to Republic Ministry of health of Serbia. In next regulatory step, after getting demand of Ministry of health of Serbia, ALIMS experts have to re-evaluate all registration documentation and their own decision in order to issue final decision.

Disclosure of Interest: None declared.

PP249—BRINAVESS® – ARGUMENTS OF REGULATORY SUSPENSION IN SERBIA

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Introduction: BRINAVESS® /vernakalant/ is an antiarrhythmic medicine that acts preferentially in the atria to prolong atrial refractoriness and to rate dependently slow impulse. Anatomical Therapeutic Chemical Classification/ATC/ is: C01BG11.

Patients (or Materials) and Methods: According to Serbian Law on Medicinal Products and Medical Devices, regulatory procedural steps taken for getting Marketing Authorisation Approval in Serbia, started on 2011 year.

Results: After evaluation and reevaluation of submitted documentation/Module 1-5 Common Technical Document/, Advising Working Group for medicinal products of Medicines and Medical Devices Agency of Serbia suggested refusal application. On June 2012, year ALIMS issued the final decision/No. 515-01-0020-11-003/ about withdrawing registration of BRINAVESS® in Serbia.

Conclusion: Impossibility to submit requested additional relevant regulatory data caused applicant’s claim on March 2013.year for withdrawing registration of BRINAVESS® in Serbia.

Disclosure of Interest: None declared.

PP252—ETHICS OF RELATIONSHIPS IN THE SPHERE OF PHARMACEUTICAL SERVICES

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Introduction: Study of ethical aspects of relationships of pharmacists and patients during rendering of pharmaceutical services for the purpose of improving effectiveness and safety of pharmacotherapy of patients.

Patients (or Materials) and Methods: A social poll using a method of selective anonymous survey of pharmacists and customers. The objects of research were the chemist’s shops of the city of Bishkek determined randomly. The analysis is based on the survey of 121 pharmacists and 207 patients. The pharmacists were 45 (37.2%) specialists with university education and 76 (62.8%) with college education, the average age was 31.4 and the work of experience in pharmacy was 7.2 years. The patients were respondents older 18 years old. The age distribution was 28.8% for 18–27; 34.6% for 28–37; 9.7% for 38–47; 22.7% for 48–57 and 4.2% for older 60. In terms of gender, the customers broke down into 133 (64.3%) female and 76 (35.7%) male. 45.3% of them had a university education, 32.7% had a college education, and 21.9% were students. The received data were processed with the help of specialized SPSS statistical software package.

Results: According to the processed data most pharmacists (72.7%) know about the Code of Ethics for pharmacy practice and its contents. All specialists (100%) admit that customers have the right to receive the information about the medicine they buy. As pharmacists note (64.5%), customers are most often interested in dosage and proper use of medicines. 63.6% of patients need professional assistance when they choose a medicine. However, 27.1% of patients say pharmacists give consultations reluctantly. In the course of the research, customers of the chemist’s shops were suggested to evaluate some indices reflecting the degree of their satisfaction by pharmacists’ work (10-point scale). The average evaluation of the indices, such as appearance, consideration, tactfulness, patience and the ability to turn medical notions into plain language was 7.5. According to 23.4% of pharmacists the most often reason of conflicts in chemist’s shops is patients’ dissatisfaction with a price of a medicine. This is confirmed by 67.7% patients thinking that most pharmacists are oriented for selling expensive and advertised medicines regardless of other affordable generics which do not concede in quality and effectiveness.

Conclusion: The research has revealed significant gaps in professional ethics of pharmacists. This allows us to make a conclusion that measures of interference in relationships of pharmacists and patients in the process of rendering pharmaceutical services need to be taken.

Disclosure of Interest: None declared.

PP255—IFN-GAMMA INTERFERE THE EFFECT OF BETA-2 AGONIST ON TNF-ALPHA INDUCED CXCL10 THROUGH CREB PHOSPHORYLATION IN HASM CELLS

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Introduction: CXCL10 is a potent mast cell chemoattractant responsible for the mast cell myositis characteristic of asthma. We have identified human airway smooth muscle (HASM) as a rich source of CXCL10 which is increased by TNF-alpha and IFN-gamma. We have previously shown that beta-agonists inhibit TNF-alpha induced CXCL10 release but the effect is lost when IFN-gamma is given concomitantly through poorly defined mechanisms. Here we defined the mechanism involved.

Patients (or Materials) and Methods: HASM cells taken from 3 normal donors were cultured using standard techniques. ELISA was used for quantitative measurement of CXCL10 release. Cyclic AMP assay was used to measure the cAMP level. Western Blot was used to indicate CREB phosphorylation.

Results: We found that salmeterol time dependently increased cAMP generation. TNF-alpha or IFN-gamma alone or in combination had similar effects on salmeterol time dependently induced cAMP generation suggesting that the inhibitory effect of IFN-gamma on beta-2 agonist signaling was not at the level of cAMP generation but rather was likely to be an effect on downstream signaling pathways. Next we looked at the phosphorylation of CREB by Western blot and found that salmeterol and caused phosphorylation of CREB but this was differentially affected by the cytokines. Whereas TNF-alpha

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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
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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 ml/kg–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 mg/kg–1 PO daily for 2 weeks before induction of ulcerative colitis. Group 5: Taken valsartan dissolved in Arabic gum at a dose of 30 mg/kg–1 PO daily for 2 weeks before induction of ulcerative colitis. Group 6: Taken captopril HCl at a doses of 30 mg/kg–1 PO once daily for 2 weeks after induction of UC. Group 7: Taken valsartan in a doses of 30 mg/kg–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-1β), 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 mg/kg–1 body weight (prophylactic groups) and continuously for 2 weeks after induction (therapeutic groups) significantly reduce MDA, TNF-α, PAF, TGF-1β, 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
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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 algesia 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
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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 sigma 1 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,