

ABSTRACTS
OF
CHIEF ASSIST. PROF. GEORGI ST. POPOV, PhD

Presented for participation in a competition for academic position "Associate Professor"

, in Department "Internal non-infectious diseases, pathology and pharmacology", in the scientific field 6. Agricultural sciences and Veterinary medicine, professional field 6.4.

Veterinary medicine, scientific specialty "Pathology of animals", in the discipline "Pathology (General pathomorphology)"

I. Monographs and books

Monograph

Popov G., 2024. Pathological characteristic of intoxications in domestic animals. PANEV Publishing, Sofia, pp. 136, ISBN 978-619-90789-9-0.

Abstract: The presented monograph aims to acquaint the reader with the pathological changes in the organs of domestic animals as a result of common intoxications. For this purpose, 177 scientific sources were used. Known and new data concerning the pathogenesis, clinical signs and pathomorphological changes of the presented intoxications are interpreted. Some of the changes are illustrated with original photos. The author's studies, presented in various scientific publications, as well as cases from practice are included.

Book based on a defended dissertation

Popov G., 2024. Pathomorphological and pharmacological studies on the protective effect of biologically active substances of *Astragalus* species, PANEV Publishing, Sofia, pp. 136, ISBN 978-619-92707-0-7.

Abstract: In the book are presented pathomorphological and pharmacological effects of two flavonoids obtained from *Astragalus monspessulanus* and of purified saponin fraction and mixture obtained from *Astragalus glycyphyllos* and *Astragalus glycyphylloides* in different in vitro and in vivo pathological conditions. 281 scientific sources were used for the interpretation. Some of the studies are illustrated with 62 author's macroscopic and microscopic original photographs.

II. Scientific publications

- 1. Dimitrov, D., V. Manov, I. Ralchev, K. Hristov, G. Popov. 2016. Cytological characteristics of endometritis in dairy cattle. Tradition and Modernity in Veterinary Medicine, 1, 27–32.**

Abstract: In the last decades, related to increased milk yield, the reproductive performance has rapidly decreased in dairy cows, especially in the Holstein breed. Although milk yield is negatively associated with reproductive-performance, there are other additional factors which affect the fertility in dairy cattle, such as animal health-condition, management and balanced rations. Additionally, physiologic dysfunctions, such as uterine infections, are elements which are responsible for decreased reproductive performance and fertility in dairy cattle. The objective of this study was to obtain a clear view over normal cell clusters in cow's vagina and uterus, so this information will be useful for comparison in future examination related to rapid

cytology diagnosis. Neutrophils are the first and most significant inflammatory cell involved in endometritis, but are also foremost during normal uterine involution. The inflammatory cell response in cases of subclinical endometritis is widely believed to be quantifiably more severe than that associated with normal involution yet milder than clinical endometritis. Such cytological diagnostic approach is useful for both – normal and infected vagina/uterus with or without presence of discharge. Vaginoscopy is a rapid and simple technique for the diagnosis of purulent vaginal discharge. Clear mucus is normal, whereas purulent and foul-smelling discharge are indicative of disease. Other ways of detecting uterine discharge have been studied, including the gloved hand and the Metricheck device (Simcrotech, Hamilton, New Zealand). The results show clear relation between cytological positive diagnosis and affected condition of the re-productive function.

2. Kondeva-Burdina, M., I. Krasteva, G. Popov, V. Manov. 2019. Neuroprotective and anti-oxidant activities of saponins' mixture from *Astragalus glycyphylloides* in a model of 6-hydroxydopamine-induced oxidative stress on isolated rat brain synaptosomes *Pharmacia*, 66, 233-236.

Abstract: The aim of the study was to investigate the possible neuroprotective and antioxidant activity of purified saponins' mixture (PSM), isolated from *Astragalus glycyphylloides* (Fabaceae), in a model of 6-hydroxydopamine (6-OHDA)-induced oxidative stress on isolated rat brain synaptosomes. Synaptosomes were incubated with 3 different concentrations of PSM: 60 µg/mL; 6 µg/mL; 0.6 µg/mL. The effects of PSM were compared to those of silymarin (S), at the same concentrations. The main parameters, characterized functional and metabolic status of synaptosomes, were investigated: viability (MTT-test) and level of reduced glutathione (GSH). At isolated rat brain synaptosomes, in conditions of 6-OHDA-induced oxidative stress (150 µM), PSM revealed statistically significant, concentration-dependent, neuroprotective and antioxidant effects, compared to those of silymarin. Effects were most prominent at concentration 60 µg/mL. These neuroprotective effects of PSM might be due to the possible activity as scavenger of reactive oxygen species (ROS), produced by p-quinone (toxic metabolite of 6-OHDA).

3. Al Sharif M., V. Vitcheva, R. Simeonova, I. Krasteva, V. Manov, P. Alov, G. Popov, A. Shkondrov, I. Pajeva. 2019. *In silico* and *in vivo* studies of *Astragalus glycyphylloides* saponin(s) with relevance to metabolic syndrome modulation. *Food and Chemical Toxicology*, 130, 317-325.

Abstract: Triterpenoids are well known modulators of metabolic syndrome. One of the suggested modes of action (MoAs) involves peroxisome proliferator-activated receptor gamma (PPAR γ) binding. In this study we aimed to: (i) evaluate *in silico* potential metabolites and PPAR γ -mediated MoA of the sapogenin of the main saponin present in a purified saponins' mixture (PSM) from *Astragalus glycyphylloides*; (ii) estimate *in silico* and *in vivo* PSM's toxicity; and (iii) investigate *in vivo* antihyperglycaemic, hypolipidaemic, antioxidant and hepatoprotective effects of PSM. Metabolites and toxicity were predicted using Meteor and Derek Nexus expert systems (Lhasa Limited) and PPAR γ binding was investigated using the software MOE (CCG Inc.). PSM's acute oral toxicity was evaluated in mice and the

pharmacological effects were assessed in streptozotocin-induced diabetic spontaneously hypertensive rats (SHRs). Liver histopathology was studied as well. PPAR γ weak partial agonism was predicted in silico for 24 probable/plausible Phase I metabolites which docking poses were clustered in 12 different binding modes with characteristic protein-ligand interactions. PSM's beneficial effects on the levels of blood glucose, triglycerides, and total cholesterol, on oxidative stress markers and liver histology in diabetic SHRs were comparable to those of the PPAR γ ligand pioglitazone. PSM's safety profile was confirmed in silico and in vivo.

4. **Kondeva-Burdina M., R. Simeonova, A. Shkondrov, I. Krasteva, G. Popov, V. Manov. 2022. Hepatoprotective and antioxidant effects of alcesefoliside from *Astragalus monspessulanus*. *Brazilian Journal of Pharmaceutical Sciences*, 58, e18902**

Abstract: The hepatoprotective potential of alcesefoliside (AF) from *Astragalus monspessulanus* was investigated. Iron sulphate/ascorbic acid (Fe²⁺/AA) lipid peroxidation was induced in rat liver microsomes and pre-incubated with AF and silybin (100, 10 and 1 μ mol). Pronounced effects were observed in 100 μ mol. In vivo experiments were carried out on rats, challenged orally with carbon tetrachloride (CCl₄) alone and after pre-treatment and followed by curative treatment with AF (10 mg/kg). The activity of the serum and antioxidant enzymes, together with reduced glutathione (GSH) levels and malonedialdehyde (MDA) quantity were measured. Microsomal incubation with Fe²⁺/AA increased MDA production. The pre-incubation with AF reduced the formation of MDA, comparable to silybin. These findings were supported by the in vivo study where CCl₄-induced liver damage was discerned by significant increase in serum enzymes and in MDA production as well as by GSH depletion and reduced antioxidant enzymes activity. The AF pre-treatment and consecutive curative treatment normalizes the activity of the serum and antioxidant enzymes alike, as well as the levels of GSH and MDA. Histological examination of AF-treated livers showed a decrease in the abnormal accumulation of lipids in hepatocytes as well as reduced alterative changes in their structure in a model of CCl₄-induced toxicity.

5. **Georgieva A., G. Popov, A. Shkondrov, R. Toshkova, I. Krasteva, M. Kondeva-Burdina, V. Manov. 2021. Antiproliferative and antitumour activity of saponins from *Astragalus glycyphyllos* on myeloid Graffi tumour. *Journal of Ethnopharmacology*, 267, 113519.**

Abstract: Ethnopharmacological relevance: *Astragalus glycyphyllos* L. has been extensively used in Bulgarian folk medicine as an antihypertensive, diuretic, anti-inflammatory, anti-tumour, in cases of cardiac insufficiency, renal inflammation, calculosis, etc.

Aim of the study: To evaluate the possible in vitro/in vivo anti-proliferative/anti-tumour activity of a purified saponins' mixture (PSM) obtained from the plant.

Materials and methods: Viability and proliferative activity of the Graffi myeloid tumour cells was assessed by MTT test. The morphological alterations were visualized and analysed by

fluorescent microscopy after intravital double staining. An in vivo model of Graffi tumour bearing hamsters was used to examine the influence of PSM on transplantability, tumour growth, survival and mortality as well as to observe pathomorphological changes.

Results: Graffi tumour cells were sensitive to purified saponins' mixture after 24 and 48 h treatment. The treatment induced a statistically significant decrease of the viability/proliferation of the Graffi tumour cells. These effects were concentration- and time-dependent. Fluorescent microscopy studies showed that these antiproliferative effects were connected to the induction of apoptosis. The in vivo study showed the presence of a stromal component, single mononuclear cells in the stroma. Multiple incorrect mitotic figures were observed in the tumour tissue from the control group. Well-formed stroma with accumulation of mononuclear cells and mitotic cells were found in the group, treated with PSM. The tumour weight was decreased in the group, treated with PMS.

Conclusion: The results indicate that PSM exhibited in vitro/in vivo antiproliferative/anti-tumour effects.

6. Popov G., 2021. Seminoma in dancing, brown, Eurasian bear (*Ursus arctos*). *Tradition and Modernity in Veterinary Medicine*, 6, 25-29.

Abstract: In the present research, a pathomorphological study of testicular tumor formation in a dancing, Eurasian, brown bear was performed. There was a significant enlargement of the right testis, which had a pale pink, rough and slightly prominent cut surface with multiple necrotic-degenerative areas and hemorrhages. Microscopic examination revealed a diffuse tumor formation composed mainly of densely arranged, oval neoplastic cells with round nuclei and a small amount of cytoplasm. Notable lymphocyte accumulations were observed around some of the blood vessels. Based on the established morphological finding, the tumor was diagnosed as unilateral, diffuse seminoma.

7. Sapundzhiev E., M. Chervenkov, G. Popov, K. Todorova. 2021. Adrenal glands histological structure in brown bear (*Ursus arctos*, Linnaeus, 1758). *Acta morphologica et anthropologica*, 28, 32-37.

Abstract: The adrenal glands exhibit species specific differences in the outer layer of the glandular parenchyma cortex where in ruminants, some laboratory animals and human the cells form glomeruli, but in carnivores, horse and pig they are arranged in arches. The purpose of this study was to examine histologically adrenal gland of a deceased adult male Brown bear during summer time and to compare its morphology with those of other domesticated animals and human. In our study we found endocrine cell clusters in the capsule of the gland which was described only in horse adrenal gland. We also established that in outer cortical zone of the adrenal glands parenchyma the cells form arches which resembled the shape and the height of the dog's glands. The remaining inner cortical zones and the medulla were situated similarly to those of the bovine, horse, pig, dog and human adrenal glands and did not show structural peculiarities.

8. Chakuleska L., A. Shkondrov, G. Popov, N. Zlateva-Panayotova, R. Petrova, M. Atanasova, I. Krasteva, I. Doytchinova, R. Simeonova. 2022. Beneficial effects of the fructus Sophorae extract on experimentally induced osteoporosis in New Zealand white rabbits. *Acta Pharmaceutica*, 72, 289-302.

Abstract: Sophora japonica is a source of several flavonol, flavone and isoflavone glycosides that are reported to positively affect menopausal symptoms including osteoporotic complications. In the present study fructus Sophorae extract (FSE) was administered orally for three months at a dose of 200 mg kg⁻¹ in ovariectomized (OVX) New Zealand rabbits. 3D computed tomography scans and histopathological images revealed microstructural disturbances in the bones of the castrated animals. FSE recovered most of the affected parameters in bones in a manner similar to zoledronic acid (ZA) used as a positive control. The aglycones of the main active compounds of FSE, daidzin, and genistin, were docked into the alpha and beta estrogen receptors and stable complexes were found. The findings of this study provide an insight into the effects of FSE on bone tissue loss and suggest that it could be further developed as a potential candidate for the prevention of postmenopausal osteoporotic complications.

9. Rafailov R., G. Popov, K. Kanchev, V. Manov. 2022. Pathomorphological findings in dogs with spontaneous heartworm disease. *Tradition and Modernity in Veterinary Medicine*, 7, 53-59.

Abstract: Study reveals the pathomorphological findings of 6 dogs, 3 males and 3 females, diagnosed with Heart-worm disease. By necropsies were found a total number of 144 adult stages (74 male and 70 female) of the nematode *Dirofilaria immitis*, located in *a. pulmonalis*, right ventricle and atrium and *sulcus vena cavae*. The gross pathology shows right-sided enlargement of the heart, dilated pulmonary arteries, and single petechial hemorrhages in the lungs. Histopathologically, degenerative changes in the pulmonary arteries, thickening of the pulmonary valves, interstitial reactions in the lungs and protein precipitates in the kidneys were found.

10. Karabelyov V., V. Angelova, M. Sharkov, R. Mihaylova, G. Popov, T. Pencheva, V. Manov, M. Dangalov, N. Todorova, M. Kondeva-Burdina. 2023. *In vitro/in vivo* effects of some new 2,5-disubstituted 1,3,4-oxadiazole and hydrazone analogues targeting Parkinson's disease. *Journal of Molecular Structure*, 1288, 135755.

Abstract: A series of new 1,3,4-oxadiazole 3a-3k and hydrazone hybrids 5a-5m were synthesized and their activity against both the A and B isoforms of hMAO was evaluated in vitro. The compounds were synthetically accessible in high yields by three different methods. The investigation indicated that some of them, especially 3a and 3d, exhibited effective in vitro inhibition of hMAO-B. Experimental compound 3a had a greater enzyme-inhibiting effect, exhibiting a half-inhibitory concentration (IC₅₀) of 0.55 μM upon a 2 h exposure. The half-inhibitory concentration (IC₅₀) of selegiline (classical MAO-B inhibitor) of hMAO-B activity on human recombinant MAO-B (hMAO-B) is 0.32 μM. All compounds tested at concentration 1 μM, did not reveal a statistically significant inhibitory effect on the activity of hMAO-A, so

malonedialdehyde production (MDA), and the activity of ethylmorphine-N-demethylase (EMND) were measured in liver homogenate. A histopathological examination was performed on the livers, brains and kidneys of all animals. Administered alone, mauritianin had no toxicity. Both biochemical and pathoanatomical findings were similar to those in the silymarin-treated group. CCl₄ caused severe organ damage – increased MDA production, decreased GSH and EMND levels, lipid accumulations in the liver, pericellular oedemas in the brain and interstitial haemorrhages, accompanied by necrotic changes in the kidneys. In animals pre-treated with mauritianin, exposed to CCl₄ and treated 14 days more, minimal biochemical and pathological changes were found, compared to the latter group. A well-preserved histoarchitectonic was found, commensurable to observation of the organs of silymarin and CCl₄ treated rats.

13. Popov G., V. Manov, T. Popova. 2023. Multiple organ mycosis and neoplasia in an Indian elephant (*Elephas Maximus Indicus*). *Tradition & Modernity in Veterinary Medicine*, 8, 19-25.

Abstract: A 58-year-old female Indian elephant (*Elephas maximus indicus*), owned by the Zoological Garden in Sofia, was examined postmortem. The pathomorphological, imaging and microbiological studies revealed lob-ular exudative pneumonia and zonal interstitial fibrosis with supramiliary calcifications and single extensive ossified areas. The uterine musculature was neoplastically transformed, and the endometrium with catarrhal-purulent inflammation. The results of the performed microbiological tests show the probable development of mycosis in the lungs and uterus of the animal, with the causative agent *Penicillium oxalicum*. The obtained results are not described in the available worldwide literature, for the wild and circus and zoo-bred representatives of the elephant family.

14. Popov G. 2024. Canine and feline oral tumors and tumor-like lesions a retrospective study of 206 cases (2018 – 2022). *Tradition & Modernity in Veterinary Medicine*, in press

Abstract: Tumor and tumor-like lesions in the oral cavity of dogs and cats are common in the clinical practice. Their diagnosis requires pathomorphological examination, because of the similar macroscopic appearance. The aim of the present study was to retrospectively analyze tumors and tumor-like lesions of the oral cavity in dogs and cats, and to assess the prevalence, as well as age, sex and breed predisposition. A total of 206 cases of oral cavity lesions (126 dogs; 80 cats) diagnosed cytopathologically and histopathologically between 2018 and 2022 were included. The malignant tumors were predominated in dogs, mainly melanomas and fibrosarcomas. In cats, tumors and tumor-like masses in the oral cavity were of approximately equal prevalence, with lymphoplasmacytic gingivitis and squamous cell carcinomas predominating, respectively.

19.04.2024

Prepared:


/chief assist. Georgi Popov, PhD/