NASTAVNO-NAUČNOM VEĆU FARMACEUTSKOG FAKULTETA UNIVERZITETA U BEOGRADU

TO THE ACADEMIC COUNCIL OF THE FACULTY OF PHARMACY -UNIVERSITY OF BELGRADE

KOMISIJI ZA POSLEDIPLOMSKE STUDIJE

TO THE COMMITTEE FOR POSTGRADUATE STUDIES

Na sednici Nastavno-naučnog veća Farmaceutskog fakulteta u Beogradu, održanoj 22.12.2016. godine imenovani su članovi Komisije za ocenu i odbranu završene doktorske disertacije, kandidata dipl. farm. Musbah Salem Mohamed Shenger, pod naslovom:
The Academic Council of the Faculty of Pharmacy at the University of Belgrade on the meeting held on December 22, 2016 has nominated the Commission for evaluation and defence of doctoral dissertation of the candidate BSc in pharmacy Musbah Salem Mohamed Shenger, entitled:

"Kvantitativni odnosi strukture i retencionih osobina odabranih liganada alfa adrenergičkih i imidazolinskih receptora u tankoslojnoj hromatografiji"

"*Quantitative structure retention relationships of selected alpha adrenergic and imidazoline receptors ligands in thin layer chromatography*"

Komisija u sastavu/*Commission including*:

1. Dr Danica Agbaba, redovni profesor/*full professor*, mentor

Univerzitet u Beogradu – Farmaceutski fakultet/*University of Belgrade – Faculty of Pharmacy*

2. Dr Slavica Oljačić, docent/*assistant professor*, mentor

Univerzitet u Beogradu – Farmaceutski fakultet/*University of Belgrade – Faculty of Pharmacy*

3. Dr Katarina Nikolić, docent/*assistant professor*

Univerzitet u Beogradu – Farmaceutski fakultet/*University of Belgrade – Faculty of Pharmacy*

4. Dr Živoslav Tešić, **redovni profesor/*full professor***

Univerzitet u Beogradu – Hemijski fakultet/*University of Belgrade – Faculty of Chemistry*

pregledala je priloženu disertaciju i podnosi Nastavno-naučnom veću Farmaceutskog fakulteta Univerziteta u Beogradu sledeći/

based on detailed review of the submitted dissertation, presents to the Academic Council of the Faculty of Pharmacy-University of Belgrade the following

IZVEŠTAJ/*REPORT*

A. PRIKAZ SADRŽAJA DOKTORSKE DISERTACIJE/*THE CONTENT OF THE DOCTORAL DISSERTATION*

Doktorska disertacija dipl. farm. Musbah Salem Mohamed Shenger pod nazivom „**Kvantitativni odnosi strukture i retencionih osobina odabranih liganada alfa adrenergičkih i imidazolinskih receptora u tankoslojnoj hromatografiji"** napisana je na 110 strana A4 formata, proreda 1,5 i fonta Times New Roman (veličina 12). Disertacija se sastoji od sledećih poglavlja: 1. Uvod, 2. Cilj rada, 3. Eksperimentalni deo, 4. Rezultati i diskusija, 5. Zaključak, 6. Literatura, 7. Prilozi, 8. Biografija. Disertacija sadrži 23 slike, 24 tabele (od toga 5 u Prilogu) i 131 literaturni navod.

*Doctoral dissertation of the candidate BSc in pharmacy Musbah Salem Mohamed Shenger, entitled: **"Quantitative structure retention relationships of selected alpha adrenergic and imidazoline receptors ligands in thin layer chromatography"**, is written on 110 pages of A4 format with line spacing 1.5 and using Times New Roman font (font size 12). Doctoral dissertation comprises following chapters: 1. Introduction, 2. Objectives, 3. Experimental part, 4. Results and Discussion, 5. Conclusion, 6. Literature, 7. Supplementary material, 8. Biography. Dissertation comprises 23 figures, 24 tables (5 of them in the Supplementary material) and 131 references.*

B. OPIS POSTIGNUTIH REZULTATA/*DESCRIPTION OF THE OBTAINED RESULTS*

Rezultati ove doktorske disertacije izloženi su u dve celine u kojima je prikazana primena hemometrijskog pristupa u ispitivanjima lipofilnosti i retencionog ponašanja odabranih liganada alfa adrenergičkih i imidazolinskih receptora u uslovima hromatografije na tankom sloju, kao i u kvantitativnoj analizi moksonidina i njegovih nečistoća.

The results of this doctoral dissertation are presented and discussed in two parts in which application of chemometric approach for estimation of lipophilicity and retention behaviour of selected alpha adrenergic and imidazoline receptors ligands by thin layer chromatography have been presented as well as in quantitative analysis of moxonidine and its impurities.

Hromatografsko ponašanje 16 odabranih jedinjenja (klonidin, moksonidin, gvanfacin, brimonidin, efaroksan, idazoksan, harman, harmin, tizanidin, nafazolin, ksilometazolin, tetrahidrozolin, oksimetazolin, tramazolin i amilorid) ispitano je metodom reverzno-fazne tankoslojne hromatografije (RP-TLC). Oktadecil- (RP-18) i cijano- (CN) modifikovani silika gel su korišćeni kao stacionarna faza dok su metanol i tetrahidrofuran (THF) korišćeni kao organski modifikatori u mobilnoj fazi. Retencioni podaci (R_M^0, m i C_0) dobijeni ispitivanjima u tri hromatografska sistema (metanol-voda/RP-18, tetrahidrofuran-amonijak-voda/RP-18 i tetrahidrofuran-amonijak-voda/CN) su ispitani kao mogući parametri u proceni lipofilnosti odabranih jedinjenja. Korelacijom dobijenih hromatografskih parametara sa izračunatim log *P* vrednostima utvrđeno je da je R_M^0 najpouzdaniji parametar za procenu lipofilnosti odabranih liganada alfa adrenergičkih i imidazolinskih receptora, pri čemu prednost treba dati R_M^0 vrednostima dobijenim u tetrahidrofuran-amonijak-voda/CN (r=0,933 između R_M^0 i ACD/log *P*) i tetrahidrofuran-amonijak-voda/RP-18 (r=0,916 između R_M^0 i ACD/log *P*) hromatografskim sistemima, dok je metanol-voda/RP-18 sistem manje pouzdan za procenu lipofilnosti ispitivanih jedinjenja (r =0,580 između R_M^0 i Clog *P*).

Chromatographic behaviour of 16 selected compounds (clonidine, moxonidine, guanfacine, brimonidine, efaroxan, idazoxan, harmane, harmine, tizanidine, naphazoline, xylometazoline, tetrahydrozoline, oxymetazoline, tramazoline, and amiloride) was examined by reverse phase-thin layer chromatography (RP-TLC). Octadecyl- (RP-18) and cyano- modified silica gel were used as stationary phase while methanol and tetrahydrofuran (THF) were used as organic modifier in mobile phase. Retention parameters (R_M^0, m i C_0) obtained in three examined chromatographic systems (methanol-water/RP-18, tetrahydrofuran-ammonia-water/RP-18, and tetrahydrofuran-ammonia-water/CN) were tested as potential parameters in the evaluation of lipophilicity of selected compounds. Correlation between determined chromatographic parameters and calculated log P values revealed that R_M^0 is the most reliable parameter for estimation of lipophilicity of selected alpha adrenergic and imidazoline receptors ligands whereby priority should be given to R_M^0 values obtained for tetrahydrofuran-ammonia-water/CN (r=0.933 between R_M^0 and ACD/logP) and tetrahydrofuran-ammonia-water/RP-18 (r=0.916 between R_M^0 and ACD/logP) chromatographic systems while methanol-water/RP-18 system is less reliable for the evaluation of lipophilicity of the tested compounds (r =0.580 between R_M^0 and Clog P).

Primenom analize osnovnih komponenti (PCA) ispitane su sličnosti i razlike u lipofilnosti testiranih jedinjenja. Dobijeni rezultati su pokazali da se na osnovu eksperimentalno određenih (R_M^0) i izračunatih parametara lipofilnosti (log *P*) ispitivana jedinjenja mogu klasifikovati u četiri različite lipofilne grupe.
Principal Component Analysis (PCA) was applied for examination of similarity and differences in lipophilicity between the tested compounds. Obtained results showed that according to experimentally determined (R_M^0) and calculated lipophilicity (log P) parameters, 16 examined compounds can be classified into four different lipophilicity groups.

Utvrđivanje kvantitativnih odnosa između strukture i retencionog ponašanja (QSRR) analiziranih jedinjenja u ispitivanim hromatografskim sistemima izvršeno je metodom parcijalne regresije najmanjih kvadrata (PLS). U svim formiranim QSRR modelima logaritam particionog koeficijenta, log *P* je izdvojen kao važan parametar koji je u pozitivnoj korelaciji sa retencionim ponašanjem u testiranim sistemima. Pored lipofilnosti, važni deskriptori koji utiču na retenciono ponašanje analiziranih jedinjenja u RP-TLC sistemu su *the average molecular weight (AMW), P_VSA-like on van der Waals volume, bin 3 (P_VSA_v_3) descriptors* i *hydrogen bonding properties* testiranih jedinjenja. Svi formirani modeli su validirani primenom ukrštene i eksterne validacije, a dobijeni statistički parametri potvrdili su njihovu pouzdanost u predviđanju retencionog ponašanja i lipofilnosti novih liganada alfa adrenergičkih i imidazolinskih receptora.
The Quantitative Structure Retention Relationship (QSRR) modeling of analysed compounds was performed with aid of the Partial Least Squares regression (PLS). In all devised QSRR models, logarithm of the partition coefficient, log P is selected as the important property with positive influence on the retention in the tested chromatographic RP-TLC systems. In addition to the logarithm of the partition coefficient, the average molecular weight (AMW), P_VSA-like on van der Waals volume, bin 3 (P_VSA_v_3) descriptors and hydrogen bonding properties of the tested compounds are the most relevant descriptors influencing the retention behavior in the RP-TLC systems. All created models were validated by cross and external validation and obtained statistical parameters confirmed their reliability in prediction of the retention behaviour and lipophilicity of related alpha adrenergic and imidazoline receptors ligands.

U drugom delu doktorske disertacije prikazana je optimizacija i validacija TLC metode za kvantitativnu analizu moksonidina i njegove četiri nečistoće (nečistoća A: 6-hlormoksonidin, nečistoća B: 4-metoksimoksonidin, nečistoća C: 4-hidroksimoksonidin i nečistoća D: 6-demetilmoksonidin). Primenom eksperimentalnog dizajna u fazi optimizacije metode identifikovani su hromatografski parametri kao i njihove interakcije, koji imaju najznačajniji uticaj na retenciono ponašanje moksonidina i njegovih nečistoća. Primenom normalno-faznog hromatografskog sistema (NP-TLC) gde je polaran silika gel korišćen kao stacionarna faza, a smeša metanol-toluen-dihloretan-amonijak 2:3:3:0.1 (v/v/v/v) kao mobilna faza omogućeno je brzo razdvajanje svih analiziranih jedinjenja. Predložena metoda je zadovoljila sve postavljene kriterijume validacije (osetljivost, selektivnost, linearnost, preciznost, tačnost i robusnost), a dobijeni rezultati su pokazali da se može koristiti za kvantitativnu analizu moksonidina i njegovih nečistoća u tabletama.

In the second part of the doctoral dissertation the optimization and validation of TLC method for quantitative analysis of moxonidine and its four impurities (impurity A: 6-chloromoxonidine, impurity B: 4-methoxymoxonidine, impurity C: 4-hydroxymoxonidine and impurity D: 6-desmethylmoxonidine) was presented. During the optimization of chromatographic conditions by applying experimental design the most important chromatographic parameters and their interactions with the highest impact on the retention behaviour of moxonidine and its impurities were identified. Separation of all examined compounds was achieved by normal-phase thin layer chromatography (NP-TLC) where polar silica gel was used as stationary phase and mixture of methanol-toluene-dichloroethane-ammonia 2:3:3:0.1 (v/v/v/v) was used as mobile phase. The proposed TLC method fulfilled all validation requirements (with respect to sensitivity, selectivity, linearity, precision, accuracy, and robustness) and can be used for quantitative analysis of moxonidine and its impurities in tablets.

C. UPOREDNA ANALIZA REZULTATA SA PODACIMA IZ LITERATURE/ *COMPARISON OF THE OBTAINED RESULTS WITH THE PUBLISHED DATA*

U dosadašnjim studijama koje su se bavile ispitivanjima liganada alfa adrenergičkih i imidazolinskih receptora lipofilnost je ispitivana metodama tečne i tankoslojne hromatografije.[1,2] Retenciono ponašanje i lipofilnost 26 liganada alfa adrenergičkih i imidazolinskih receptora ispitani su primenom pH zavisne gradijentne RP/HPLC metode.[1] Korelacijom eksperimentalno određenih logK_w vrednosti sa izračunatim log *P* vrednostima nisu dobijene značajnije zavisnosti.[1] Lipofilnost 11 liganada alfa adrenergičkih i imidazolinskih receptora ispitana je i TLC metodom gde je kao nepolarna stacionarna faza korišćena RP-18 faza, dok su različite frakcije metanola u dioksanu korišćene kao mobilna faza.[2] Nešto bolja korelacija sa izračunatim log *P* vrednostima (r^2 = 0,612) je postignuta u poređenju sa metodom tečne hromatografije.[2]

In previous studies related with investigation of alpha adrenergic and imidazoline receptors ligands, lipophilicity of tested compounds was examined using liquid and thin layer chromatographic methods. [1,2] *A pH/organic modifier gradient RP-HPLC method has been applied for simultaneous determination of lipophilicity of 26 alpha adrenergic and imidazoline receptors ligands.*[1] *Correlation between experimentally determined logK_w values and calculated log P values did not result in significant relationship. Lipophilicity of 11 alpha adrenergic and imidazoline receptors ligands was also investigated by TLC method where nonpolar RP-18 plates were used as stationary phase while different fractions of methanol in dioxane were used as mobile phase. In comparison with HPLC method something higher correlation was observed (r^2 = 0.612).*[2]

U ovoj doktorskoj disertaciji u cilju optimizacije i odabira najpogodnijeg hromatografskog sistema lipofilnost je ispitana korišćenjem RP-18 i CN stacionarnih faza i metanola i THF kao organskih modifikatora. Dobijeni rezultati su ukazali na prednost korišćenja THF u odnosu na metanol tako da se oba hromatografska sistema tetrahidrofuran-amonijak-voda/CN (r =0,933 između R_M^0 i ACD/log P) i tetrahidrofuran-amonijak-voda/RP-18 (r=0,916 između R_M^0 i ACD/log P) mogu smatrati pouzdanim i pogodnijim sistemima, od već opisanih u literaturi, za procenu lipofilnosti liganada alfa adrenergičkih i imidazolinskih receptora.

In this doctoral dissertation, in order to optimize and select the most appropriate chromatographic system for investigation of lipophilicity, different stationary (RP-18 and CN) and mobile phases (methanol and THF as organic modifier) were tested. The obtained results showed the adventages of THF as organic modifier compare to methanol, so that the both chromatographic systems, tetrahydrofuran-ammonia-water/CN (r=0.933 between R_M^0 and ACD/log P) and tetrahydrofuran-ammonia-water/RP-18 (r=0.916 between R_M^0 and ACD/log P) can be considered as more reliable and convenient compare to the systems already described in the literature for the assessment of lipophilicity of alpha adrenergic and imidazoline receptors ligands.

Kvantitativni odnosi između strukture i retencionih osobina (QSRR studije) su uspostavljeni za 11 liganada alfa adrenergičkih i imidazolinskih receptora čije retenciono ponašanje je ispitano u RP-TLC sistemu. Primenom višestruke linearne regresije formiran je QSRR model u kojem su kao najznačajniji deskriptori izdvojeni elektrostatički, geometrijski deskriptori, lipofilnost i sposobnost građenja vodoničnih veza.[2] U ovoj doktorskoj disertaciji QSRR modeli su formirani primenom PLS metode. Za razliku od postojeće metode svi modeli su validirani primenom interne i eksterne validacije. Dobijeni validacioni parametri su potvrdili da se na osnovu formiranih modela pouzdano može predvideti retenciono ponašanje strukturno sličnih liganada alfa adrenergičkih i imidazolinskih receptora. Sposobnost građenja vodoničnih veza je takođe izdvojena kao važna osobina koja opisuje retenciju u datim sistemima. Pored konstitucionih deskriptora i elektronegativnosti, parametar lipofilnosti jedinjenja se izdvaja kao najznačajniji deskriptor u svim formiranim modelima.

Quanitative Structure Retention Relationship (QSRR) study was performed for 11 alpha adrenergic and imidazoline receptors ligands in RP-TLC. QSRR model was created by Multiple Linear Regression and electrostatical and geometrical descriptors as well as lipophilicty and hydrogen bonding ability were selected as the most important molecular properties with influence on the retention behavior.[2] In this doctoral dissertation the QSRR modeling of 16 alpha adrenergic and imidazoline receptor ligands was performed with aid of the PLS regression. In contrast to the existing method, in this thesis all models were validated by using internal and external validation. The obtained validation parameters were confirmed reliability of created QSRR models in prediction of retention behaviour of structurally related alpha adrenergic and imidazoline receptors ligands. Hydrogen bonding ability was also selected as an important feature which describes retention in the examined systems. In addition to constitutional and electronegativity descriptors, lipophilicity parameter was selected as the most important feature in all devised QSRR models.

Od hromatografskih metoda koje se odnose na analizu moksonidina i njegovih nečistoća u literaturi se mogu naći podaci o validiranoj HPLC metodi koja je primenjena za određivanje moksonidina i njegove 4 nečistoće,[3] kao i o UPLC metodi koja je korišćena za praćenje i određivanje degradacionih proizvoda nastalih tokom studije forsirane degradacije.[4] Pored toga, razvijena je, ali ne i validirana, HILIC metoda u kojoj je moksonidin razdvojen od 5 srodnih supstanci.[5] Podaci koji se odnose na ispitivanje čistoće moksonidina u doziranim oblicima primenom tankoslojne hromatografije su još uvek ograničeni. U literaturi se može naći samo jedna TLC metoda u kojoj su sprovedene studije forsirane degradacije i u kojima je

moksonidin određen u prisustvu degradacionih proizvoda nastalih u kiseloj, baznoj i neutralnoj sredini ili oksidativnom degradacijom. U radu nije određena struktura nastalih degradacionih proizvoda.[6]

Among chromatographic methods relating to the analysis of moxonidine and its impurities the HPLC method was developed and validated for the determination of moxonidine and its four impurities,[3] and the UPLC method was devised as a stability indicating method for the determination of moxonidine and its degradation products in pharmaceuticals.[4] In addition, HILIC method was developed but not validated for the separation of moxonidine in the presence of five related compounds.[5] There is still limited information on an assessment of the moxonidine purity in pharmaceuticals by TLC. Literature survey revealed one TLC stability indicating method where moxonidine was determined in the presence of its degradation products formed from acidic, alkaline, neutral and oxidative degradation. The structures of degradation products were not resolved.[6]

U ovoj doktorskoj disertaciji razvijena je i validirana TLC metoda za određivanje moksonidina i njegove 4 nečistoće (nečistoće A, B, C i D) u doziranim oblicima. Metodom eksperimentalnog dizajna ispitani su hromatografski parametri i njihove interakcije sa najvećim uticajem na rezoluciju analiziranih jedinjenja. Utvrđeni limiti detekcije i kvantifikacije su u poređenju sa validiranim metodama tečne hromatografije nešto viši,[3,4] što je u skladu sa manjom osetljivošću planarne hromatografije, ali je metoda dovoljno osetljiva da se odrede nečistoće u skladu sa specifikacijama koje daje proizvođač.

In this doctoral dissertation optimization and validation of TLC method for determination of moxonidine and its four impurities (impurities A, B, C and D) in tablets was performed. Experimental design was applied for investigation of chromatographic parameters and their interactions with the highest influence on the resolution of tested compounds. The determined limits of detection and quantification were slightly higher compared with validated methods of liquid chromatography, [3,4] which is in accordance with lower sensitivity of the planar chromatography, but the method is enough sensitive for determination of impurities in accordance with the specification provided by the manufacturer.

Citirana relevantna literatura/*Cited literature*

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D. OBJAVLJENI REZULTATI KOJI ČINE DEO DISERTACIJE /*PUBLISHED RESULTS WHICH ARE PART OF THE DOCTORAL DISSERTATION*

Rezultati ove doktorske disertacije publikovani su u dva rada štampana u međunarodnim časopisima kategorije **M23,** dva saopštenja sa međunarodnog skupa štampana u izvodu (**M34**) i jednom saopštenju sa međunarodnog skupa štampanom u celini **(M33)**.
*The results presented in this doctoral dissertation were published in the form of two papers published in international scientific journals of category **M23**, as well as in the form of two abstracts (**M34**) and one proceeding **(M33)** presented on international congresses.*

Radovi objavljeni u celini u časopisima međunarodnog značaja (M23)/ Article published in international scientific journal (M23)

1. Shenger, M.S.M.; Filipic, S.; Nikolic, K.; Agbaba, D. Estimation of lipophilicity and retention behaviour of some alpha adrenergic and imidazoline receptor ligands using reversed phase-thin layer chromatography. *J. Liq. Chromatogr, R. T.* **2014**, *37*, 2829-2845.

2. Filipic, S.; Shenger, M.S.M.; Nikolic, K.; Agbaba, D. Determination of moxonidine and its impurities by thin-layer chromatography. *J. Liq. Chromatogr, R. T.* **2015**, *38*, 1121-1125.

Saopštenja sa međunarodnih skupova štampana u izvodu (M34)/Abstract on international congresses (M34)

1.Shenger, M.S.M.; Filipic, S.; Nikolic, K.; Agbaba, D. Determination of moxonidine and its impurities by thin layer chromatography. *VI Serbian Congress of Pharmacy with international participation*, October 15-19, **2014**, Belgrade, Serbia.

2.Filipic, S.; Shenger, M.S.M.; Nikolic, K.; Agbaba, D. Optimization of chromatographic condition for separation of moxonidine and its impurities by TLC. *3rd congressof pharmacycst'of Bosnia and Herzegovina with international participation,* May 14-17, **2015**, Sarajevo, Bosnia i Herzegovina.

Saopštenja sa međunarodnih skupova štampana u celini (M33)/Proceedings on international congresses (M33)

1.Filipic, S.; Shenger, M.S.M.; Vucicevic, J.; Popovic, M.; Agbaba, D. RP-TLC in Quantitative Structure-Retention Relationships of some alpha adrenergic and imidazoline receptor ligands. *12th International Conference on Fundamental and Applied Aspects of Physical Chemistry*, September 22-26, **2014**, Belgrade, Serbia.

E. OBRAZLOŽENJE NAUČNOG DOPRINOSA DISERTACIJE / *JUSTIFICATION OF SCIENTIFIC CONTRIBUTION OF THE DOCTORAL DISSERTATION*

Rezultati prikazani u doktorskoj disertaciji daće značajan naučni doprinos primeni hemometrijskog pristupa i metode tankoslojne hromatografije u proučavanju hromatografskog

ponašanja, retencionih mehanizama, lipofilnosti i farmaceutske čistoće liganada alfa adrenergičkih i imidazolinskih receptora.
The results presented in the doctoral dissertation will give a significant scientific contribution to the implementation of chemometric approache and thin layer chromatography method in the investigation of chromatographic behavior, retention mechanisms, lipophilicity and pharmaceutical purity of alpha adrenergic and imidazoline receptors ligands.

Uspostavljeni kvantitativni odnosi između hemijske strukture i retencionih osobina omogući će da se korišćenjem formiranih matematičkih modela izvrši brzo i jednostavno predviđanje retencionog ponašanja i lipofilnosti srodnih jedinjenja. Pored toga, dobijeni rezultati predstavljaju značajnu smernicu u dizajnu novih liganada sa potencijalnom aktivnošću na alfa adrenergičke i imidazolinske receptore kao i sa željenim lipofilnim karakteristikama koje predstavljaju važan parametar za postizanje njihove biološke aktivnosti.
The performed quantitative structure retention relationships study will enable fast and easilly prediction of retention behavior and lipophilicity of structurally related compounds by using created mathematical models. In addition, the obtained results are a significant guideline in the design of new ligands with potential activity on alpha adrenergic and imidazoline receptors ligand as well as with the desired lipophilic characteristics which are an important parameter for achivement of their biological activity.

Nova validirana metoda tankoslojne hromatografije je ekonomična, brza, jednostavna i osetljiva i može se koristiti u kontroli kvaliteta moksonidina u doziranim oblicima.
New validated TLC method is economic, fast, simple and sensitive and can be used in quality control of moxonidine in dosage forms.

F. ZAKLJUČAK I PREDLOG KOMISIJE ZA OCENU ZAVRŠENE DOKTORSKE DISERTACIJE / *CONCLUSION AND THE COMMISSION'S OPINION ON THE COMPLETED DOCTORAL DISSERTATION*

Na osnovu izloženog može se zaključiti da rezultati kandidata diplomiranog farmaceuta Musbah Salem Mohamed Shenger prikazani u ovoj doktorskoj disertaciji predstavljaju originalan i značajan naučni doprinos za oblast Farmaceutske-medicinske hemije i strukturne analize.

Based on the presented results it can be concluded that results of candidate Musbah Salem Mohamed Shenger presented in this doctoral dissertation represent original and significant scientific contributions to the field of pharmaceutical-medicinal chemistry and structural analysis.
Rezultati ove doktorske disertacije publikovani su u dva rada štampana u međunarodnim časopisima kategorije **M23,** dva saopštenja sa međunarodnog skupa štampana u izvodu (**M34**) i jednom saopštenju sa međunarodnog skupa štampanom u celini **(M33)**.
*The results presented in this doctoral dissertation were published in the form of two papers published in international scientific journals of category **M23**, as well as in the form of two abstracts (**M34**) and one proceeding **(M33)** presented on international congresses.*

Komisija u navedenom sastavu predlaže Nastavno-naučnom veću Farmaceutskog fakulteta u Beogradu da prihvati pozitivan Izveštaj o izrađenoj doktorskoj disertaciji kandidata Musbah Salem Mohamed Shenger i uputi ga Veću naučnih oblasti medicinskih nauka Univerziteta u Beogradu radi dobijanja saglasnosti za javnu odbranu doktorske disertacije pod nazivom:

"Kvantitativni odnosi strukture i retencionih osobina odabranih liganada alfa adrenergičkih i imidazolinskih receptora u tankoslojnoj hromatografiji"

Therefore, the Commission advises the Academic Council of the Faculty of Pharmacy in Belgrade to accept this positive Report on the completed doctoral dissertation of candidate Musbah Salem Mohamed Shenger and after being given the appropriate approval by the University of Belgrade permit the candidate to defend his doctoral dissertation entitled:

"*Quantitative structure retention relationships of selected alpha adrenergic and imidazoline receptors ligands in thin layer chromatography*"

Beograd/*Belgrade*, 19.1.2017.

Članovi Komisije/*Commission Members*:

Dr Danica Agbaba, redovni profesor/*full professor*, mentor
Univerzitet u Beogradu - Farmaceutski fakultet/
University of Belgrade – Faculty of Pharmacy

Dr Slavica Oljačić, docent/*assistant professor*, mentor
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Dr Katarina Nikolić, docent/*assistant professor*
Univerzitet u Beogradu - Farmaceutski fakultet/
University of Belgrade – Faculty of Pharmacy

Dr Živoslav Tešić, redovni profesor/*full time professor*
Univerzitet u Beogradu – Hemijski fakultet/
University of Belgrade – Faculty of Chemistry