer acetate, Copaxone®, Teva, Israel, n = 20) was administered intramuscularly (4 mg/kg) from the 2nd to the 25th day after EAE induction.

Results: The severity of neurologic symptoms was assessed in points: muscle weakness, tremor (0.5 point); resistant paresis (1 point); paralysis (1.5 points). Clinical Index (CI) was calculated as a sum of the symptoms for 4 limbs. CI was defined as zero if visible clinical signs were absent, and as 6 in case of animal's death. Cumulative index for each rat was calculated as a sum of individual CI for the total disease period (30 days). Time to disease onset (days) and the mean severity of the disease (points) were recorded in each group.

The key results of the study are presented in the **Table**.

	Groups, the number of animals	Proportion of Animals With Symptoms	Severity of Symptoms	Time to Disease Onset, days	Mean Cumulative CI, Points (M ± m)	
		Mild, %	Average, %	Severe %		
Control, n = 20	80	20	25	35	9.5 (8.0–11.3)	27.53 ± 7.19
Glatiramer acetate, n = 20	65	5	40	20	10.0 (9.0–11.0)	18.03 ± 6.20
Anti-S100, n = 20	85	40	40	5*	12.0 (8.0–14.0)	18.96 ± 5.94

*The difference with control is significant at $P < 0.05$ (chi-square test).

Conclusion: Anti-S100 ameliorated clinical symptoms of EAE in Wistar rats: they both significantly reduced the severity of the disease and delayed the disease onset. The results give promise to patients in a search of a treatment option for multiple sclerosis.

Disclosure of Interest: J. Dugina: Employee of Materia Medcia Holding Company. I. Abdurasulova: Grant/research support from Materia Medcia Holding Company. I. Ertuzun: Employee of Materia Medcia Holding Company. O. Epstein: Shareholder of Materia Medcia Holding Company.

PP261—UTILIZATION OF TRIPTANES IN SWEDEN; ANALYSES OF OVER THE COUNTER AND PRESCRIPTIONS SALES

M. Von Euler[1*]; S. Keshani[2]; K. Baatz[3]; and B. Wettermark[4]

[1]Clinical Science and Education, Södersjukhuset; [2]Karolinska Institutet; [3]National Board of Health and Wellfare; and [4]Laboratory Medicine-clinical pharmacology, Karolinska Institutet, Stockholm, Sweden

Introduction: In Sweden, some triptans became available over the counter (OTC) in 2008. The present study describes the utilization pattern of prescribed and OTC triptans in Sweden over time.

Patients (or Materials) and Methods: Wholesaler and aggregated sales data from the National Corporation of Swedish Pharmacies between 1991 and 2006, and patient identity data on dispensed prescriptions between 2006 and 2010 from the National Prescribed Drug Register were used to investigate volume and expenditure of triptans over time. Prevalence was calculated for 2007 and 2011, measured as the number of patients/1000 inhabitants dispensed at least 1 triptan prescription. To illustrate proportions of patients dispensed large and small amounts of the drug, respectively, Lorentz percentiles and Lorentz curves were used. Analyses were done by age and gender.

Results: Volumes of triptans sold has increased continuously to 7.0 million defined daily doses (DDD) dispensed on prescriptions and 0.7 million DDDs OTCin 2011. The prevalence of triptan utilization was 10.0 in 2007 and increased slightly to 10.1 in 2011. A marked gender difference was found with a 3.6 times higher prevalence of triptan use in women both years. The mean number of DDD increased with 10%, from 67 DDD per patient in 2007 to 74 DDD per patient in 2011. The median volume per patient increased even more, 20%, from 30 DDD per patient in 2007 to 36 DDD per patient in 2011. Dispensed triptans were unevenly distributed within the population. In 2007, in women, 46% of the volume was purchased by 10% of those consuming the largest amounts. In men, the corresponding proportion consumed by 10% heavy users was 50%.

Conclusion: Triptans OTC has increased since the introduction as has the purchases of prescribed triptans. The number of patients dispensed triptans on prescription remained stable during the period studied even though the volumes increased.

Disclosure of Interest: None declared.

PP262—CAN AUTHORITIES TAKE FULL ADVANTAGE OF THE AVAILABILITY OF GENERIC ATYPICAL ANTIPSYCHOTIC DRUGS? IMPLICATIONS FOR THE FUTURE

B. Godman[1,2*]; M. Persson[3]; J. Miranda[4]; C. Barbui[5]; M. Bennie[2,6]; K. Bennett[7]; A. Bucsics[8]; S. Simoens[9]; C. Zara[10]; and L.L. Gustafsson[1]

[1]Division of Clinical Pharmacology, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden; [2]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, United Kingdom; [3]Drug Management Department; [4]Department of Healthcare Development, Stockholm County Council, Stockholm, Sweden; [5]WHO Collaborating Centre for Research and Training in Mental Health and Service Evaluation, Department of Public Health and Community Medicine, Section of Psychiatry, University of Verona, Verona, Italy; [6]Information Services Division, NHS National Services Scotland, Edinburgh, United Kingdom; [7]Department of Pharmacology and Therapeutics, Trinity College, Dublin, Ireland; [8]HVB, Vienna, Austria; [9]Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven, Belgium; and [10]Barcelona Health Region, Catalan Health Service, Barcelona, Spain

Introduction: There could be an opportunity for health authorities to take advantage of oral generic atypical antipsychotic drugs (AAPs) given their considerable expenditure across countries. However, schizophrenia and bipolar disorders (BPD) are complex to treat, with the need to tailor treatments. Consequently, there is a need to assess changes in risperidone utilization before and after oral generic risperidone was reimbursed among European countries, as well as the utilization of generic versus originator risperidone, to provide future guidance.

Patients (or Materials) and Methods: We principally used an interrupted time series design of monthly aggregated AAP utilization (2011 DDDs) up to 2 years before generic risperidone became available and reimbursed and up to 6 years after in Austria, Belgium, Ireland (GMS population), Scotland, Spain (Catalonia), and Sweden; (ii) Demand-side measures captured and categorised using the 4Es (Education, Engineering, Economics and Enforcement). Expenditure was also measured. Only administrative databases were used.

Results: There were generally no specific measures among the various authorities to preferentially encourage the prescribing of oral