РЕЗЮМЕТА НА ОТПЕЧАТАНИ В ПЪЛЕН ТЕКСТ НАУЧНИ ТРУДОВЕ
/публикации, глави от монографии, книги/
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ДИСЕРТАЦИЯ

Регулаторни аспекти на лечение на остеопороза и аналитични характеристики на някои лекарствени продукти със стероидна структура
Диплома No/дата: 152 - ДМ/08.09.2016, Фармацевтичен факултет (Медицински университет - Пловдив), Първично звено: Фармакогнозия и Фармацевтична химия.

Анотация: Остеопорозата е широко разпространено социално значимо заболяване и рисков фактор за общественото здраве. Класическият терапевтичен подход е с антирезорбтивни антиостеопорозни средства. Перспективна терапевтична тенденция е проучването и аналитично охарактеризиране на съединения с ниска токсичност и потенциални свойства за повлияване едновременно на патогенетичните механизми на заболяването и оксидативния стрес като лекарствени продукти със стероидна структура. Важността на заболяването изисква достъпни аналитични подходи за доказване показатели на прилаганите в терапията лекарства, поради конфиденциалността на фирмените методики и липсата на такива във Фармакопеите. С настоящия труд освен мониторинг на лекарствената терапия във връзка с фармацевтичните грижи, са разработени и валидирани дензитолитрични, високоефективни течнохроматографски и такава с хидрофилно взаимодействие, както дензитолитрични, високоефективни течнохроматографски и такава с хидрофилно взаимодействие, както и в съчетание с газ - мас спектрометрия. Мултидисциплинарният характер на труда, освен с научни приноси го прави приложим в Добрата фармацевтична практика.

ПУБЛИКАЦИИ /извън дисертационния труд/:

1.Obreshkova, D. P., Ivanov, K. V., Tsvetkova, D. D., Pankova, St. A. Quality control of aminoacids in organic foods and food supplements. International Journal of Pharmacy and Pharmaceutical Sciences, ISSN: 0975-1491, 2012; 4(2):404-409.
Scopus

Abstract: The variety of manufactured and proposed on the market food supplements, containing L – Glutamic acid and L – Arginine, set the pattern for the necessity of the developement of method, which can provide the possibility for their simultaneous determination with great selectivity, accuracy and precision. In accordance with this requirements, the aim of current study is to validate an isocratic HPLC method with UV – detection, which can be appropriate for simultaneous quality control of this aminoacids in different dosage food supplements. Results. The data for the degree of recovery (R) are: L – Glutamic acid: 98.15 % (G80), 97.60 % (G100), 104.7 % (G120); L – Arginine: 100.15 % (A750), 100.13 % (A1000), 100.28 % (A1250). For the obtained quantity of aminoacids, SD is lower than 0.01 (L – Glutamic acid) and 0.08 (L –

Arginine). Linearity is presented by the regression equations, which show proportional accordance AUC = f (C) in respective concentration ranges: y = 2.109.x – 458796 (R2 = 0.9956) for L – Glutamic acid in 8.10–4 ÷ 1.2.10–3 g/ml and y = 9.108.x + 699739 (R2 = 0.9977) for L – Arginine in 2.25.10–3 ÷ 3.75.10–3 g/ml. Conclusion. The applied HPLC method with UV – detection is appropriate for quality control of L – Glutamic acid and L – Arginine with great accuracy and precision in food additives.

1. Georgieva, M., Andonova, L., Zlatkov, B., Pankova, St., Koleva, Y., Zlatkov, Al. Synthesis, druglikeness and electrooptical parameters estimation of some monoterpenic ester derivatives of Theophylline 7-acetic acid. Pharmacia, ISSN: 0428-0296 (print), 2014; 61(3):47-56.
Scopus, WoS

Abstract: A series of monoterpenic ester derivatives of theophylline 7-acetic acid with a chosen monoterpene alcohol were synthesized, according to two synthetic pathways. The structure of the new products was elucidated with TLC characteristics, IR and 1 H-NMR spectra. By evaluation of some electro-optical parameters of the studied compounds was established, that the hydrophilicity and the values of HOMO/LUMO energies are of great importance for the biological activity. An elucidation of their drug likeness was made, based on Lipinski's Rule of Five parameters. It was determined, that the newly synthesized products are in good agreement with Lipinski's Rule of Five limitations, which is a premise for good pharmacokinetics. This was also conformed from the results for the %ABS parameter, whereas the target compounds are with commensurable %ABS. The possible enzymatic activity of the newly obtained products was determined. It was found, that compound 3c expresses good enzyme inhibitory activity comparable to the one obtained for the already published product 3a. The obtained values showed that both products are 2-4 times more active, than the initial compound. Using PBT profiler web server, the potential persistence, bioaccumulation and toxicity for the newly synthesized compounds was determined, as part of the EPA criteria. It was concluded that the target structures are not PBT, whereas the synthesized derivatives are persistent, do not bioaccumulate and are toxic, where the least toxic products are 3b,c.

2. Ivanova, S. S., Ivanov, K., Ivanova, S. A., Papanov, S., Obreshkova, D. The effect of treatment with Prasterone (DHEA) on circulating hormones, body composition and muscle strength in men and women. Pharmacia, ISSN: 0428-0296 (print), 2015; 62(4):36-43.
Scopus, WoS

Abstract: Nowadays many individuals are using "performance-enhancing" nutritional supplements. Many professional and nonprofessional athletes take the popular supplements, containing the hormone DHEA (Prasterone), to increase their testosterone levels and improve their performance. Even DHEA has been considered as a hormone with multiple effects, it is sold as a dietary supplement in many countries. Dehydroepiandrosterone (DHEA), a 19-carbon steroid, is situated along the steroid metabolic pathway. It is the most abundant circulating hormone in the body and can be converted to either androgens or estrogens. The physiological function of Dehydroepiandrosterone remains poorly understood and not enough analyzed. In this work we

have analyzed the beneficial effects of a supplementation with Prasterone in order to alleviate its decrease in ageing and improve well-being. We have summarized the results of clinical trials including more than 1000 women and men.

3. Tsvetkova, D., Obreshkova, D., Ivanova, St., Hadjieva, B. Application of TLC-densitometry for analysis of Estradiol hemihydrate in dosage forms. Indian Journal of Pharmaceutical Education and Research (IJPER), ISSN: 0019-5464, 2016; 50(3):482-488.
Scopus, Web of Science

Abstract: The aim of current study was the application of validated TLC-densitometric method for identification and determination of Estradiol hemihydrate in dosage forms. The applied TLC conditions were: Silicagel G60F254 glass plates; mobile phase: chloroform : acetone = 90 : 10 v/v, migration distance of mobile phase: 120 mm, UV-detection at λ = 254 nm. All of the experimental results for the content of Estradiol hemihydrate correspond to the respective confidence interval: Estrofem table: 1.78 mg ÷ 2.12 mg; Femoston F1 table: 1.88 mg ÷ 2.2 mg; Femoston F2 table: 1.99 mg ÷ 2.19 mg; Trisequens T1 table: 1.78 mg ÷ 2.18 mg; Trisequens T2 table: 1.92 mg ÷ 2.12 mg; Trisequens T3 table: 0.97 mg ÷ 1.17 mg. The proposed validated TLC-densitometric method is appropriate for quality control of Estradiol hemihydrate in commercially available tablets.

4. Maslarska, V., Bozhanov, S., **Ivanova, S**., Angelova, V. T. Development and Validation of a liquid chromatographic method for aroylhydrazones at hydrolytic conditions. Current Pharmaceutical Analysis, ISSN: 1573-4129:2021:17(4)528-536.
Scopus, Web of Science

Abstract: The indol-containing derivatives 3a-c with potent antimycobacterial activity against a referent strain M.tuberculosis H37Rv and low cytotoxicity were evaluated for their stability via the precide and HPLC analytical method in aqueous media of pH (2.0; 7.0; 9.0 and 12.0).
The study describes the development and validation of a simple and reliable HPLC- UV procedure for the determination of aroylhydrazone derivatives and their hydrolytic stability. Additionally, to recognize if hydrolysis leads to generating undesired products, the degradation processes were identified.

5. Ivanova, St., Ivanov, K., Pankova, St., Atanasov, P., Obreshkova, D., Petkova, V. Analytical methods for the determination of non-labeled anabolic androgenic steroids supplements. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), ISSN: 2278-4357, 2015; 4(3):10-23
Scopus

Abstract: Analytical methods for the determination of non-labeled anabolic androgenic steroids supplements. World J. Pharm. Pharm. Sci., 2015; 4(3):10-2SJIF (2015) = 6.041 ABSTRACT Recent studies showed that non-hormonal supplements such as vitamins, minerals and amino acids or other food additives can contain anabolic androgenic steroids not declared on the labels of the products. These undeclared substances (often prohormones of testosterone or 19- nortestosterone) can cause health risks to consumers and might lead to positive results in sports doping control. The

analysis of nutritional supplements for anabolic steroids has proven to be rather difficult due to the different matrices in the various products. To conduct a broadbased analysis, a few robust methods capable of analyzing various matrices are needed. To obtain a sensitive gas chromatography-mass spectrometry (GC-MS) analysis, a method including extraction and purification of the analytes followed by GC-MS analysis of the trimethylsilyl (TMS) derivatives of the steroids was developed. In this review we summarized some of the most used methods for determination of steroids in food additives.

7.Tsvetkova, D., Obreshkova, D., Ivanova, S., Hadjieva, B. Evaluation of separation of steroids in combined forms by RP HPLC with UV-detection and gas chromatography. Bulgarian Chemical Communications, ISSN: 0861-9808 (Print); ISSN: 2534-9899 (Online), 2017; 49(2):377-383. Scopus, Web of Science

Abstract: The aim of the current study is the evaluation of the separation of steroids from accompanying substances in drug products as follows: estradiol hemihydrate from didrogesterone (in Femoston tabl.) and estradiol valerate from levonorgestrel (in Climonorm tabl.) and ciproterone acetate (in Climen tabl.). Reversed phase (RP) HPLC with UVdetection and gas chromatography were applied. For the RP HPLC method with UV-detection the following conditions were used: a) column: Nova Pack C18; isocratic elution with mobile phase: acetonitrile : methanol : water = 40 : 5 : 55 v/v/v; flow rate: 1 ml/min; UV-detection at λ = 204 nm; b) column Nova Pack C18; gradient elution with: 0-10 min: acetonitrile : methanol : water = 35 : 5 : 60 v/v/v; 10-20 min; acetonitrile : methanol : water = 70 : 5 : 25 v/v/v, flow rate: 1 ml/min, UV-detection at λ = 230 nm. Although RP-HPLC separation at isocratic conditions allows determination of estradiol hemihydrate with high reproducibility with the highest sensitivity at λ = 204 nm, the analysis in medicinal products requires additional time for elution of components more non-polar than estradiol hemihydrate, which are present in the sample: in Femoston tabl.: tR = 13.42 min for didrogesterone; tR = 4.85 min for estradiol hemihydrate. The experimental results showed that RP HPLC separation with gradient elution is characterized by higher selectivity. It is found that the detection wavelength λ = 230 nm is optimal for the achievement of high sensitivity and it is universal for the identification of other active principles and for obtaning of a stable base line with gradient elution. For the GC method: a column HP-35 (30 m × 0.25 mm × 0.25 μm), temperature program from 100 o C to 330 °C and mass detection were used. Degradation of analytes at high temperature, their different degree of ionization and the different sensitivity of their detection lead to uncertainty in the GC/MS analysis, therefore, HPLC is the more suitable method for analysis of steroid components.

8.Tsvetkova,D. D., Ivanova, St. A., Saso, L., Obreshkova, D., Dimitrov, M. Estimation of linearity and precision of HPLC-HILIC method for analysis of Estradiol hemihydrate. Bulgarian Chemical Communications, ISSN: 0861-9808 (Print); ISSN: 2534-9899 (Online), 2017; 49(2):384-389. Scopus, WoS

Abstract: The aim of the present study was the estimation of linearity and precision of an isocratic HPLC-HILIC method with UV-detection for identification and determination of estradiol hemihydrate in pharmaceutical dosage forms. Linear regression analysis was performed. The regression calibration curve was built. Linearity accordance between concentration and peak area in the range: 3.10-6 g/ml ÷ 4.10-5 g/ml was proved by the regression equation: y = 2698.99 x – 2307.98. The least squares regression yielded a correlation coefficient R2 = 0.999. LOD = 8.10-7

g/ml, LOQ = 8.10-6 g/ml. The results for the accuracy at P = 99 % (t = 4.03) were presented by the percent recovery R [%] within the confidence interval: RC: 97.16 % ÷ 101.84 % (RSD = 1.42). Precision was estimated by standard deviation, relative standard deviation and confidence interval. All data for the obtained quantity of estradiol hemihydrate correspond to the confidence interval: 1.96 mg/100 ml ÷ 2.02 mg/100 ml (SD = 0.03; RSD = 1.51). The high selectivity and efficiency of separation by HPLC-HILIC with UV-detection at λ = 230 nm in an Aminocolumn and the elution of non-polar analytes before the polar ones (estradiol) shortens the time for analysis and leads to high repeatability. Keywords: HPLC-HILIC, estradiol hemihydrate, linearity, precision.

9.Popova, T. M., Ivanova, St. A., Dimitrov, M. V. Characterization and drug release from extended release matrix pellets with Montelukast sodium. Bulgarian Chemical Communications, ISSN: 0861-9808 (Print); ISSN: 2534-9899 (Online), 2018; 50(3):405-410.
Scopus, WoS

Abstract: The undisputable benefits of pellets, associated with improved bioavailability, make them ideal for presenting in extended-release formulations. Unfortunately, despite the many advantages of wet extrusion and spheronization, extended release is difficult to be achieved, even with commonly used release modifying agents like cellulose derivates, polyethylene oxides, sodium alginate, etc. In order to sort out this problem, we included ethanol in the kneading liquid and investigated its influence on the properties of ethylcellulose (EC) pellets and the release behaviour of montelukast sodium. Differential scanning calorimetry of EC showed increase in heat capacity, associated with increased amount of ethanol, which proved that ethanol changes the thermo-mechanical properties of EC. Moreover, evaporation of ethanol during spheronization caused partial melting and dissolution of EC provoking agglomeration, rounding and smoothing, which reflected in the formation of a hydrophobic film around the particle. As a result, the increase in ethanol concentration in the kneading liquid led to obtaining pellets with narrower particle size distribution, higher dimensions, improved sphericity, flatter surface, longer mean dissolution time (MDT) and slower release of montelukast sodium.

10.Tsvetkova, D., Ivanova, St. Estimation of validation parameters of UV-spectrophotometric method for analysis of Valsartan. Journal of Advanced Pharmacy Education and Research, E-ISSN: 2249-3379, 2018; 8(3):37-42.
Scopus

Abstract: The aim of recent investigation was the estimation of the validation analytical parameters selectivity, linearity, LOD, LOQ, accuracy and precision for UV-spectrophotometric method for analysis of Valsartan at λmax = 252 nm (99.98 % ethanol) and λmax = 250 nm (methanol). Selectivity was proved by the fact that in UV-spectra of blank solution was not observed the measured absobance at Valsartan specific wavelengths. The experimental results were subjected to a linear regression analysis: 99.98 % ethanol: y = 81628.x – 0.0226 (A > 0.2); y = 88004.x – 9.10-5 (A < 0.2); methanol: 39508.x + 0.095 (A > 0.2); 53659.x + 0.008 (A < 0.2). Linearity is characterized by coefficient of linear regression: R2 > 0.98. In 99.98 % ethanol LOD = 1.84.10–9 g/ml; LOQ = 6.12.10–9 g/ml; in methanol: LOD = 9.4.10–8 g/ml; LOQ = 3.16.10–7 g/ml. Accuracy is represented by the degree of recovery, which suit confidence intervals: 1) 99.98 % ethanol: RCV160 : 97.51 % ÷ 99.11 %; 2) methanol: RCV160: 97.74 % ÷ 100.06 %. Results

for precision correspond to the relevant interval: 1) 99.98 % ethanol: CV160: 157.06 mg ÷ 157.94 mg; 2) methanol: CV160: 157.52 mg ÷ 158.90 mg. K

11.Tsvetkova, D. D., Ivanova, S. A. GC determination of fatty acids in fish supplements. International Journal of Pharmaceutical Research and Allied Sciences, ISSN: 2277-3657, 2018; 7(3):153-165.
Web of Science

Abstract: Omega-3 fatty acids (especially Docosahexaenoic acid and Eicosahexaenoic acid) are important for humans, due to their health benefits that include: supporting neurodevelopment, preventing from aging process and cognitive decline, reducing the abnormal heart rhythm and stroke in people with heart disease, possessing hypotriglyceridemic effect on type 2 diabetes, and decreasing inflammation. The aim of the current study was the application of optimized GC method for complete separation of fatty acids methyl esters in different trade supplements with fish oil, and their determination by percentage method at the following chromatographic conditions: flow rate of hydrogen: 45 ml/min, inlet pressure of carrier gas: 15 Psi and temperature program: holding on at 140 °C for 5 min, increasing the temperature to 240 °C at a rate of 4 °C/min., maintaining at 240 °C for 20 min, increasing the temperature to 280 °C at a rate of 6 °C/min and holding on at 280 °C for 10 min. After hydrolysis of esters of fatty acids, the free forms in supplements with fish oil were preesterificated with methanol solution of 14 % boron trifluoride. The content of methyl esters of fatty acids in fish food supplements was obtained by the application of percentage method. The experimental results showed that in comparison with other supplements, in Omega-3 Fish Oil Softgel, the highest concentrations of the following acids: Linolenic acid (50.71 %), Stearic acid (10.71 %) and Linoleic acid (15.49 %), were found. The suitability of the system was: Linolenic acid (50.71 %), Stearic acid (10.71 %) and Linoleic acid (15.49 %), were found. The suitability of the system was confirmed by the lack of a statistically significant difference between the values of the chromatographic parameter retention time in the analysis of 3 samples of tR. The advantages of the current study were: the determination of fatty acids without derivatization and application of not expensive hydrogen as a carrier gas. The advantage of the percentage method which was used was providing very fast complete quantitative analysis of all the fatty acids. The GC percentage method which was described can be applied for routine analysis of fatty acids in fish oil food additives, after derivatization to the respective methyl esters.

12.Tsvetkova, D. D., Pankova, St. A. DPPH radical-scavenging activity of Galantamine hydrobromide and Pymadine alone and in combination. Bulgarian Chemical Communications, ISSN: 0861-9808 (Print); ISSN: 2534-9899 (Online), 2018; 50(C):338-344.
Scopus, WoS

Abstract: The overproduction of reactive oxygen species and the weakness of the antioxidant defense mechanisms in the human body are the main reasons for the oxidative stress, which underlies the development of neurodegenerative Alzheimer's disease. Alkaloid Galantamine is nonselective acetylcholinesterase inhibitor with antioxidant activity. Pymadine is nondepolarizing potassium channel blocker having a synergistic effect with Galantamine on the symptomatic

treatment of Alzheimer's disease. The aim of the current study was the evaluation of the radical-scavenging activity (RSA) of Galantamine hydrobromide, Pymadine and the combination Galantamine hydrobromide/Pymadine towards 2,2- diphenyl-1-picrylhydrazyl (DPPH) radical. The decrease in the absorbance of 0.05 mM methanol solution of DPPH at λ = 516 nm in presence of methanol solution of: 1 mM Butylhydroxytoluene (BHT) (standard); 1 mM ÷ 5 mM Galantamine hydrobromide; 1 mM ÷ 5 mM Pymadine and 5 mM Galantamine hydrobromide/5 mM Pymadine was monitored by spectrophotometry in equal intervals of 5 s for a total period of 30 min. The regression equations were used for calculation of the RSC50: RSA (Galantamine hydrobromide) = 3.419.e0.293.c, RSC50 (Galantamine hydrobromide) = 9.16 mM; RSA(Pymadine) = 0.460.e0.411.c, RSC50 (Pymadine) = 11.41 mM. RSA of the investigated compounds was compared with the effect of standard BHT and the relative radical-scavenging activity (RRSA) and relative decrease of radical-scavenging activity (RDRSA) were calculated. The experimental results showed that the combination of 5 mM Galantamine hydrobromide/5 mM Pymadine has a higher RSA (20.19 %), compared to 5 mM Galantamine hydrobromide (15.44 %) and 5 mM Pymadine (2.48 %) itself.

13.Tsvetkova, D. D., Ivanova, S. A. Application of UV-spectrophotometric method for determination of Losartan Potassium in tablets. Indo American Journal of Pharmaceutical Sciences (IAJPS), ISSN: 2349-7750, 2018; 5(8): 8393-84
WoS

Abstract: The aim of current study was to validate spectrophotometric method with UV-detection for identification and determination of Losartan Potassium 99.8 % ethanol in respect of analytical parameters: selectivity, linearity, limit of detection (LOD), limit of quantification (LOQ), accuracy and precision (repeatability). For Losartan Potassium in 99.8 % ethanol at λ max = 298 nm for A1% 1cm and ε the obtained results for A > 0.2 and A < 0.2 are: 1) A > 0.2: at 3.10–6 g/ml ÷ 1.25.10–5 g/ml; A 1% 1cm: 725 ÷ 823; ε: 37347 ÷ 42335 2) A < 0.2: at 2.5.10–7 g/ml ÷ 1.10–6 g/ml; A1% 1cm: 1201 ÷ 1567; ε: 61816 ÷ 80651 Analytical parameter accuracy is represented by the degree of recovery, which in the corresponding confidence possibility suit the confidence interval: R CT60: 100.31 % ÷ 102.05 %; R CT80: 99.22 % ÷ 103.18 %; R CT100 : 93.58 % ÷ 101.9 %. For precision is proved that all results for the quantities correspond to the relevant confidence interval: CT60: 60.31 mg ÷ 60.77 mg; CT80: 79.82 mg ÷ 82.18 mg; CT100: 94.22 mg ÷ 101.58 mg.

14.Tsvetkova, D., Ivanova, S. Investigation of HPLC behaviour and system suitability estimation for combination Galantamine hydrobromide and Pymadine. Journal of Advanced Pharmacy Education and Research, E-ISSN: 2249-3379, 2019; 9(2):82-88.
Scopus

Abstract: The aim of the current study was the investigation of HPLC behaviour, separation and system suitability for the combination of Galantamine hydrobromide/Pymadine in model mixtures, in accordance with the new trend of multi-target therapy of Alzheimer's disease by combining acetylcholinesterase inhibitor with its potential synergist. The system suitability test for the simultaneous determination of the components was carried out by the following criteria: 1)

retention times in the analysis of 6 model mixtures; 2) the change of values for separation degrees in minor changes of the ratio of mobile phase components and mobile phase flow rates. The system suitability was confirmed by the lack of the statistically significant differences between the values of parameter retention time tR [min.]: tR = 3.179 (Galantamine hydrobromide), tR = 5.272 (Pymadine). In changing the ratio of mobile phase components, the data for separation degree were in the range of 1.76 ÷ 1.83, and the symmetry factor (T) was in the range of 0.94 ÷ 1 (Galantamine hydrobromide), 0.96 ÷ 1.03 (Pymadine). Upon varying the mobile phase velocity, T values varied between 0.94 ÷ 1 (Galantamine hydrobromide) and 0.95 ÷ 1.06 (Pymadine). The system suitability was confirmed by the fact that minor changes in the ratio of the mobile phase components or in the mobile phase flow rate didn't decrease the degree of separation.

15. Ivanova, St., Ivanov, K., Pankova, St., Zlatkov, Br., Stoychev, K. Sport supplementation: beneficial effects of vitamin E and Creatine on exercise performance. Pharmacia, ISSN: 0428-0296 (print), 2015; 62(2):40-49.
Scopus, Web of Science

Abstract: Most athletes use food supplements to obtain a well-trained, athletic, and healthy looking body. Supplementation practices vary between sports and individual athletes. Many athletes take food additives, containing vitamin E and food additives with creatine because of their favorable effects on muscle mass. Vitamin E deficiency leads to serious damage to the body, especially the muscles. Antioxidant supplementation with Vitamin E is likely to provide beneficial effects against exercise-induced oxidative tissue damage. Many studies have examined the effects of creatine supplementation on exercise performance. This article reviews the literature on vitamin E and creatine supplementation in sport and shows their beneficial effect on exercise performance.

16. Ivanova, S., Ivanov, K., Mladenov, R., Papanov, S., Ivanova, St., Obreshkova, D., Atanasov, P., Petkova, V. Food supplements with anabolic and androgenic activity – UHPLC analysis of food additives, containing Tribulus terrestris extracts. World Journal of Pharmaceutical Research, ISSN: 2277-7105: 2016;5(3):6-13.
WoS

Abstract: Over the last 50 years AAS have been used by many sportsmen to improve physical endurance and better results in sport. The widespread use of AAS is a problem because of the serious side effects of these medicines. Long-term effects affect the cardiovascular system, mental health, endocrine system. Infertility defects, feminization and masculinization are often irreversible side effects. Rate risk - benefit shows that any kind of AAS abuse is extremely dangerous. AAS can be used legally only like prescribed medicines and only for medical purposes. Many athletes prefer taking food supplements with androgenic effects instead of conventional steroids because of their safety profile. By the end of 2004 Prohormones have been one of the most attractive supplements with anabolic and androgenic effects. In 2005 the use and distribution of the majority of these Prohormones became illegal. Nowadays there is a big interest about food additives, containing extract of Tribulus Terrestris because of their androgenic and anabolic activity. In this work we have demonstrated a UHPLC method of analysis of FA and OTC, containing extract of Tribulus Terrestris with mass spectral detection with high resolution (HRMS)

and atmospheric pressure ionization "electrospray". This combination gives as quickly and as efficiently split and the possibility of identifying the separated components of the samples analyzed by the exact weight of their molecular ions.

17.Пенчева И., Обрешкова Д., Пейкова Л., Папанов С., Петкова Е., Иванов К., Петров Г., Трайкова Н., Божкова М., Панкова Ст., Григоров Л. Комплексообразование фитина с железными и калциевыми ионами (спектрофотометрическое исследование). XX международная заочная научно-практическая конференция, СИБАК, Новосибирск 01.07.2013 – 152 с., Современная медицина: актуальные вопросы, ISSN: 2309-3552, 2013, 20, с. 123-130, https://www.elibrary.ru/item.asp?id=19142751

Абстракт: Разработеният и описан метод за анализ при прилагане на инфрачервена и ултравиолетова спектрофотометрия дава възможност за определяне и комплексообразуване на новополучени комплекси при взаимодействие на фитина със соли на желязо и калций. Описани са аналитичните подходи и характеристики, както и спектралните характеристики на образуваните комплекси и сравнени с тези на фитина. Изследвано е и комплексообразуването както на субстанция фитин, така и на лекарството Фитин капсули. Описаните и визуализирани спектри са представени.

18. Pankova, St., Tsvetkova, D. Role of phytoestrogens in prevention of osteoporosis. International Journal of Current Pharmaceutical Research, ISSN: 0975-7066, 2015; 7(2):1-6.

Abstract: Articles pertinent to the metabolism of phytoestrogens, including female reproduction (in particular menstruation and menopause), cardiovascular disease, **osteoporosis**, and cancer were assessed including relevant case control or cohort studies, as well as randomized trials and review articles. Epidemiological studies regarding human data were included, as well as human cell line and animal studies when there were no relevant human data available. We conclude that phytoestrogens exhibit physiological effects in humans. Mild estrogenic changes occur in postmenopausal women. Benefits are seen regarding hypercholesterolaemia. Epidemiological, animal, and *in vitro* data encourage further assessment of the role of phytoestrogens in cancer prevention.

19. Ivanov, K., Ivanova, St., Doncheva, D., Georgieva, M., **Pankova St**., Zlatkov, B., Pencheva, I., Papanov, S. Analytical methods for quality and quantity control of energy drinks and food supplements, containing amino acids. International Journal of Nutrition and Food Sciences, ISSN: 2327-2694 (Print); ISSN: 2327-2716 (Online), 2015; 4(1):9-13.

Abstract: The need for analytical control of food supplements and “energy“ drinks containing amino acids is huge. In the literature there are describes various analytical techniques for their qualitative and quantitative analysis. Most preferred methods is HPLC because of its range, accuracy and speed. Despite the wide variety of methods, there isn’t coherent analytical system associated with the standardization of food additives containing amino acids.

20. Papanov, S., Pankova, St., Ivanov, K., Ivanova, St., Doncheva, D., Pencheva, I. Analytical methods for quality and quantity control of food supplements, containing Caffeine. International Journal of Nutrition and Food Sciences, ISSN: 2327-2694 (Print); ISSN: 2327-2716 (Online), 2015; 4(1):14-17.

Abstract: Many beverages such as soft drinks, coffee and tea contain the mild stimulant caffeine (C8H10N4O2). The caffeine content varies widely from about 100 µg/mL (100 ppm) in sodas to over 1000 µg/mL in certain types of coffee. For this reason the caffeine and the content in they need to be analyzed. A rapid and selective high-performance liquid chromatographic (HPLC) method is developed for the separation and determination of caffeine.

21.Tsvetkova, D.D., Klisurov, R.C., Pankova, St. A., Zlatkov, B.A. Investigation of some pharmacological effects of Caffeine and Taurine in food supplements. International Journal of Nutrition and Food Sciences, ISSN: 2327-2694 (Print); ISSN: 2327-2716 (Online), 2015; 4(1):18-23.

Abstract: In modern times in all age groups energy supplements containing different amounts of Caffeine and Taurine are applied. Caffeine is purine alkaloid, which stimulates central nervous system action, enhances the strength and frequency of the cardiac contractions and increases the excretion of urine. Taurine is a sulfur containing amino acid, which possesses many fundamental biological roles including: effect on synaptic transmission in the central nervous system, cardiotropic action, antioxidant and anticonvulsant activity, improvement of energy processes, stimulation of reparative processes in tissues, protection of eyes cataract, decrease of cholesterol and stimulation of immune system. The combination of Caffeine and Taurine provide benefit due to obtaining synergism of pharmacological effects in increasing of physical activity, stimulation of brain action, cognition, memory and attention. In connection with the significant enlarging of the consumption of energy drinks, especially by children and young qualities valued especially in the 20th century apple fruit is preferred worldwide. Objective: The current work presents the antioxidant specifications of several varieties of apples distributed in Republic of Bulgaria and also methodology/equipment and method for the preparation of the apples for the experiment/ used to determine the antioxidant characteristics. Methods: We use the following methods: spectrophotometric people in recent years the requirements for regulation and control of the labeling of these products in many countries are enlarged. In many food additives Caffeine and Taurine are added in not labeled high concentrations, which can provoke and increase their side effects. High consumption of Caffeine enhances its adverse effects on body: anxiety, headache, insomnia, nervousness, respiratory disorders, tachycardia, tremor, dehydration. In children the adverse reactions of Caffeine in much lower doses than adults are occurred. In high concentrations Taurine has adverse effects on brain activity and can induce psoriasis. The result of combination of Caffeine and Taurine is associated with increased diuretic effect and loss of water and salts from the body, especially in children and young people. Because of these facts the quality and quantity control of included compounds in food supplements is important for their health safety.

22.Papanov, St., Petkova, Ek., Pankova, St., Traykova, N., Hadjidekov, G., Grudeva, V.

Antioxidant characteristics of different varieties distributed in Bulgaria. International Journal of Technical Research & Applications, ISSN: 2321-7332, ISSN: 2320-8163, 2015; 3(2):33-36.

Abstract: Background: Because of its wonderful taste, as well as numerous nutritional and medicinal qualities valued especially in the 20th century apple fruit is preferred worldwide. Objective: The current work presents the antioxidant specifications of several varieties of apples distributed in Republic of Bulgaria and also methodology/equipment and method for the preparation of the apples for the experiment/ used to determine the antioxidant characteristics.

23.Tsvetkova, D. D.,Ivanova , S. A. Investigation and estimation of spectrophotometric values specific and molar absorbances for Losartan Potassium and Valsartan. Journal of Applied Science – IJRDO, 2018; 4(9):13-20, ISSN: 2455-6653.

Abstract. The aim of current investigation was the investigation and estimation of spectrophotometric values specific (A 1% 1cm) and molar (ε) absorbances for angiotensin receptor blockers Losartan Potassium and Valsartan. The following experimental results were obtained: for solutions of referense standards Losartan Potassium (λmax = 208 nm) at A > 0.2 (3.10–7 g/ml ÷ 6.75.10–7 g/ml): A 1% 1cm: 12113 ÷ 12778; ε: 558441 ÷ 589064; for Valsartan in 99.8 % ethanol at λmax = 252 nm for A > 0.2 (6.10–6 g/ml ÷ 1.10–5 g/ml): A 1% 1cm : 774 ÷ 800; ε: 33730 ÷ 34840. For Valsartan in methanol at λmax = 250 nm for A > 0.2 (3.5.10–6 g/ml ÷ 1.10–5 g/ml): A 1% 1cm: 480 ÷ 628; ε: 20885 ÷ 27368. Specific (A 1% 1cm) and molar (ε) absorbances for A < 0.2 were: [C] g/ml A 1% 1cm ε 3.5.10–8 ÷ 1.10–7 13107 ÷ 16710 604252 ÷ 770348 Losartan Potassium 5.10–7 ÷ 2.10–6 877 ÷ 880 38221 ÷ 38304 Valsartan (99.8 % ethanol) 1.2.10–6 ÷ 2.5.10–6 574 ÷ 617 24997 ÷ 26875 Valsartan (methanol).

24.Ivanova, S., Ivanov, K., Mladenov, R., Obreshkova, D., Ivanova, St., Stoyanov, P. HPLC detection of Dehydroepandrosterone food additives by using normal-phase HPLC. Scripta Scientifica Pharmaceutica, Medical University of Varna, 2016; 3(1):54-59, ISSN: 2367-5500 (online), ISSN: 2367-6000 (print).

Abstract: A normal-phase High Performance Liquid Chromatography (HPLC) method was developed for the determination of dehydroepiandrosterone (DHEA) in food supplements. We have used an HPLC 200 (Perkin Elmer, USA) with a spectrophotometric detector LC-785A (Bioanalytical systems, USA) and a thermostat (Perkin Elmer, Waltham, MA, USA). We have chosen isocratic HPLC elution, column: LiChrospher (100 DIOL 250 x 4 mm x 5 μm), mobile phase: acetonitrile: water = 98: 2 v/v, flow rate: 1 ml/min. and detection at λ = 202 nm. We have found that this method allows fast and selective qualitative and quantitative determination of DHEA in pharmaceutical products.

25.Tsvetkova, D., Ivanova, St., Obreshkova, D. P., Atanasov, P., Yordanova-Laleva, P. D., Pashev, A. S. Antioxidant activity, pharmacological effects and distribution in food products of vitamins C, A and E. Science Pharmacology = Наука Фармакология, 2020; (2):15-19.- https://publishing.arbilis.com/p=3166 ISSN: 1314-2674 (print).

Abstract

Oxidative stress leads to development of chronic diseases, including cardiovascular disease, stroke, neurodegenerative diseases (Alzheimer, Parkinson), carcinogenesis, artrtitis, macular

degeneration and cataractogenesis. Vitamins C, A and E are an important dietary antioxidants, which significantly decrease the adverse effect of reactive species. Ascorbic acid is a potent water soluble antioxidant capable of scavenging an array of reactive oxygen species, hydroxyl, alkoxyl, peroxyl, superoxide anion, hydroperoxyl radicals and reactive nitrogen radicals such as nitrogen dioxide, nitroxide, peroxynitrite. By regenerating Vitamin E, Vitamin C indirectly prevents lipid peroxidation. The mechanism of the antioxidant action of Vitamins A is due to the direct binding of peroxide radicals. Vitamin E protects low-density lipoproteins, cell membrane lipids and other lipidcontaining components from oxidation by direct binding to free radicals. Vitamin E blocks the synthesis of free radicals by inhibiting the active site of the enzyme 12-lipoxygenase.

Vitamins C, A and E are involved in the maintenance and regulation of various metabolic processes in the body: protein synthesis and metabolism of carbohydrates and fats. Vitamin C and Vitamin A are found in fruits, vegetables, and animal products, while Vitamin E is found in cereals, dried oils, eggs and fish. The use as a nutritional supplement of multivitamin products containing the antioxidant Vitamins C, A and E is recommended for preventive or restorative therapy, for infectious diseases, for metabolic disorders, for neuritis, intoxication and osteoporosis.

26. Papanov, S. I., Petkova, Ek. G., Ivanova, St. D., Ivanova, St. A. Caffeine – the most abused psychoactive substance (survey conducted among students and their parents). International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS), 2016; 5(2):504-512 ISSN: 2277-4998.

Abstract:Caffeine is a widely used psychoactive substance in both adults and children that is legal, easy to obtain, and socially acceptable to consume. Although once relatively restricted to use among adults, caffeine-containing drinks are now consumed regularly by children. Unfortunately, our knowledge of the effects of caffeine use on behavior and physiology remains understudied and poorly understood. The purpose of this article is to review what to discuss why children and adolescents may be particularly vulnerable to the negative effects of caffeine, and to propose how caffeine consumption within this population may potentiate the rewarding properties of other substances.

27. Ivanova, St., Peikova, L., Koleva, P., Tsvetkova, D., Petkova, V. Applying HPLC-HILIC as method for analysis of pharmaceutical compounds. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), 2016; 5(1):1-12 ISSN: 2278-4357.

Abstract: In this investigation, hydrophilic interaction liquid chromatographic (HILIC) applications for pharmaceutical analysis are discussed. The HPLC-HILIC technique uses an aqueous/organic modifier mobile phase with a high organic modifier fraction and a hydrophilic stationary phase, chemically bonded silica particle, and monolithic phases. The bare-silica columns are most frequently used. The much less applied polymer-based columns are also divided into particle and monolithic phases. There are many stationary phases that can be used in HILIC mode and many phases are generally described as independently of their chemistry.

28. Tsvetkova, D. D., Obreshkova, D. P., Ivanova, S. A., Yankov, V. P., Atanasov, P., Petkova, V. B. Current trends in pharmacological applications of sartans. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), 2016; 5(7):317-350, ISSN: 2278-4357.

Abstract: The aim of current study is to summarize the application of sartans for thetapy of hypertension and related cardiovascular diseases. Arterial hypertension is a widespread disease with more than 1 billion cases worldwide. Hypertension is one of the most significant social disease, leading to stroke, myocardial infarction and high mortality. A major advantage of sartans in comparison with ACE-inhibitors in the treatment of essential hypertension, is that not inhibit the degradation of bradykinin and other kinins and thus not cause the side effects (cough and angioedema) on, hypertension with left ventricular dysfunctioof ACE-inhibitors. Sartans are applied in a number of heart diseases: heart failure, atrial fibrillatin, acute coronary syndrome, for protection o of ACE-inhibitors. Sartans are applied in a number of heart diseases: heart failure, atrial fibrillation, hypertension with left ventricular dysfunction, acute coronary syndrome, for protection of vascular endothelium and platelet aggregation, for prevention of stroke, cerebral ischemia, Alzheimer, Parkinson; and migraine. Blood pressure control is optimized by fixed-dose formulations of sartans with thiazide diuretic Hydrochlorothiazide (HCTZ): Candesartan (Atacand HCoT), Irbesartan (Avapro HCT) Olmesartan medoxomil (Benicar HCTZ), Valsartan (Co-Valsacor).

29. Papanov, St., Petkova, E., Ivanova, S., Obreshkova, D., Petkova, V. Apples from variety Golden Delicious, Red Delicious, Grey-Smith – an antioxidant characteristics. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), 2016; 5(8):8-13, ISSN: 2278-4357.

ABSTRACT. The apple is among the best fruit foods for human, widely used from all societies. This is due to its diverse chemical composition. The phytonutrient content of apple does not change notably throughout the period of their storage.That is why the aim of this study is to establishe the antioxidant properties of apples from variety Grey Smith, Golden and Red Delicious, distributed in Bulgaria.The scientific methods applied include systematic approach and critical analysis of the available scientific periodicals; mathematical and statistical methods and technical analysis / spectrophotometric method.The esukts showthat the apples combine flavonoids, fiber and antioxidants intounique and incomparable way. We determine the antioxidant activity by the difference of absorption of the control sample and the sample with the corresponding apple juice.The studied varieties of apples can be arranged according their antioxidant activity as follows: Grey smith, Golden Delicious(Ognyanovo), Golden Delicious (Katunitza), Red Delicious.

30.Tsvetkova, D., Obreshkova, D., Ivanova, St., Yankov, V., Atanasov, P., Hadjieva, B. Telmisartan quality control by validation of UV-spectrophotometric method. International Journal of Innovative Research in Medical Science (IJIRMS), 2016; 1(4):113-123, ISSN: 2455-8737.

Abstract The aim of current study was to validate spectrophotometric method with UV-detection for identification and determination of Telmisartan in 99.8 % ethanol in respect of analytical parameters: selectivity, linearity, limit of detection (LOD), limit of quantification (LOQ), accuracy

and precision (repeatability). For Telmisartan in 99.8 % ethanol at □ max = 298 nm for $A^{1\%}_{1cm}$ and □ the obtained results for A □ 0.2 and A □ 0.2 are: 1) A 0.2: at 3.10^{-6} g/ml $1.25.10^{-5}$ g/ml; $A^{1\%}_{1cm}$: 725 □ 823; □: 37347 □ 42335 2) A □ 0.2: at $2.5.10^{-7}$ g/ml □ 1.10^{-6} g/ml; $A^{1\%}_{1cm}$: 1201 □ 1567; □: 61816 □ 80651 .Analytical parameter accuracy is represented by the degree of recovery, which in the corresponding confidence possibility suit the confidence interval: R C_{T60}: 100.31 % □ 102.05 %; R C_{T80}: 99.22 % □ 103.18 %; R C_{T100} : 93.58 % □ 101.9 %. For precision is proved that all results for the quantities correspond to the relevant confidence interval: C_{T60}: 60.31 mg □ 60.77 mg; C_{T80}: 79.82 mg □ 82.18 mg; C_{T100}: 94.22 mg □ 101.58 mg.

31. Tsvetkova, D., Ivanova, St. Validation parameters of densitometric method for simultaneous determination of Galantamine hydrobromide and Pymadine. Journal of Advanced Pharmacy Education and Research, E-ISSN: 2249-3379, 2018; 8(4):1-8.

ABSTRACT:The aim of the current study was the validation of a TLC-densitometric method for quality control of Estradiol valerate in drug combination dosage forms. The TLC conditions were: glass plates with silicagel $G_{60}F_{254}$; mobile phase: chloroform : water = 90 : 10 v/v. The TLC-densitometric method was validated with respect to the analytical parameters: limearity, LOD, LOQ, accuracy and precision (repeatability). Linear regression analysis was performed. The regression calibration curve was built. Linearity accordance between the concentration and spot area in range:
5.10^{-4} g/ml ÷ 3.10^{-3} g/ml was proved by the regression equation: y = 28874286.x + 14290. LOD = $3.15.10^{-4}$ mg/ml; LOQ = $9.54.10^{-3}$ mg/ml.
For estimating the accuracy the recovery is presented in R [%] □ RSD [%] with the respective confidence interval:
R[1.5 mg]: 95.92 % □ 103.98 %; R[2 mg]: 93.35 % □ 108.89 %; R[2.5 mg]: 95.37 % □ 103.77 %. Precision is estimated by standard deviation, relative standard deviation and confidence interval. All data for the obtained quantity correspond to the confidence interval: 1.88 mg □ 2.17 mg. The proposed validated TLC-densitometric method is appropriate for quality control of Estradiol valerate in commercially available tablets.

32. Tsvetkova, D., Obreshkova, D., Ivanova, S., Yankov, V., Atanasov, P. Quality control of impurities and comparison of pharmacokinetic parameters of angiotensin receptor antagonists. Journal of Multidisciplinary Engineering Science Studies (JMESS), ISSN: 2458-925X, 2016;2(7):647-661.

***Abstract*—**The major risk for mortality from chronic heart and kidney disease worldwide is an inadequate treatment of hypertension. Therapy of hypertension becomes successfully by the developed in recent years a new class compounds – sartans (angiotensin II-receptor antagonists), specifically blocking renin angiotensin aldosteron system. Benefits of sartans in hypertensive patients include reduction in left ventricular hypertrophy, improvement of diastolic function, decrease of ventricular arrhythmias, reduction of microalbuminuria, improvement of renal function, cardioprotective effect in patients with heart failure. The impurity profiling of

active pharmaceutical ingredients is an important quality control parameter. Impurities are analysed by high performance liquid chromatography, thin layer chromatography, capillary electrophoresis and spectrophotometry. For estimation of impurities of sartans the most applied methods, due to highest selectivity and specificity in separation and detection, are: HPLC-MS, HPLCMS/MS, HPLC-ESI/MS and HPLCTOF/MS. The important pharmacokinetic data of sartans are:1.suitability to the criteria of the rule of Christopher A. Lipinski (Rule 5): a) Mr □ 500; b) H – donors (NH, OH) □ 5; c) H – acceptors (N, O) □ 10; d) logP□5: LogP = 4.9 (Candesartan); 3.58 (Eprosartan); LogP = 4.52 (Irbesartan); LogP = 4.68 (Losartan); LogP= 4.31 (Olmesartan); LogP = 4.66 (Telmisartan); LogP = 3.68 (Valsartan) high plasma protein binding, which provide to be obtained once daily; Telmisartan is with the highest oral bioavailability and with the longest half-life;the bioavailability of other sartans is: Candesartan (3-11 %); Tasosartan (3-7 %); Zolasartan (20 %); Enoltasosartan (36-72 %).

33. Ivanova, S. A., Tsvetkova, D. D., Obreshkova, D. P. GC determination of Docosahexaenoic acid, Eicosapentaenoic acid and other fatty acids in food supplements by percentage method. Scholars Academic Journal of Pharmacy, ISSN: 2347-9531 (print), ISSN: 2320-4206 (online), 2018; 7(9):425-433.

Abstract: The aim of current study was the application of GC method for separation of Docosahexaenoic acid and Eicosahexaenoic acid from other fatty acids in food supplements and their further determination by percentage method. This method for quantitative analysis is based on the measuring of the area of all peaks in the chromatogram of the hydrolyzed and methylated samples and calculation of their sum, whereby the area of each peak is calculated as a percentage of the total area of the chromatographic peaks. After hydrolysis of fatty acid esters, the free forms were preesterificated with methanol solution of 14 % boron trifluoride. For separation of Docosahexaenoic acid and Eicosahexaenoic acid from other fatty acids was applied GC method: flow rate of carrier gas: hydrogen: 45 ml/min., inlet pressure: 15 Psi, temperature programm: 140 □C for 5 min, increasing the temperature to 240 □C at a rate of 4 □C/min, 240 □C for 20 min, increasing the temperature to 280 □C at a rate of 6 □C/min and 280 □C for 10 min. The suitability of the system was confirmed by the lack of a statistically significant difference between the values of the chromatographic parameter retention time in the analysis of Methylmyristate (SD = 0.185, RSD = 1.22 %), Methylpentadecanoate (SD = 0.39, RSD = 2.18 %), Methylheptadecanoate (SD = 0.31, RSD = 1.34 %), Methyldocosahexanoate (SD = 0.017, RSD = 0.05 %), Methyleicosapentaenoate (SD = 0.013, RSD = 0.04 %), Methylbehenate (SD = 0.15, RSD = 0.43 %), Methylerucate (SD = 0.13, RSD = 0.37 %. Maximum concentration was found for Methyleicosapentaenoate (20.58 %) and minimun concentration was observed for Methylnonadecanoate (0.30 %). The described GC persentage method can be applied for rutine analysis of Docosahexaenoic acid and Eicosahexaenoic acid in combination with other fatty acids in food additives.

34. . Obreshkova, D. D,. Tsvetkova, D. D., Ivanova, S. A**.**, Yordanova-Laleva, P. D. Comparison of different modifications of DPPH method for the estimation of radical scavenging activity of

Silybum marianum L. International Journal of Current Advanced Research, ISSN: 2319-6475, 2020;9(1):21060-21065.

Silybum marianum (L.) is a medicinal plant containing Silymarin – a complex of flavonolignans: Silybin A, Silybin B, Isosilybin A, Isosilybin B, Silychristin A, Silychristin B, Silydianin, Silandrin, Isosilandrin, Silychermin, Neosilychermin, Siliamandine and Siliymonine. Silymarin possesses antioxidant, anticarcinogenic, anti-inflammatory, antifibrotic, hepatoprotective, immunomodulatory and neuroprotective activity and is applied in liver cirrhosis, acute and chronic viral hepatitis. Hepatoprotective action is a result of antioxidant, anti-lipid peroxidative activity and of reduction of glutathione oxidation.
Objective: The aim of cuttent study was to compare the different modificated DPPH methods for determination of free radical scavenging activity of Silybum marianum L. extracts.
For the estimation of free radical scavenging activity of Silybum marianum L. extract, the modifications of DPPH method comprise the changing of :
reaction time(from 30 min. to 90 min.)
solvent for DPPH (methanol, ethanol, butanol)
concentration of DPPH (from 0.1 M to 0.006 mM, 0.15 mM, 0.2 mM, 0.3 mM, 1 mM)
proportion between volumes of DPPH and plant extracts
absorption maximum: from λ = 517 nm to λ = 515 nm or λ = 520 nm.
For different modifications of DPPH method for the assessment of free radical scavenging activity of Silybum marianum L. extract, the following most important conclusions can be summarized:
the most often applied modifications are in connection with the changing of:
concentration of DPPH solution: 0.1 mM to 0.006 mM, 0.15 mM, 0.2 mM, 0.3 mM, 1 mM,
proportion between volumes of DPPH and plant extract
the most often used conditions for DPPH method are:
30 min. reaction time between DPPH solution and plant extracts
application of methanol as solvent,absorption maximum: λ = 517 nm.

35. **.** Ivanova, St., Vasileva, L. Current and emerging strategies in osteoporosis management Current Pharmaceutical Design, ISSN: 1381-6128, e-ISSN: 1873-4286, 2017; 23(41):6279-6287.

Abstract:

The abnormal loss of bone tissue is defined as osteoporosis. Increased risk of fractures, low bone mineral density (BMD) and loss of the structural and biomechanical properties of the bone tissue characterize this pathological condition. Physiologically bone undergoes a continuous remodeling process involving balance between the activity of osteoblast and osteoclast. Disruption in this balanced condition increases the risk of osteoporosis. Both sexes are affected, but with higher prevalence in women after menopause. This review aims to enlighten the established and emerging trends in prevention and treatment of bone loss. Herbal supplementation and physical exercises are suggested as addition to the well-established therapy in prevention and management of osteoporosis. Treatment strategies of osteoporosis include non- pharmacological treatment - diet rich of calcium and vitamin D, healthy lifestyle, proper exercise plan, and pharmacological therapy. Preventive and treatment strategies have to consider combination of non-pharmacological and pharmacological approaches for minimization of the fracture risk in osteoporosis.

36.Yankov, V. P., Tsvetkova, D. D., Obreshkova, D. P., Ivanova, S. A, Petkova, V. B. Recent applications of spectrophotometric and thin layer chromatographic methods for quality control of fixed dosage combinations of sartans with Hydrochlorthiazide. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), ISSN: 2278-4357, 2016; 5(6):18-43**.**

ABSTRACT The aim of current study is to summarize the application of spectrophotometric and thin layer chromatographic methods for simultaneous determination of sartans and thiazide diuretic Hydrochlorothiazide in fixed dosage preparations. Hypertension is one of the most significant social disease, leading to stroke, myocardial infarction and high mortality. Combination therapy with antihypertensive drugs from different classes: beta-blochers, calcuium antagonists, angiotensine-converting enzyme inhibitors, angiotensine II receptor antagonis (sartans) and duiretics improves blood pressure by synergistic effect. The theatment with fixed-dose formulations in a single-dosage form allows to optimize the blood pressure control. The very modern trends in hypertension therapy is the application of fixed dosage preparations of sartans with a thiazide diuretic Hydrochlorothiazide (HCTZ): Candesartan (Atacand HCT), Irbesartan (Avapro HCT), Olmesartan medoxomil (Benicar HCTZ), Valsartan (Co-Valsacor). For improvement of blood pressure control in hypertension current trends include triple fixed-dose combinations with an angiotensin II receptor blocker, a calcium channel blocker.

37. Petkova, V., Obreshkova, D., Hadzhieva, B., Ivanova, St. Regulatory aspects of Omega polyunsaturated fatty acids in dietary supplements. Journal of Pharmaceutical Research International, ISSN: 2456-9119, 2017; 18(2):1-7.

Absrtact:Food additives are subject to certain regulatory requirements, as in some countries, the control is very strict, while in others there is almost no control. Some food supplements can affect existing diseases or interact with some medications, food and beverage, a fact that is not mentioned on the packaging or in product instructions.The aim of the study is to analyze the legislative framework for authorization and use of omega polyunsaturated fatty acids in the US and the European Union. The documents of 10 pieces of legislation were analyzed.

38. Tsvetkova, D., Ivanova, St. Validation parameters of densitometric method for simultaneous determination of Galantamine hydrobromide and Pymadine. Journal of Advanced Pharmacy Education and Research, E-ISSN: 2249-3379, 2018; 8(4):1-8.

Abstract: The aim of the current investigation was the development and validation as per ICH requirements of the TLC-densitometric method with the detection at λ = 282 nm for the simultaneous determination of Galantamine hydrobromide and Pymadine in model mixtures. The

aim was in accordance to the perspectives of multi-target therapy of Alzheimer's disease, and due to the fact that in the literature and pharmacopoeial articles the methods for simultaneous analysis of these components haven't been described. Selectivity was confirmed by the fact that in blank solution, Rf data weren't observed corresponding to Rf data of the active ingredients. The regression equations obtained demonstrated the linear relationship between the peak area and concentration: y = 2.107 .x + 25364 (Galantamine hydrobromide) (LOD = 1.87.10-3 g/ml; LOQ = 6.22.10-3 g/ml); y = 2.107 .x + 65930 (Pymadine) (LOD = 2.5.10-3 g/ml; LOQ = 8.35.10-3 g/ml). All the experimental data for the degree of recovery were included in the corresponding confidence interval: 93.54 % ÷ 97.32 % (Galantamine hydrobromide); 100.05 % ÷ 103.11 % (Pymadine). The results of precision suited the relevant intervals. System suitability was confirmed by the lack of a statistically significant difference between the Rf values: 0.663 (Galantamine hydrobromide); 0.433 (Pymadine). The method was appropriate for the simultaneous determination of Galantamine hydrobromide and Pymadine in the model mixtures.

39. Ivanova, S. A., Tsvetkova. Application of validated TLC-densitometric method for determination of Estradiol valerate in tablets. Scholars Academic Journal of Pharmacy, ISSN: 2347-9531 (print), ISSN: 2320-4206 (online), 2020; 9(2):75-81.

A**bstract**:The aim of current study was the application of validated TLC-densitometric method for quality control of pharmaceutical dosage products, containing steroid component Estradiol valerate. The used materials were: Climonorm tabl. CN1 (Estradiol valerate 2 mg); Climonorm tabl. CN2 (Estradiol valerate 2 mg/Levonogestrel 0.15 mg); Climen tabl. CM1 (Estradiol valerate 2 mg); Climen tabl. CM2 tabl. (Estradiol valerate 2 mg/Ciproterone acetate 1 mg). Thin layer chromatographic-densitometric method was applied. The used instrumentation was densitometer VILBER LOURMAT CN-15 LC. Chromatographic system used was: stationary phase: Silicagel G60F254 glass plates; mobile phase: chloroform: acetone = 90: 10 v/v, migration distance of mobile phase: 120 mm, detection at λ = 254 nm. The amount of Estradiol valerate in Climonorm tabl. and Climen tabl. was determined by method of calibration curve by using of regression equation: y = 28874286.x + 14290 in concentration range: 5.10–4 g/ml ÷ 3.10–3 g/ml. LOD = 3.15.10-4 g/ml; LOQ = 9.54.10-3 g/ml. Analytical parameter precision (repeatability) is presented by standard deviation (SD) and related standard deviation (RSD) and is proved by the fact that all of the experimental results for the content of Estradiol valerate correspond to the respective confidence interval: ___ X ± t.S ___ X : Climonorm CN1 tabl.: 1.78 mg ÷ 2.1 mg; SD = 0.09; Climonorm CN2 tabl.: 2 mg ÷ 2.16 mg; SD = 0.08; Climen CM1 tabl.: 1.81 mg ÷ 2.13 mg; SD = 0.09; Climen CM2 tabl.: 1.77 mg ÷ 2.09 mg; SD = 0.09. The proposed TLC-densitometric method is appropriate for identification and determination of Estradiol valerate in commercially available tablets. Keywords: Estradiol valetate, TLC, densitometry, tablets, determination.

40. Tsvetkova, D. D**.**, Ivanova, S. A., Obreshkova, D. P., Petkova, V. B., Atanasov, P., Yordanova-Laleva, P. D., Pashev, A. S. Methods for analysis of Galantamine hydrobromide. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), ISSN: 2278-4357, 2020; 9(2):1-19**.**

ABSTRACT
The overproduction of reactive oxygen species and the weakening of the antioxidant defense mechanisms in human body are the main reason for the oxidative stress, which underlies the development of neurodegenerative Alzheimer's disease. The important strategy for treatment of Alzheimer's disease is with compounds such as natural product Galantamine which increases acetylcholine, inhibites γ-secretase and inflammation and scavenges the free radicals. In European and USP Pharmacopoeias is recommended a gradient HPLC method for the determination of the maximum content of related substances in Galantamine hydrobromide substance. For analysis of Galantamine hydrobromide substance, HPLC methods with UV and mass-detection have been developed. For determination of Galantamine hydrobromide in tablets, the following methods have been described: UV-spectrophotometry at λ = 287 nm and λ = 289 nm; UV-spectrophotometry – first derivative at λ = 277.4 nm and λ = 284.8 nm; fluorimetry at λexcitation = 282 nm and λemmmsion = 607 nm; HPLC with UV and fluorescence detection. For quantification of Galantamine hydrobromide in biological fluids, the following methods have been presented: 1) fluorimetry; 2) capillary zone electrophoresis (serum, urine); 3) micellar electrokinetic chromatography; 4) HPLC methods with UV, fluorescence and mass detection. For the quantification of Galantamine hydrobromide in plasma after liquid-liquid extraction with hexane : ethylacetate, diethyl ether, toluene, trichloromethane or ethylacetate, an HPLC-methods with UV-detection at λ = 224 nm, fluorescence and mass detection with ionization at atmospheric pressure have been proposed. Sulpiride, Loratadine, isotopically labeled Galantamine or Glimepride have been applied as internal standards.

41. Kobakova, Y. A., Moneva-Sakelarieva, M., Atanasov, P., Ivanova, St., Obreshkova, D. The role of immunostimulants in the complex therapy of Covid 19 – a clinical case. Pharmacia, ISSN: 0428-0296 (print), 2020; 67(4): 233-23

Abstract: The aim of current study was the investigation of complex treatment including nutritional supplement with recognized antioxidant and immunomodulatory properties (malic, glycyrrhizic, ascorbic and folic acids, glucosamine, arginine, glycine, calcium pantothenate, cyanocobalamine, zinc sulfate, pyridoxal) and purely plant systemic protease supplement (Serrapeptase, Bromelaim, Boswellia, Uncaria tomentosa, Quercetin) as a strategy against Covid 19. A clinical case of a 33-year-old patient treated in Internal Clinic Diseases "Pirogov" against atypical bilaterally viral pneumonia with RT-PCR proven coronavirus have been presented. A complex treatment strategy was applied: Doxycycline, Amikacin sulfate, food additive containing malic and glycyrhizic acids, aminoacids, B-vitamins, antioxidants, proteolytic agent, Methylprednisolone, anticoagulant: Nadroparin calcium, hepatoprotector: Ademethionine. After 16 days hospitalization and two negative RT-PCR tests the patient was discharged in improved condition and home treatment with Levofloxacin hemihydrate, vitamins, probiotics, immunomodulatory and proteolytic products for one month was recommended. Immunostimulating, proteolytic and other products have an important role in complex treatment.

42 .Ivanova, St., Pankova, St., Petkova, V., Dimitrov, M. Food additives with beneficial effects in the treatment of erectile disfunction, containing L-arginine, Pycnogenol and Ginseng extract. World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS), ISSN: 2278-4357, 2014, 11 (3), 234-245

Abstract: The market of products for erectile dysfunction treatment or improving sexual performance is growing. Drugs as Viagra and Cialis have revolutionized treatment for erectile dysfunction. These medications work by increasing tissue sensitivity to the blood-vessel-dilating substance nitric oxide (NO) in the penis. These drugs may not be appropriate for patients with heart disease because of the danger of interacting with the nitrates. Men who have any of the following conditions should also avoid taking these drugs: severe heart or liver problems , recent stroke or heart attack ,low blood pressure ,certain rare inherited eye diseases.For this group of patients the only alternative is to take food additives for improving sexual performance .These food supplements very often contain L-arginine , Ginseng ,Pycnogenol. This review is focused on some food additives containing :L-arginine , Pycnogenol and Ginseng used for improvement of potency .We made an observational study based on information in medical sources for the benefits of use of these substances in the treatment of erectile dysfunction.

43.Moneva-Sakelarieva, M. G., Kobakova, Y. A., Atanasov, P. Y., Obreshkova, D. P., Ivanova, S. A., Stankova, E. K. Pharmacia.ISSN: 0428-0296 (print), 2021; 68(1):155-161. COVID-19 – the challenge to treat a disease and not a positive RT-PCR test.

Abstract: The new pandemic disease COVID is quick spread worldwide.The primary method used for diagnosing of COVID-19 is detecting viral nucleic acids. The main problem with RT-PCR test is the false negative results. The negative RT-PCR does not exclude a SARS-CoV-2 infection and this method should not be used as the only diagnostic criteria. The RT-PCR result does not change the complex treatment of the disease. The aim of the current study is to compare the four groups clinical cases of the different parameters: RT-PCR test, rapid test, clinical picture, laboratory tests as hematology, inflammatory markers, coagulation status and chemistry and imaging examinations: Chest X-ray at and Chest CT scan. Complex therapeutic approach has been implemented: antibiotic, inflammatory, anticoagulants, oxygen therapy, hepatoprotectors, antimycotics, fibrinolytics, probiotics, essential oils, vitamins. During the follow-up period, a tendency for significant reduction and resorption of the pulmonary changes on the CT scans has been seen.

44. Ivanova, St., Kirkoiva-Bogdanova, A., Becheva, M. V. Prophylactics of osteoporosis. Iranian Journal of Public Health, ISSN: 2251-6085 (print), ISSN: 2251-6093 (online), 2020; 49(12):2426-2427. Scopus, WoS

Abstract: Osteoporosis is a progressive disease characterized by a decrease in bone density. It is considered a public health problem, a socially significant disease, due to its “epidemic” prevalence among middle-aged women causing osteoporotic fractures and leading to disability. It is estimated that globally every third woman and every fifth man over 50 yr receive an osteoporotic fracture for the rest of their lives. Risk factors for fractures. Although bone growth stops in adults, there is

evidence that exercises result in a moderate increase in BMD of 1-2% (4). For good bone health, it is necessary to toinclude adequate amounts of calcium, vitamin D, proteins and other nutrients. Calcium supplements should be limited to 500-600 mg per day. Vitamin D intake should be between 800 and 1000 mg per day in people over 60 yr of age to prevent fractures. The administration of hormone replacement therapy over 10 yr in women with naturally occurring menopause helps prevent fracture risk without increasing the risk of breast cancer.

45. Tsvetkova, D. D., Ivanova, S. A., Yankov, V. P., Atanasov, P. Y. Telmisartan content determination in pharmaceutical dosage forms by UV-spectrophotometry, Scholars Academic Journal of Pharmacy, ISSN: 2347-9531 (print), ISSN: 2320-4206 (online), 2019;8(2):38-43.

Abstract: Original Research Article Antihypertensive effect of Telmisartan is result of it's action by specific blockage of angiotensin II receptors. The aim of current study was the application of the validated UV-spectrophotometric method for determination of Telmisartan at λ = 298 nm in 99.98 % ethanol. UV-VIS diode array spectrophotometer was used. From the homogenized tablets of Telmisartan tabl. 80 mg accurately were measured samples, containing an amount, equivalent to 80 mg Telmisartan and were dissolved to 100.0 ml with 99.98 % ethanol in volumetric flasks. From the obtained solutions, an aliquot parts of 1.0 ml were diluted separatelly with the same solvent to 100.0 ml. Data for Chauvenet's criterion are lower than maximum permissible value (U = 1.73; N = 6), which was applied for the assessment of the need for the removal of sharply different results. Analytical parameter precision was proved by the fact, that all results for the quantities in model mixtures and in tablets correspond to the relevant confidence interval: model mixtures: 80.06 mg ÷ 81.34 mg; tablets 80 mg: 77.79 mg ÷ 81.09 mg. Standard deviations were lower than 1.2; related standard deviations were lower than 1.6 % and relative errors were lower than 0.7 %. The validated method can be applied for the determination of Telmisartan in dosage drug preparations. Keywords: Telmisartan, UV-spectrophotometry, determination, pharmaceutical dosage preparations, tablets.

Глави от сборници и глави от книги:

1. **Pankova, S.**, Zhelev, I., Peykova, L., Papanov, S., Ivanov, K., Andonova, V., Penkov, D., Kassarova, M., Obreskova, D., Petkova, E. Antioxidant against Free Radicals. Public Health and Health Care in Greece and Bulgaria: the Challenge of the Cross-border Collaboration in Times of Financial Crisis. Athens: Papazissis Publishers, 2011, 2, pp. 335-338, ISBN 978-960-02-2630-0

Резюме: Интересът към участието на свободните радикали в процесите в човешкия организъм значително се увеличава през последните десетилетия. Всички фактори, които могат да намалят или да предпазят от окислително увреждане на биологичните молекули най-общо се разглеждат като антиоксиданти. Настоящото проучване представя спецификата на свободните радикали и антиоксиданти, българските растителни продукти с антиоксидантна активност и възможността за благоприятното им приложение като радиопротектори. Представена е класификация на свободните радикали по различни признаци и отнасяния. Всички окислителни процеси, които водят към модификация на нормалната химическа структура на биологичните молекули и на нормалните функции на биологичните процеси, са опасни за човешкия организъм. Установено е, че синергизъм на антиоксидантната активност има по-силно влияние от отделните антиоксиданти. Балансирането на комбинации от антиоксидантни хранителни субстанции може ефективно да предпази увреждането от свободните радикали и различните състояния, които те причиняват.

2. Константинов, С., Атанасов, П., **Иванова, Ст.** Фармакотерапевтични подходи в спешната медицина. Фармакотерапия, под редакцията на Константинов С., Момеков Г., Софтрейд, 2019, ISBN: 978-954-334-211-2, 869-880.

Резюме: Разглеждат се фундаментални принципи на лекарствената терапия, общи симптоми и синдроми. Фармакологичните средства за лечение на спешните състояние изискват компетентност и отговорност както не само от лекаря, а и от фармацевта, които имат един и същ основен приоритет диагностика и лечение на спешните животозастрашаващи състояния. Фармакотерапевтичният подход при шок включва корекция при хиповолемията-рехидратация с глюкозни и солеви разтвори, колоидни разтвори; възстановяване и стабилизиране на сърдечната дейност с кардиоинтропни средства: сърдечни гликозиди, катехоламини, инхибитори на фосфодиестазата; борба с болката /аналгетици/; противомикробна терапия- внимателен подход при използване на антибиотици. Хеморагичният шок има специфика по отношение на патогенезата,

диагностиката и самото лечение. За повлияване на шоковите състояния се прилагат не само лекарствени продукти, а и еритроцитен концентрат, тромбоцитен концентрат, плазмени компоненти. Коматозните състояния често са свързани с увреждане на мозъка при което главна задача е поддържане на основните жизнени функции, при което се прилагат глюкокортикостероиди, диуретична терапия, ноотропни средства. Основен проблем е и острата дихателна недостатъчност като приоритетна отново е глюкокортикостероидната терапия. В настоящата глава са разгледани редица остри състояния в спешен порядък и медикаментозната терапия като е отредено място на качествения състав и свойства на лекарствените продукти и необходимостта от активната позиция на фармацевта и познаването от него на всички качествени характеристики на лекарствата.