9. Annotation of the materials under Article 65 (1) of the Rules for Academic Staff Development at Plovdiv University "Paisii Hilendarski," including self-assessment of contributions.

of Chief Assist. Prof. Stanimir Petrov Manolov, PhD

regarding participation in the competition for the academic position of "**Associate Professor**" in the field of higher education **4. Natural Sciences, Mathematics, and Informatics**, professional area **4.2. Chemical Sciences**, scientific specialization **Organic Chemistry (Organic Analysis)**, as announced in the State Gazette, issue 98, dated November 19, 2024.

In connection with the annotation of materials under Article 65 of the Rules for the Development of Academic Staff at Plovdiv University "Paisii Hilendarski" (RDASPU).

The Rules for the Development of Academic Staff at Plovdiv University "Paisii Hilendarski" (RDASPU) were adopted by a decision of the Academic Council of Plovdiv University on April 18, 2011, amended by a decision of the Academic Council on June 20, 2011, amended by a decision of the Academic Council on October 20, 2014, amended by a decision of the Academic Council on October 15, 2018, amended by a decision of the Academic Council on March 25, 2019, amended by a decision of the Academic Council on June 10, 2019, amended by a decision of the Academic Council on November 22, 2021, amended by a decision of the Academic Council on October 30, 2023, amended by a decision of the Academic Council on December 18, 2023, amended by a decision of the Academic Council on July 22, 2024, and amended by a decision of the Academic Council on December 16, 2024.

Чл. 65. (1) (Изм. – 20.10.2014 г., изм. – 15.10.2018 г., изм. – 22.11.2021 г.) Кандидатите за заемане на академичната длъжност „доцент“ трябва да отговарят на следните изисквания:

1. Да изпълняват съответните минимални национални и допълнителни факултетни изисквания.
2. (Изм. – 22.11.2021 г.) Да са придобили ОНС „доктор“, която за специалностите от регулираните професии трябва да бъде по същата специалност.
3. (Изм. – 22.11.2021 г.) Не по-малко от две години:
   а) да са заемали академичната длъжност „асистент“ или „главен асистент“ или
   б) да са били преподаватели, включително хонорувани, в Университета или в друго висше училище или научна организация, или да са били членове на научноизследователски екип в Университета или друго висше училище или научна организация,
   или
   в) да са упражнявали художественотворческа дейност,
   или
   г) да са били специалисти от практиката и да имат доказани постижения в своята област.
4. Да са представили публикуван монографичен труд и/или равностойни публикации в специализирани научни издания (вкл. техни цитирания) или доказателства за съответни на тях художественотворчески постижения в областта на изкуствата.
5. Да са представили и други публикации (вкл. техни цитирания) или доказателства за съответни на тях художественотворчески постижения в областта на изкуствата.
6. (Изм. – 30.10.2023 г.) Да нямат доказано по законоустановения ред плагиатство или недостоверност на представените научни данни в научните трудове.

(2) (Нова – 22.07.2024 г.) Материалите от т. 3 и т. 4 не трябва да повтарят други, с които кандидатът е участвал в успешни процедури за придобиване на ОНС „доктор“ и на НС „доктор на науките“.

(3) (Изм. – 15.10.2018 г.) Всеки факултет има право да определи и допълнителни изисквания за заемане на академичната длъжност „доцент“, отразяващи спецификата на професионалното направление. Тези изисквания се приемат от ФС и задължително се депозират в Отдела. При определяне на допълнителните изисквания факултетите се съобразяват с установените показатели за оценка и финансиране на присъщата на държавните висши училища научна и художественотворческа дейност, както и показателите от рейтинговата система на висшите училища в България.

The implementation of Article 65 (1), items 1, 2, and 3 of the Rules can be seen in the presented materials, respectively in points 8, 4, and 12.

At the Department of Organic Chemistry at Plovdiv University, I have been tutoring laboratory practicals since 2008, when I was a 4th-year student in the Bachelor Programme of Computer Chemistry. In the provided report on teaching activity, I have presented my teaching workload from 2015 to 2024.

In 2015, after successfully defending my doctoral dissertation in the scientific area of Organic Chemistry and winning a competition for the position of Chief Assistant Professor in Organic Chemistry, I was appointed to a permanent employment contract at Plovdiv University.

For participation in the competition for the academic position of "**Associate Professor**" in the scientific field of Organic Chemistry (Organic Analysis), I am presenting a total of 21 scientific papers that have not been used in the procedure for obtaining the academic degree "**Doctor**" or for the position of "**Chief Assistant Professor**". They are classified into the following groups (according to the list of scientific papers):

- Scientific publications indexed in *Scopus/Web of Science* – 20 items;
- Published book based on the defended doctoral dissertation for the award of the educational and scientific degree "Doctor" – 1 item.

I. Scientific publications indexed in Scopus/Web of Science

1. Ivanov, I.; Manolov, S.; Bojilov, D.; Stremski, Y.; Marc, G.; Statkova-Abeghe, S.; Oniga, S.; Oniga, O.; Nedialkov, P. Synthesis of Novel Benzothiazole–Profen Hybrid Amides as Potential NSAID Candidates. *Molecules* **2025**, *30*, 107. https://doi.org/10.3390/molecules30010107

Abstract: Herein, we report the synthesis of a series of new compounds by combining 2-aminobenzothiazole with various profens. The compounds were characterized using techniques such as ^{1}H- and ^{13}C-NMR, FT-IR spectrometry, and high-resolution mass spectrometry (HRMS), with detailed HRMS analysis conducted for each molecule. Their biological activities were tested in vitro, revealing significant anti-inflammatory and antioxidant effects, comparable to those of standard reference compounds. Lipophilicity was experimentally determined through partition coefficient (R_M) measurements. To understand their binding affinity, molecular docking studies were perfsormed to analyze interactions with human serum albumin (HSA). The stability of these predicted complexes was further evaluated through molecular dynamics simulations. The results highlight the compounds' promising biological activity and strong affinity for HSA. The new hybrid molecule between 2-ABT and ketoprofen **3b** demonstrates significant promise based on the experimental data and is further supported by *in silico* calculations. Compound **3b** exhibits the best hydrogen peroxide scavenging activity among the

tested compounds, with an IC_{50} of 60.24 µg/mL. Furthermore, **3b** also displays superior anti-inflammatory activity, with an IC_{50} of 54.64 µg/mL, making it more effective than the standard ibuprofen (76.05 µg/mL).

2. Ivanov, I.; Manolov, S.; Bojilov, D.; Marc, G.; Dimitrova, D.; Oniga, S.; Oniga, O.; Nedialkov, P.; Stoyanova, M. Novel Flurbiprofen Derivatives as Antioxidant and Anti-Inflammatory Agents: Synthesis, In Silico, and In Vitro Biological Evaluation. *Molecules* **2024**, *29*, 385. https://doi.org/10.3390/molecules29020385

Abstract: In this study, we present the synthesis of five novel compounds by combining flurbiprofen with various substituted 2-phenethylamines. The synthesized derivatives underwent comprehensive characterization using techniques such as ^{1}H- and ^{13}C-NMR spectroscopy, UV-Vis spectroscopy, and high-resolution mass spectrometry (HRMS). Detailed HRMS analysis was performed for each of these newly created molecules. The biological activities of these compounds were assessed through *in vitro* experiments to evaluate their potential as anti-inflammatory and antioxidant agents. Furthermore, the lipophilicity of these derivatives was determined, both theoretically using the c*Log*P method and experimentally through partition coefficient (R_M) measurements. To gain insights into their binding affinity, we conducted an in silico analysis of the compounds' interactions with human serum albumin (HSA) using molecular docking studies. Our findings reveal that all of the newly synthesized compounds exhibit significant anti-inflammatory and antioxidant activities, with results statistically comparable to the reference compounds. Molecular docking studies further explain the observed in vitro results, shedding light on the molecular mechanisms behind their biological activities. Using *in silico* method, toxicity was calculated, resulting in LD_{50} values. Depending on the administration route, the novel flurbiprofen derivatives show lower toxicity compared to the standard flurbiprofen.

3. Divya Mohan, R.; Anaswara, S.A.; Kulkarni, N.V.; Bojilov, D.G.; Manolov, S.P.; Ivanov, I.I.; Al-Otaibi, J.S.; Sheena Mary, Y. Synthesis, Characterization and Assessment of Antioxidant and Melanogenic Inhibitory Properties of Edaravone Derivatives. *Antioxidants* **2024**, *13*, 1148. https://doi.org/10.3390/antiox13091148

Abstract: A series of edaravone derivatives and the corresponding Cu(II) complexes were synthesized and characterized using spectroscopic and analytical techniques such as IR, UV, NMR and elemental analysis. Antioxidant activities of all compounds were examined using free radical scavenging methods such as hydrogen peroxide scavenging activity (HPSA), 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 2-2'-azino-bis-(3-ethylbenzothiazoline-6-sulfonate) (ABTS) assays. All of the tested compounds exhibited good antioxidant

activity. Further, the frontier orbital energy levels, as well as various chemical properties, were determined using the density functional theory (DFT) calculations. The MEP maps of all of the derivatives were plotted to identify the nucleophilic and electrophilic reactive sites. Further, binding energies of all of the organic compounds with the protein tyrosinase was investigated to determine their potential anti-melanogenic applications. The selected ligand, **L6** was subjected to molecular dynamics simulation analysis to determine the stability of the ligand–protein complex. The MD simulation was performed (150 ns) to estimate the stability of the tyrosinase–**L6** complex. Other key parameters, such as, RMSD, RMSF, Rg, hydrogen bonds, SASA and MMPBSA were also analyzed to understand the interaction of L6 with the tyrosinase protein.

4. Manolov, S.; Ivanov, I.; Bojilov, D.; Nedialkov, P. Synthesis, In Vitro Anti-Inflammatory Activity, and HRMS Analysis of New Amphetamine Derivatives. *Molecules* **2023**, *28*, 151. https://doi.org/10.3390/molecules28010151

Abstract: Herein, we report the obtaining of new hybrid molecules of amphetamine with different profens (amfens). The obtained amfens are characterized by their melting points, UV, ^{1}H–, ^{13}C–NMR, and HRMS spectra. A complete and detailed mass spectral analysis of the newly obtained derivatives of amphetamine with ibuprofen, flurbiprofen, ketoprofen, naproxen, and carprofen was performed. *In vitro* inhibition of albumin denaturation of each new compound was assessed, and they showed significant activity. The IC_{50} values of the obtained amphetamine-profen derivatives ranged from 92.81 to 159.87 µg/mL. This indicates that the new hybrids inherit the anti-inflammatory properties of profens. Using *in silico* method, the toxicity was also calculated. The obtained results are given in LD_{50} values. Depending on the route of administration, the amfens are less toxic compared to the standard amphetamine.

5. Manolov, S.; Ivanov, I.; Bojilov, D. Microwave-assisted synthesis of 1,2,3,4-tetrahydroisoquinoline sulfonamide derivatives and their biological evaluation. *Journal of the Serbian Chemical Society* **2021** *86*, 2, 139-151. https://doi.org/10.2298/JSC200802076M

Abstract: Herein we report an alternative eco-friendly method for the synthesis of 1,2,3,4-tetrahydroisoquinoline sulfonamide derivatives. All obtained compounds were screened for their *in vitro* inhibition of albumin denaturation, antioxidant, antitryptic and antibacterial activity, and have shown significant results. The lipophilicity was established using both reversed-phase thin layer chromatography and *in silico* calculations.

6. S. Manolov, D. Bojilov, and I. Ivanov, "Evaluating the in Vitro Biological Efficacy of Novel Ketoprofen Hybrids against Inflammation, Arthritis, and Oxidative Stress", *C. R. Acad. Bulg. Sci.* **2024**, *77*, 824–830. https://doi.org/10.7546/CRABS.2024.06.05

Abstract: In this study, we disclose the outcomes of the biological assessment of recently synthesized hybrids of ketoprofen with 2-phenylethylamines and 1,2,3,4-tetrahydroisoquinolines. These hybrids were obtained using an environmentally friendly method that minimizes the generation of waste products. The newly acquired hybrids were analysed to evaluate their antioxidant, anti-inflammatory, and anti-arthritic activities. Additionally, as potential drugs exhibiting favourable results, their experimental partition coefficient in a biphasic system of lipids and water (logP) was determined.

7. Dimitrova, D.; Manolov, S.; Ivanov, I.; Bojilov, D.; Kasamova, L.; Nedialkov, P. N-(2,2-Diphenylethyl)-4-nitrobenzamide. *Molbank* **2024**, *2024*, M1775. https://doi.org/10.3390/M1775

Abstract: In this study, we outline the eco-friendly mechanosynthesis of *N*-(2,2-diphenylethyl)-4-nitrobenzamide by reacting 2,2-diphenylethan-1-amine with 4-nitrobenzoyl chloride. The resulting bio-functional hybrid compound was meticulously characterized through the analysis of ^{1}H-, ^{13}C-NMR, UV, and detailed mass spectral analysis.

8. Ivanov, I.; Manolov, S.; Bojilov, D.; Dimitrova, D.; Nedialkov, P. Synthesis of Novel Sulfonamide Derivatives Featuring 1-(Methylsulfonyl)-4-(2,3,4-Trimethoxybenzyl)Piperazine Core Structures. *Molbank* **2024**, *2024*, M1879. https://doi.org/10.3390/M1879

Abstract: Herein we report the synthesis of three novel sulfonamide derivatives of trimetazidine—medication primarily used to treat angina pectoris. The new compounds have been fully characterized with their melting point, ^{1}H- and ^{13}C-NMR, UV, and mass spectrometry. The collected data confirm the successful synthesis and structural integrity of the new molecules.

9. Mollova, S.; Stanev, S.; Bojilov, D.; Manolov, S.; Mazova, N.; Koleva, Y.; Stoyanova, A. Chemical composition and antioxidant actuvuty of Roman Chamomile (Anthemis nobilis L.) Essential oil. *Oxidation Communications* **2024**, *47*, 264-271.

Abstract: *Roman chamomile* is a wild and cultivated plant in many countries worldwide and is mainly used in folk medicine. The flower's essential oil is used in various cosmetic, perfumery and aromatherapy

products. In recent years in Bulgaria, the plant has been cultivated in the experimental field of the Institute of Roses, Essential and Medical Plants, Kazanlak. The present work aims to prepare essential oil and determine its chemical composition and antioxidant activity to reveal new possibilities for its application. The essential oil was obtained under laboratory conditions by steam distillation (yield 0.14%) and its main components determined by GC/MS were: isobutyl angelate (37.22%), 2-methylbutyl angelate (18.71%), methylallyl angelate (11.85%), isobutyl isobutyrate (5.86%), pentan-2-yl 2-methylbut-2-enoate (5.48%), 2-metylbutyl isobutyrate (3.47%), and (Z)-pinocarveol (2.86%). The antioxidant activity of the essential oil was also determined by three methods – ABTS (1.54 µM TE/g), DPPH (1.09 µM TE/g), and CUPRAC (2.26 µM TE/g). The results show that *Roman chamomile* can be successfully cultivated in Bulgaria. Its essential oil has an interesting chemical composition and antioxidant activity, a prerequisite for use in various food and cosmetic products, a novelty for our country.

10. Mollova, S.; Stanev, S.; Bojilov, D.; Manolov, S.; Kostova, I.; Damianova, S.; Fidan, H.; Stoyanova, A.; Ercisli, S.; Assouguem, A.; Ullah, R.; Bari, A. Chemical composition and biological activity of essential oil from anise hyssop. *Biotechnology & Biotechnological Equipment* **2024**, *38*. https://doi.org/10.1080/13102818.2024.2358995

Abstract: Anise hyssop (*Agastache foeniculum* (Pursh) Kuntze) is a perennial plant belonging to the *Lamiaceae* family mainly used in folk medicine to treat various ailments. This study determined the chemical composition of the essential oil and evaluated its antimicrobial and antioxidant activity. The essential oil was obtained from plants cultivated in the experimental field at the Institute of Roses, Essential and Medical Plants, Kazanlak, Bulgaria. The plants were processed by steam distillation, with the essential oil yielding 0.37%, and its main components being methyl chavicol (82.03%) and limonene (9.90%). The most potent antimicrobial action was observed against the gram-positive bacteria *Staphylococcus aureus* (25.7 mm inhibition zone) and *Bacillus cereus* (12.3 mm), the yeast *Saccharomyces cerevisiae* (16.3 mm) and *Candida albicans* (16.5 mm). The remaining gram-positive bacteria (*Staphylococcus epidermidis* and *Bacillus subtilis*), gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella ebony*), and fungi (*Aspergillus brasiliensis* and *Fusarium moniliforme*) were resistant to the action of the essential oil. The antioxidant activity of the essential oil was ABTS (32.36 µmol TE/mL), DPPH (21.61 µmol TE/mL), CUPRAC (19.94 µmol TE/mL), and FRAP (29.56 µmol TE/mL) *in vitro*. Overall, the results from this study revealed the biological potential of anise hyssop as a source in pharmaceutical, food, and cosmetic applications.

11. Bojilov, D.; Manolov, S.; Ahmed, S.; Dagnon, S.; Ivanov, I.; Marc, G.; Oniga, S.; Oniga, O.; Nedialkov, P.; Mollova, S. HPLC Analysis and In Vitro and In Silico Evaluation of the Biological Activity of Polyphenolic Components Separated with Solvents of Various Polarities from Helichrysum italicum. *Molecules* **2023**, *28*, 6198. https://doi.org/10.3390/molecules28176198

Abstract: *Helichrysum italicum* has piqued the interest of many researchers in recent years, mostly for its essential oil, but increasingly for its polyphenolic content as well. In the current study, we examine the polyphenolic composition of *H. italicum* grown in Bulgaria. The polyphenolic complex was fractionated with solvents of various polarities, including hexane, chloroform, ethyl acetate, and butanol, in order to assess the biological impact of the components. HPLC-PDA and UHPLC-MS/MS were used to examine all fractions. The green coffee fingerprint profile was employed as a "surrogate standard" in the polyphenolic components detection approach. From the UHPLC-MS/MS analysis, we identified 60 components of the polyphenolic complex such as quercetin 3-*O*-glucuronide, quercetin acetyl-glycoside, isorhamnetin acetyl-glycoside, isorhamnetin caffeoyl-glycoside, quercetin caffeoyl-malonyl-glycoside, isorhamnetin coumaroyl-glycoside, coumaroyl-caffeoylquinic acid, and diCQA-acetyl-derivative were first reported in the composition of *H. italicum*. The biological activity of the fractions was evaluated *in vitro* and *in silico*, which included the fight against oxidative stress (hydrogen peroxide scavenging activity (HPSA), hydroxyl radical scavenging activity (HRSA), metal-chelating activity (MChA)) and nitrosative (nitric oxide scavenging activity) (NOSA)), *in vitro* anti-inflammatory, and anti-arthritic activity. Results are presented as IC_{50} ± SD μg/mL. The analysis showed that the EtOAc fraction was characterized by highest HPSA (57.12 ± 1.14 μg/mL), HRSA (92.23 ± 1.10 μg/mL), MChA (5.60 ± 0.17 μg/mL), and NOSA (89.81 ± 2.09 μg/mL), while the hexane and chloroform fractions showed significantly higher *in vitro* anti-inflammatory activity (30.48 ± 2.33 μg/mL, 62.50 ± 1.69 μg/mL) compared to the standard ibuprofen. All three fractions showed potential anti-arthritic activity (102.93 ± 8.62 μg/mL, 108.92 ± 4.42 μg/mL, 84.19 ± 3.89 μg/mL).

12. Bojilov, D.; Manolov, S.; Nacheva, A.; Dagnon, S.; Ivanov, I. Characterization of Polyphenols from Chenopodium botrys after Fractionation with Different Solvents and Study of Their In Vitro Biological Activity. *Molecules* **2023**, *28*, 4816. https://doi.org/10.3390/molecules28124816

Abstract: In the present work, we have investigated the polyphenolic composition of *Chenopodium botrys* from Bulgaria. The polyphenols were fractionated with solvents of varying polarity (*n*-hexane, chloroform, ethyl acetate, and *n*-butanol). The fractions were analyzed by HPLC-PDA and UHPLC-MS. The ethyl acetate

fraction contained mono- and di-glycosides of quercetin, di-glycosides of kaempferol, and isorhamnetin and monoglycosides of hispidulin and jaceosidine. We found quercetin triglycosides in the butanol fraction. The ethyl acetate and butanol fractions contained 168.82 mg/g Extr and 67.21 mg/g Extr of quercetin glycosides, respectively. The main components of the polyphenolic complex in *C. botrys* were 6-methoxyflavones (355.47 mg/g Extr), which were found in the chloroform fraction. The flavonoids pectolinarigenin, demethylnobiletin, and isosinensetin, and the glycosides of quercetin (triglycosides, acylglycosides), kaempferol, isorhamnetin, hispidiulin, and jaceosidine, were discovered and reported in *Chenopodium botrys* for the first time. We used *in vitro* methods to assess the biological activity against oxidative stress (hydrogen peroxide scavenging activity (HPSA) and hydroxyl radical scavenging activity (HRSA)), nitrosative stress (nitric oxide scavenging activity (NOSA)), anti-inflammatory activity (IAD inhibition), and anti-tryptic activity (ATA). Quercetin mono- and di-glycosides exhibited greater HPSA and HRSA (IC_{50} = 39.18, 105.03 µg/mL), while 6-methoxyflavones had a greater NOSA (IC_{50} = 146.59 µg/mL). The same components showed the highest ATA (IC_{50} ranging from 116.23 to 202.44 µg/mL).

13. Mollova, S.; Dzurmanski, A.; Fidan, H.; Bojilov, D.; Manolov, S.; Dincheva, I.; Stankov, S.; Stoyanova, A.; Ercisli, S.; Assouguem, A.; Marc, R.A.; Ullah, R.; Bari, A. Chemical Composition of Essential Oils from Nepeta transcaucasica Grossh. and Nepeta cataria L. Cultivated in Bulgaria and Their Antimicrobial and Antioxidant Activity. *ACS Omega* **2023**, https://doi.org/10.1021/acsomega.3c00704

Abstract: The genus *Nepeta*, belonging to the family *Lamiaceae*, includes about 300 species, most of which are used in folk medicine due to their pronounced biological properties. The aim of the present study was to evaluate the agrobiological characteristics of *Nepeta transcaucasica* (*N. transcaucasica*) Grossh. and *Nepeta cataria* (*N. cataria*) L., cultivated in Bulgaria, and obtain their essential oils and determine their antimicrobial and antioxidant activities. The agrobiological characteristics of the two species growing in Kazanlak were analyzed; therefore, high variability in the population of *N. transcaucasica* and comparative homogeneity in *N. cataria* was shown. The species *N. transcaucasica* contained 0.28% essential oil with main components β-citronellol (52.05%), eucalyptol (7.34%), β-citronellal (6.06%), germacrene D (5.45%), (Z)-β-ocimene (5.14%), and β-caryophyllene (3.06%). The species *N. cataria* consisted of 0.19% essential oil with main components β-citronellol (26.31%), geraniol (15.92%), neral (11.45%), nerol (9.56%), carvacrol (6.04%), and β-citronellal (5.35%). The antibacterial activity against Gram-positive bacteria *Listeria monocytogenes* and *Staphylococcus aureus* and Gram-negative bacteria *Escherichia coli* (*E. coli*) and *Salmonella enterica* subsp. enterica serovar Abony was determined. The essential oils showed

antimicrobial activity only against *E. coli*. The diameters of the inhibition zones were found to be 26 mm for the species *N. transcaucasica* and 10 mm for the species *N. cataria*. The antioxidant activity of the two essential oils was also determined by four different methods, DPPH, ABTS, FRAP, and CUPRAC, with the highest values for the ABTS radical, for the species *N. transcaucasica* (48.72 µM TE/mL), and the species *N. cataria* (310 µM TE/mL).

14. Manolov, S.; Ivanov, I.; Bozhilov, D.; Voynikov, Y. Evaluation of antioxidant, anti-inflammatory and anti-arthritic activity of new ibuprofen derivatives. *Bulgarian Chemical Communications* **2021**, *53*, 1, 66-71. https://doi.org/10.34049/bcc.53.1.5320

Abstract: Herein, we present the synthesis and *in-vitro* anti-inflammatory, antioxidant, and anti-arthritic activities of new ibuprofen derivatives. All structures were confirmed by spectral analysis (^{1}H NMR, ^{13}C NMR, UV, IR and HRMS). The lipophilicity was established using reversed-phase thin layer chromatography and *in silico* calculations. The anti-inflammatory and anti-arthritic activities correlated with the lipophilicity of the compounds.

15. Angelov, P.; Manolov, S.; Yanev, P.; Naydenov, M. Oxygenated Analogues of Santacruzamate A. *Molbank* **2021**, *2021*, M1188. https://doi.org/10.3390/M1188

Abstract: A new approach for the synthesis of Santacruzamate A analogues is demonstrated. The method allows functionalization at position 3 of the gamma-aminobutyric fragment and carbon chain variation.

16. Manolov, S.; Ivanov, I.; Bojilov, D. N-(2-(1H-Indol-3-yl)ethyl)-2-(6-methoxynaphthalen-2-yl)propanamide. *Molbank* **2021**, *2021*, M1187. https://doi.org/10.3390/M1187

Abstract: The title compound was obtained in high yield in the reaction between tryptamine and naproxen. The newly synthesized naproxen derivative was fully analyzed and characterized *via* ^{1}H, ^{13}C-NMR, UV, IR, and mass spectral data.

17. Manolov, S.; Ivanov, I.; Bojilov, D. N-(2-(1H-Indol-3-yl)ethyl)-2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanamide. *Molbank* **2021**, *2021*, M1177. https://doi.org/10.3390/M1177

Abstract: *N*-(2-(1H-Indol-3-yl)ethyl)-2-(2-fluoro-[1,1'-biphenyl]-4-yl)propanamide was prepared by a reaction between tryptamine and flurbiprofen, applying *N*,*N*'-Dicyclohexylcarbodiimide, as a coupling agent. The obtained new amide has a fragment similar to Brequinar, a compound used in SARS-CoV-2 treatment trials. The newly synthesized compound was fully analyzed and characterized *via* ^{1}H, ^{13}C-NMR, UV, IR, and mass spectral data.

18. Bozhilov, D.; Petkova, Zh.; Manolov, S.; Antova, G; Angelova-Romova, M. Impact of the duration of ultrasound-assisted extraction on total phenolics content and antioxidant activity of lupin seeds. *Bulgarian Chemical Communications*, **2020**, *52*, D, 222-226.

Abstract: The influence of the duration of ultrasound-assisted extraction on antioxidant activity and total phenolics content of lupin seeds (*Lupinus angustifolius* L. cultivar 'Boregine') was investigated for the first time. Lupin seeds were with German origin but introduced in Bulgaria. They were extracted for 10, 20 and 30 min with absolute methanol and the obtained extracts were evaluated for total phenolic content and antioxidant activity. The polyphenol content of the extracts was found to be in the range of 1.65 – 2.03 mg gallic acid equivalents (GAE)/g dry weight sample, depending on the duration of the extraction process. The antioxidant activity was estimated by $ABTS^{\bullet+}$ (2,2'azinobis-(3-ethylbenzthiazoline-6-sulfonic acid)) (2.28 – 2.89 mmol Trolox Equivalent (TE)/g dw), $DPPH^{\bullet}$ (1,1-diphenyl-2-picrylhydrazyl radical) (2.01 – 2.71 mmol TE/g dw), FRAP (ferric reducing/antioxidant power) (3.76 – 4.36 mmol TE/g dw) and CUPRAC (cupric ion reducing antioxidant capacity) (3.07 – 4.69 mmol TE/g dw) methods. Generally, methanol extracts with 30 min of extraction displayed the highest total phenolic contents, while 10 min of extraction time was the least efficient ultrasound-assisted method. On the other hand, antioxidant activity of the extracts was highest in 20 min of extraction apart from CUPRAC method where 30 min of extraction depicted more antioxidant capacity of the methanol extract.

19. Manolov, S.; Ivanov, I.; Bojilov, D. N-(2-(1H-indol-3-yl)ethyl)-2-(6-chloro-9H-carbazol-2-yl)propanamide. *Molbank* **2020**, *2020*, M1171. https://doi.org/10.3390/M1171

Abstract: The titular compound was prepared by a reaction between tryptamine and carprofen, applying, as a "dehydrating" reagent, *N*,*N*'-dicyclohexylcarbodiimide. The newly synthesized compound was fully analyzed and characterized *via* ^{1}H, ^{13}C-NMR, UV, IR, and mass spectral data.

20. Manolov, S.; Nikolova, S.; Ghate, M.; Ivanov, I. A brief review of Cherylline synthesis. *Indian Journal of Chemistry, Section B* **2015**, *54B*, 1301 – 1320.

Abstract: 1,2,3,4-Tetrahydroisoquinolines are an important class of synthetic and natural compounds, which display a broad range of medicinal activities. The 1,2,3,4-tetrahydroisoquinoline system has attracted attention not only because of its biological activities, but also due to its presence as a basic framework in many naturally occurring products and drugs. Their skeletons are unique among the *Amaryllidaceae* alkaloids and they have long been alluring targets for synthetic chemists as witnessed by a number of articles dealing with biogenesis, isolation, characterization and synthesis. The alkaloid

cherylline is an optically active naturally occurring, 4-phenyl-1,2,3,4-tetrahydroisoquinoline alkaloid, isolated from *Crinum powelli*, *Amaryllidaceae* plant. There are many ways for *cherylline* synthesis. In this short review is described the different methods for synthesis of the alkaloid *cherylline*.

II. Published book based on the defended doctoral dissertation for the award of the educational and scientific degree "Doctor"

1. Alternative methods for obtaining of cherylline derivatives, Lambert Academic Publishing, **2017**, ISBN: 978-620-2-07857-3

Abstract: In this book are presentet the results from research on alternative approaches towards the synthesis of 4-aryl-1,2,3,4-tetrahydroisoquinolines as synthetic analogues of the alkaloid cherylline. Optimal conditions for the synthesis of the required 2,2-disubstituted ethylamine precursors are found. The Schotten-Bauman method for amide synthesis is then successfully applied and the synthesized amides are used in an intramolecular α-amidoalkylation reaction to obtain 4-substituted 1,2,3,4-tetrahydroisoquinolines. An eco-friendly procedure utilizing PPA/SiO_2 catalyst for the intramolecular α-amidoalkylation is developed. Microwave-assisted variant of this eco-friendly procedure is also successsfully developed. By the Bischler-Napieralski method are synthesized five new 1,4-disubstituted-1,2,3,4-tetrahydroisoquinolines. These are potential inhibitors of DHODH. It is found that the reduction of 1,4-disubstituted 3,4-dihydroisoquinolines leads to formation of diastereoisomers. The diastereoisomers are successfully separated by preparative column chromatography and 2:1 (cis:trans) ratio is determined. This ratio is not affected by the temperature at which the reaction is carried out.

10.01.2025 Signature:……

Plovdiv /Chief Assist. Prof. Stanimir Manolov, PhD/