PhD Thesis

Interactions of zearalenone and its metabolites with serum albumins and cyclodextrins

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2021

1. Introduction

Zearalenone (ZEN) is a xenoestrogenic, secondary metabolite of *Fusarium* molds, it frequently occurs as a contaminant in grains (especially in maize) and related products (e.g. food, feed, and beverages). After the oral exposure to ZEN, it is rapidly absorbed, then during its phase I metabolism α- and β-zearalenol (α- and β-ZEL) are formed via 3α/β-hydroxysteroid dehydrogenase catalyzed reactions. Further reduction of ZEN or its metabolites leads to the production of zearalanone (ZAN), α- and β-zearalanol (α- and β-ZAL). During the phase II biotransformation of ZEN, sulfate (e.g. zearalenone-14-sulfate: Z14S) or glucuronide conjugates are formed. Certain reduced ZEN metabolites (e.g. α-ZEL and α-ZAL) possess similar or more potent estrogenic activity than the parent compound. Filamentous fungi can also metabolize ZEN, during which modified mycotoxins (e.g. Z14S) are produced. In addition, mycotoxins are also metabolized by plants (defense mechanism), leading to the formation of "masked mycotoxins" (e.g. zearalenone-14-glucoside: Z14G). The analytical detection of masked mycotoxins is cumbersome, mainly due to the lack of analytical standards. Despite the lower toxicity of the conjugated ZEN derivatives, Z14G and Z14S also appear in food and feed (similarly to ZEN and its reduced metabolites). After their consumption these conjugates are hydrolyzed to ZEN in the gastrointestinal tract, thus the risk associated to their exposure is considered to be similar to the parent compound.

Serum albumin is the dominant plasma protein in the circulation, it is responsible for the maintenance of the oncotic pressure, and possessing pseudo-enzymatic and buffer activities. Albumin can bind endogenous and exogenous compounds (e.g. drugs and toxins), affecting the tissue distribution and elimination of these compounds. Sudlow's site I (subdomain IIA) and Sudlow's site II (subdomain IIIA) are the two major drug binding sites of human serum albumin (HSA). The bovine (BSA), porcine (PSA), and rat (RSA) serum albumins show high structural similarity to HSA (73-76% sequence identity). The fluorescence signals of serum albumins are mainly expressed by the tryptophan (Trp) residues (e.g. Trp-214 in HSA and RSA).

Cyclodextrins (CDs) are cyclic oligosaccharides built up from glucose units. They are frequently utilized in pharmaceutical, food, and cosmetic industries. CDs have lipophilic internal cavity, which can accommodate apolar molecules (including certain mycotoxins) leading to the formation of host-gust type complexes. The hydrophilic external part of CDs provides excellent aqueous solubility. The complex formation of fluorescent mycotoxins with CDs induces significant increase in their emission signal; therefore, CD technology seems to be suitable for the sensitization of the fluorescence detection of mycotoxins. Furthermore, CD polymers attached to water-insoluble surfaces are promising mycotoxin binders.

2. Aims

Studies on the albumin-binding of ZEN derivatives and the complexation of modified ZEN metabolites with CDs are limited to date. Therefore, I aimed to investigate the following aspects:

• Testing the interactions of ZEN, α-ZEL, β-ZEL, ZAN, α-ZAL, β-ZAL, Z14G, and Z14S with serum albumins, for the deeper understanding of their toxicokinetic properties. I aimed to determine the binding constants of the complexes formed, and to explore the species differences in the albumin binding of these mycotoxins (employing human, bovine, porcine, and rat serum albumins).

• Testing the impact of ZEN (which occupies a non-conventional binding site on HSA between IIA and IIIA subdomains) and its metabolites (α-ZEL, β-ZEL, ZAN, α-ZAL, β-ZAL, Z14G, and Z14S) on the HSA-binding of the well-known site I marker warfarin.

• Testing the interactions of masked (Z14G) and modified (Z14S) mycotoxins with native and chemically modified CDs, to determine the stability of the complexes formed and the CD-induced enhancement in fluorescence.

• Testing the extraction of ZEN and its metabolites from aqueous solutions (including beverages) with β-CD bead polymer, which may be applied for analytical sample preparation and/or mycotoxin removal.

3. Methods

Fluorescence spectroscopic measurements of mycotoxin-albumin and mycotoxin-CD interactions were performed with a Hitachi F-4500 fluorescence spectrophotometer. The UV-Vis spectra of the ligands were recorded employing a Specord Plus 210 or Jasco-V730 spectrophotometers. The experiments were performed at room temperature; fluorescence spectra were corrected to exclude the error caused by inner filter effect.

The albumin-mycotoxin interactions were investigated employing fluorescence quenching technique in PBS (phosphate buffered saline, pH 7.4; λ_{ex} = 295 nm, λ_{em} = 340 nm). The stability of the formed complexes was determined by the graphical application of the Stern-Volmer equation and by the Hyperquad2006 software. To test the species-dependent differences regarding mycotoxin-albumin complexes, these experiments were performed with HSA, BSA, PSA, and RSA. Furthermore, to confirm the complex formation of ZEN and its metabolites with HSA, high-performance affinity chromatography (HPAC) was also employed.

To examine the effects of ZEN and its metabolites on the complex formation of the site I marker warfarin with HSA, the fluorescence signal of warfarin was recorded (λ_{ex} = 317 nm, λ_{em} = 379 nm; PBS, pH 7.4) in the presence of HSA and increasing mycotoxin concentrations. Since the fluorescence signal of the albumin-bound warfarin is significantly higher compared to the free warfarin, the change in the fluorescence intensity measured at 379 nm indicates the increase or decrease in the albumin-bound fraction of warfarin.

In order to investigate the complexation of Z14G and Z14S with native and chemically modified CDs, increasing concentrations of CDs were added to standard amount of mycotoxins, then the fluorescence of the mycotoxins was recorded in different buffers (Z14G: pH 3.0-10.0; Z14S: pH 5.0-10.0). Binding constants (*K*; L/mol) of mycotoxin-CD complexes were determined by the graphical application of the Benesi-Hildebrand equation.

To investigate the extraction of ZEN and its derivatives from aqueous solutions, mycotoxin samples were incubated with β-CD bead polymer (BBP) in a thermomixer. After pulse centrifugation, the mycotoxin content of the supernatant was analyzed by HPLC-FLD.

Mycotoxin binding ability of BBP was determined based on Langmuir and Freundlich isotherms. Mycotoxin extraction from spiked corn beer samples were also investigated: after the incubation with BBP, the remaining mycotoxin content in the supernatant was detected by HPLC-FLD (after two-step extraction with dichloromethane and vacuum evaporation). In addition, the influence of BBP on the color and polyphenol content of corn beer was examined as well. After mycotoxin binding, the regenerability and reusability of BBP were also tested (with 50 *v/v%* ethanol-water mixture).

4. Results and discussion

4.1. Interaction of zearalenone and its metabolites with serum albumins

4.1.1. Fluorescence quenching studies and the stability of mycotoxin-albumin complexes

ZEN, α-ZEL, β-ZEL, ZAN, α-ZAL, β-ZAL, and Z14S decreased the fluorescence of HSA, BSA, PSA, and RSA at 340 nm, in a concentration-dependent manner. This can be explained be the partial quenching effect of the mycotoxins on the Trp-residues of albumins (which are mainly responsible for their fluorescence), suggesting the formation of mycotoxin-albumin complexes. Z14G did not influence the fluorescence signal of albumins, thus it does not interact with the protein or binds with a very low affinity. Stern-Volmer quenching constants (K_{SV}, L/mol) showed good correlation with the binding constants (K, L/mol) determined, which were in the 10^4 to 10^5 L/mol range. Typically, Z14S showed the highest affinity towards albumins (except HSA), while β-ZEL and β-ZAL formed the least stable complexes with HSA, BSA, and PSA. The parent compound binds to a non-conventional binding site on HSA (between subdomains IIA and IIIA). Based on modeling studies, α-ZEL occupies similar binding site to ZEN, while the binding site/position of β-ZEL is different, which can explain its significantly lower affinity towards HSA.

Importantly, remarkable species differences can be observed in the affinity of ZEN and its metabolites towards albumins. The least significant species-dependent alternation was shown by ZEN (approximately 7-fold higher affinity towards RSA than PSA), while the most considerable difference was noticed regarding β-ZAL (approximately 30-fold higher affinity towards RSA vs. BSA). The parent mycotoxin and its reduced metabolites bound to BSA and/or PSA with the lowest affinity, whereas the least stable complexes of Z14S were formed with HSA. Typically, ZEN and its metabolites showed the highest affinity towards RSA. Despite the high structural similarity of serum albumins investigated, different amino acids are located in the non-conventional binding site of ZEN regarding RSA compared to HSA, BSA, and PSA. These structural differences may explain the considerably higher affinity of ZEN and its metabolites towards RSA.

4.1.2. High-performance affinity chromatography of zearalenone and its metabolites

An immobilized HSA-coated HPAC column was applied to confirm the results of the fluorescence quenching studies. The mycotoxins are eluted from the column according to their affinity towards HSA: the molecules with higher affinity showing longer retention time. Similar tendency was observed in the retention time of mycotoxins to the binding constants determined by fluorescence quenching studies. Z14G eluted with the shortest retention time, indicating its very weak interaction with HSA, then followed by β-ZAL, β-ZEL, α-ZAL, α-ZEL, ZAN, ZEN, and Z14S. Interestingly, the retention time of Z14S was the longest, despite its lower affinity towards HSA compared to ZEN. This discrepancy can be likely explained by the different

experimental conditions: quenching studies were performed in PBS (pH 7.4), while HPAC experiments were carried out with the mixture of isopropanol and a low ionic strength buffer (pH 7.0; according to the manufacturer's guide).

4.1.3. Effects of zearalenone and its metabolites on warfarin-HSA interaction

The binding site of ZEN is between subdomains IIA and IIIA. Since it is close to the site I region, it can affect the interaction of site I ligands with albumin, through allosteric modulation. Similarly to ZEN, the presence of ZAN, α-ZAL, and α-ZEL induced enhancement in the emission signal of warfarin, suggesting the increased affinity of warfarin towards the protein (confirmed by ultrafiltration regarding ZEN). However, Z14G, Z14S, and β-ZAL barely affected, while β-ZEL decreased the fluorescence signal of warfarin, supporting the hypothesis regarding the allosteric mechanism of these interactions.

Since recently published toxicokinetic animal studies revealed that the affinity of ZEN and its metabolites towards albumins shows good correlation with their life-time in the circulation, albumin-binding of ZEN and its metabolites may have a significant role in their toxicokinetics.

4.2. Interaction of zearalenone and its metabolites with cyclodextrins

4.2.1. Interaction of zearalenone-14-glucoside with native and chemically modified cyclodextrins

Similarly to ZEN and ZELs, two peaks appeared in the fluorescence excitation spectrum of Z14G around 275 and 315 nm. The emission spectra of Z14G were similar at pH 3.0-7.4. However, lower fluorescence intensities and a blueshift in its fluorescence emission maximum were observed at pH 10.0. These spectral changes likely resulted from the deprotonation of the phenolic hydroxyl group of Z14G under alkaline conditions.

A significant increase was observed in the fluorescence signal of Z14G in the presence of native β-CD (BCD) and γ-CD (GCD); furthermore, a slight blueshift of the fluorescence emission maximum of Z14G was noticed (λ_{em} = 465 nm → 455 nm). Since, the CDs tested do not exert fluorescence, our observations suggest the formation of Z14G-CD complexes. The BCD-induced fluorescence enhancement was higher compared to GCD.

Similar trends were observed regarding the fluorescence enhancement of Z14G by CDs at pH 3.0-7.4. In contrast, lower fluorescence enhancement was noticed at pH 10.0, and a slight redshift (450 nm → 455 nm) was observed in the fluorescence emission maximum of the mycotoxin. The smaller increase in the fluorescence can be explained by the deprotonation of the mycotoxin under alkaline circumstances, suggesting that CDs prefer the non-ionized form of the mycotoxin. This hypothesis is also supported by the CD-induced redshift in the emission maximum of Z14G at pH 10.0, resulting in the similar emission maximum (λ_{em} = 455 nm) of the Z14G-CD complex to observed at lower pH values.

At pH 3.0-7.4, the chemically modified β-CD derivatives did not induce higher increase in the fluorescence of Z14G than the native BCD. However, under alkaline conditions (pH 10.0), random methylated β-CD (RAMEB) was the strongest fluorescence enhancer among β-CDs tested. In contrast, the hydroxypropyl (HPGCD) and random methylated (RAMEG) γ-CD derivatives induced higher fluorescence increase in the intensity of Z14G than native GCD regardless of the pH used. Typically, the RAMEG-induced fluorescence enhancement was the highest, but BCD proved to be similarly effective fluorescence enhancer at pH 3.0 and 5.0.

Z14G (pH 5: log*K* = 2,7-3,3) formed less stable complexes with CDs than ZEN (pH 5.0: log*K* = 3.8-4.8). The affinity of Z14G was higher towards γ-CDs (log*K* = 2.3-3.3) than β-CDs (log*K* = 2.0-2.9). The chemical modification of GCD resulted in a slight improvement in the

binding affinity, however, the chemically modified β-CD derivatives tested did not promote the complexation.

4.2.2. Interaction of zearalenone-14-sulfate with native and chemically modified cyclodextrins

The fluorescence excitation spectrum of Z14S showed one peak around 330 nm. However, under alkaline conditions (pH 10.0), its fluorescence signal considerably decreased. Furthermore, at pH 10.0, the redshift and the blueshift were observed in the fluorescence excitation and emission maxima, respectively. It is likely resulted from the deprotonation of the phenolic hydroxyl group of the mycotoxin.

The interaction of Z14S with CDs led to the increase in the fluorescence emission signal of the mycotoxin, and a slight blueshift was also noticed in its fluorescence emission maximum. Since CDs do not possess fluorescence properties under the applied conditions, our observations suggest the host-guest type complex formation. Under weakly acidic circumstances (pH 5.0), BCD was stronger fluorescence enhancer compared to GCD. Therefore, in our further experiments, the complex formation of Z14S with β-CDs was examined in different buffers (pH 5.0-10.0).

Similar CD-induced spectral changes were observed at pH 5.0 and 7.4. Among the chemically modified CDs, the dimethyl (DIMEB) and monoamino (MABCD) derivatives induced higher increase in the fluorescence of Z14S at pH 5.0-7.4 than the native BCD. At pH 10.0, CDs caused lower enhancement in the emission signal of the mycotoxin. Under alkaline circumstances (pH 10.0), DIMEB evoked the highest, whereas quaternary ammonium β-CD (QABCD) caused the lowest increase in the fluorescence of Z14S. In addition, a blueshift was observed in the fluorescence emission maximum of the modified mycotoxin in the presence of QABCD. The emission maximum of Z14S was recorded around 460 nm in the presence of CDs tested (except QABCD), regardless of the pH. This observation, as well as the lower fluorescence enhancer effects of CDs under alkaline conditions (pH 10.0) suggest that typically the non-ionized form of the mycotoxin is preferred during the complex formation. While the spectroscopic changes suggest that QABCD interacts with the ionized form of Z14S at pH 10.0.

According to the graphical application of the Benesi-Hildebrand equation, stable Z14S-CD complexes (log$K$ = 3.0-4.7) were formed, and the Benesi-Hildebrandt plots showed excellent fitting with the 1:1 stoichiometry model. The Z14S-BCD complexes were more stable (log$K$ = 3.6) than Z14S-GCD complexes (log$K$ = 3.1). Under acidic and physiological conditions (pH 5.0 and 7.4, respectively), DIMEB and RAMEB showed the highest affinity towards Z14S. Typically, less stable complexes were formed at pH 10.0 compared to pH 5.0 and 7.4 (except QABCD), which also suggests that CDs tested prefer the protonated form of Z14S. However, QABCD formed the most stable complexes with Z14S at pH 10.0, which also confirms that it favors the deprotonated form of the mycotoxin. This observation can be explained by the electrostatic interactions between the quaternary ammonium sidechains of QABCD and the mycotoxin anion. Interactions of certain soluble CD polymers with Z14S were also tested; however, only minor differences were noticed regarding their complex forming properties vs. the monomers.

Previously, the CD-induced fluorescence enhancement was successfully applied for the analytical determination of the mycotoxin content of ZEN-contaminated corn samples. Therefore, CD technology seems to be suitable to sensitize the fluorescence detection of the modified and masked ZEN derivatives as well.

4.2.3. Removal of zearalenone and zearalenols from aqueous solutions by β-cyclodextrin bead polymer

BBP induced a concentration-dependent decrease in the initial ZEN/ZEL concentrations in aqueous solutions, showing its suitability to considerably reduce the mycotoxin content. Approximately 70-80% decrease was noticed in the initial mycotoxin concentration after 5 min incubation with BBP. During 30-min incubation, approximately 85-90% of the mycotoxin content was extracted by BBP, which did not change significantly even after longer incubation. In contrast, the changes in the temperature used did not affect the mycotoxin extraction. Lower pH values (pH 5.0-7.4) proved to be more favorable for the extraction of ZEN and ZELs by BBP. However, at pH 10.0, BBP was a less effective mycotoxin binder, likely due to the formation of less stable complex between the CD rings and the mycotoxin anions.

4.2.4. Investigation of regenerability and reusability of β-CD bead polymer

Previous studies highlighted that organic solvents can displace ligand molecules from the apolar cavity of CDs. Therefore, after mycotoxin-binding, we tried to regenerate BBP in two washing steps with 50 *v/v%* ethanol-water mixture. The BBP-bound ZEN fraction was successfully eluted by the ethanol-water mixture, after which the regenerated BBP showed similar ability to extract ZEN during its second and third applications. Based on these observations, BBP seems to be a suitable binder for mycotoxin extraction from aqueous solutions. In addition, BBP may be suitable for analytical sample preparation/enrichment.

4.2.5. Extraction of zearalenone from corn beer by β-CD bead polymer

Since ZEN is a common contaminant in maize, and previous studies reported its presence in some beer samples (from few nmol/L to more μmol/L concentrations), the extraction of ZEN by BBP was also examined in spiked corn beer samples. Since BBP is not a selective binder of ZEN, CDs can interact with several food components. Therefore, the color and the total polyphenol content of beer samples were also investigated after their treatment with BBP. The polymer (13.3 and 26.7 mg/mL) induced approximately 90-95% reduction in the mycotoxin content, showing similar effect than 6.67 and 13.3 mg/mL BBP in aqueous buffers. BBP gradually decreased the color and total polyphenol content of beer samples. However, the BBP-induced relative decrease in ZEN content was considerably higher compared to the relative decrease in color and total polyphenol content.

4.2.6. Extraction of ZEN conjugates from aqueous solution by β-CD bead polymer

The removal of Z14G and Z14S from aqueous buffers by BBP was also investigated. BBP strongly decreased the mycotoxin content regarding both conjugates. The removal of Z14G by BBP was less effective compared to the parent mycotoxin, which is in agreement with its lower affinity towards the BCD monomer. However, the extraction of Z14S and ZEN by BBP was similarly successful, which is consistent with the binding constants determined for Z14S-BCD and ZEN-BCD complexes.

BBP seems to be suitable for the extraction of ZEN, α-ZEL, β-ZEL, and ZEN conjugates from aqueous solutions (including beverages). Since chemical modification can usually increase the binding ability of CDs regarding certain host molecules, it is possible that the selectivity and efficacy of CD polymers as mycotoxin binders can be further improved.

5. New findings

• ZEN, α-/β-ZEL, ZAN, α/β-ZAL, and Z14S form stable complexes with serum albumins (K = 10^4 to 10^5 L/mol); thus, their albumin binding may have toxicokinetic importance.

• β-ZEL/ZAL form less stable complexes with HSA compared to ZEN or α-ZEL/ZAL, which likely resulted from their different binding position/site on HSA.

• Albumin binding of ZEN and its metabolites showed considerable species-dependent differences, which should be taken into consideration regarding the extrapolation of animal studies.

• ZEN and its metabolites influence the albumin binding of the site I marker warfarin, presumably through allosteric mechanism.

• Similarly to ZEN, its conjugates also interact with CDs, resulting in the significant increase in their fluorescence signals. Therefore, CDs seems to be suitable to sensitize the fluorescent detection of Z14S and Z14G.

• Z14G forms more stable complexes with GCD than with BCD. Alkaline environment is less favorable for Z14G-CD interactions.

• Z14S formed the most stable complexes with methylated β-CDs under acidic and physiological circumstances; however, at pH 10.0, the modified mycotoxin showed the highest affinity towards QABCD.

• ZEN and its metabolites can be successfully extracted from aqueous solutions and/or from beer by BBP. The extraction is less effective under alkaline conditions.

• BBP can be regenerated by two-step washing with 50 *v/v%* ethanol-water mixture. It seems to be suitable for analytical sample preparation/enrichment.

6. Acknowledgements

I would like to say special thanks to my supervisor, Dr. Miklós Poór, for his professional guidance, advice and his dedicated work during my PhD studies. I would like to thank Prof. Dr. Gábor Pethő (Head of the Department of Pharmacology and Leader of the Toxicology Program) for his helpfulness, exemplary teaching activity and for giving me the opportunity to work at the Department. I would like to express my gratitude to Dr. Balázs Németi, the former Head of the Department of Pharmacology, and Prof. Dr. Zoltán Gregus, the former Leader of the Toxicology Program, for their exemplary professional dedication, helpfulness and conscientious work. I thank to our collaborators, Dr. Afshin Zand, Dr. Mónika Bálint, Dr. Tímea Bencsik, Dr. Chiara Dall'Asta, Dr. Gianni Galaverna, Dr. Csaba Hetényi, Dr. Sándor Kunsági-Máté, Dr. Mónika Kuzma, Dr. Beáta Lemli, Dr. Luca Dellafiora, Dr. Mátyás Mayer, Dr. Lajos Szente, and Dénes Szerencsés for their contribution in the publications related to my dissertation. In addition, I am grateful to Prof. Dr. Tamás Kőszegi and Rita Csepregi for their help in our joint work, as well as to all our collaborators who participated in our published or ongoing researches. I would like to thank my colleagues, Dr. Eszter Fliszár-Nyúl and Kata Fábián, as well as, Dr. Eszter Almásiné Rubint and István Schweibert for their assistance in HPLC measurements. I am thankful to my current and former student researchers, Renáta Skaper and Dr. Virág Vörös, respectively, for their work during fluorescence spectroscopic measurements. I am especially grateful to the co-workers of the Department of Pharmacology for providing me a joyful environment for everyday work. I would like to thank my PhD fellow student, Dr. Violetta Mohos, for her help and support in overcoming the difficulties we encountered during our studies. Furthermore, I would like to thank all the members of the Department of Pharmacology and Pharmacotherapy for providing us gracious environment.
Finally, I would like to say thank for the encouragement and immeasurable support which have been provided by my family, loved ones and friends.

7. List of publications

7.1. Publications related to the present PhD thesis:

Miklós Poór, **Zelma Faisal**, Afshin Zand, Tímea Bencsik, Lajos Szente. Removal of zearalenone and zearalenols from aqueous solutions using insoluble beta-cyclodextrin bead polymer. *Toxins* **2018**, 10, 216. **[IF: 3.895; Q1]**

Zelma Faisal, Beáta Lemli, Dénes Szerencsés, Sándor Kunsági-Máté, Mónika Bálint, Csaba Hetényi, Mónika Kuzma, Mátyás Mayer, Miklós Poór. Interactions of zearalenone and its reduced metabolites α-zearalenol and β-zearalenol with serum albumins: species-dependent alternations, binding sites, and thermodynamics. *Mycotoxin Research* **2018**, 34, 269-278. **[IF: 3.741; Q2]**

Zelma Faisal, Eszter Fliszár-Nyúl, Luca Dellafiora, Gianni Galaverna, Chiara Dall'Asta, Beáta Lemli, Sándor Kunsági-Máté, Lajos Szente, Miklós Poór. Cyclodextrins Can Entrap Zearalenone-14-Glucoside: Interaction of the Masked Mycotoxin with Cyclodextrins and Cyclodextrin Bead Polymer. *Biomolecules* **2019**, 9, 354. **[IF: 4.082; Q1]**

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Zelma Faisal, Virág Vörös, Eszter Fliszár-Nyúl, Beáta Lemli, Sándor Kunsági-Máté, Miklós Poór. Interactions of zearalanone, α-zearalanol, β-zearalanol, zearalenone-14-sulfate, and zearalenone-14-glucoside with serum albumin. *Mycotoxin Research* **2020**, 36, 389-397. **[IF: 3.164*; Q2]**

*Impact factors based on 2019 classification

Cumulative impact factor related to my thesis: 19.947

7.2. Presentations and posters related to the present PhD thesis:

Zelma Faisal, Afshin Zand, Tímea Bencsik, Lajos Szente, Miklós Poór. Removal of zearalenone and its metabolites from aqueous solutions by insoluble β-cyclodextrin bead polymer. ***4th International Cholnoky Symposium*** (Pécs, Hungary, May 10-11, 2018; oral presentation)

Zelma Faisal, Virág Vörös, Rita Csepregi, Tamás Kőszegi, Beáta Lemli, Sándor Kunsági-Máté, Mónika Bálint, Csaba Hetényi, Lajos Szente, Miklós Poór. Interactions of zearalenone and its reduced metabolites with serum albumins and cyclodextrins. ***5th International Cholnoky Symposium*** (Pécs, Hungary, April 25, 2019; oral presentation)

Faisal Zelma, Fliszár-Nyúl Eszter, Dellafiora Luca, Galaverna Gianni, Dall'Asta Chiara, Szente Lajos, Poór Miklós. Zearalenon-14-glükozid interakcióinak vizsgálata ciklodextrinekkel és béta-ciklodextrin gyöngypolimerrel – vajon a ciklodextrinek kölcsönhatásba lépnek a maszkolt mikotoxinnal? ***TOX2019 Tudományos Konferencia*** (Szeged, Hungary, October 9-11, 2019; oral presentation)

Faisal Anna Zelma, Gődér Beatrix, Szerencsés Dénes, Lemli Beáta, Poór Miklós. Zearalenon, α-zearalenol és β- zearalenol kölcsönhatásainak vizsgálata human és egyéb albuminokkal. ***TOX2017 Tudományos Konferencia*** (Bükfürdő, Hungary, October 11-13, 2017; poster)

Miklós Poór, Virág Vörös, Dénes Szerencsés, **Zelma Faisal**, Beáta Lemli, Sándor Kunsági-Máté, Mónika Bálint, Csaba Hetényi, Interaction of zearalenone and its reduced metabolites with serum albumins. ***40th Mycotoxin Workshop*** (Munich, Germany, June 11-13, 2018; poster)

7.3. Other publications:

Franziska Sueck, Miklós Poór, **Zelma Faisal**, Christoph G. W. Gertzen, Benedikt Cramer, Beáta Lemli, Sándor Kunsági-Máté, Holger Gohlke, Hans-Ulrich Humpf. Interaction of ochratoxin A and its thermal degradation product *2'R*-ochratoxin A with human serum albumin. *Toxins* **2018**, 10, 256. **[IF: 3.895; Q1]**

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Eszter Fliszár-Nyúl, **Zelma Faisal**, Violetta Mohos, Diána Derdák, Beáta Lemli, Tamás Kálai, Cecília Sár, Balázs Z. Zsidó, Csaba Hetényi, Ádám I. Horváth, Zsuzsanna Helyes, Ruth Deme, Dóra Bogdán, Andrea Czompa, Péter Mátyus, Miklós Poór. Interaction of SZV 1287, a novel oxime analgesic drug candidate, and its metabolites with serum albumin. *Journal of Molecular Liquids* **2021**, online, DOI: https://doi.org/10.1016/j.molliq.2021.115945 **[IF: 5,065*, Q1]**

7.4. Other presentations and posters:

Virág Vörös, **Zelma Faisal**, Mónika Bálint, Csaba Hetényi, Beáta Lemli, Rita Csepregi, Miklós Poór. Interactions of mycotoxin metabolites *2'R*-ochratoxin A and dihydrocitrinone with human serum albumin. ***4th International Cholnoky Symposium*** (Pécs, Hungary, May 10-11, 2018; oral presentation)

Faisal Zelma, Vörös Virág, Derdák Diána, Lemli Beáta, Bálint Mónika, Hetényi Csaba, Csepregi Rita, Sueck Franziska, Humpf Hans-Ulrich, Cramer Benedikt, Poór Miklós. Ochratoxin A és *2'R*-ochratoxin A kölcsönhatásainak vizsgálata szérum albuminnal. ***TOX2018 Tudományos Konferencia*** (Lillafüred, Hungary, October 17-19, 2018; oral presentation)

Poór Miklós, **Faisal Zelma**, Csepregi Rita, Lemli Beáta, Kunsági-Máté Sándor, Szente Lajos. Mikotoxin-ciklodextrin kölcsönhatások vizsgálata és gyakorlati hasznosíthatóságuk. ***TOX2018 Tudományos Konferencia*** (Lillafüred, Hungary, October 17-19, 2018; oral presentation)

Miklós Poór, Eszter Fliszár-Nyúl, Violetta Mohos, **Zelma Faisal**, Beáta Lemli. Pharmacological/toxicological importance of albumin-ligand interactions. ***5th International Cholnoky Symposium*** (Pécs, Hungary, April 25, 2019; oral presentation)

Zelma Faisal, Sándor Kunsági-Máté, Beáta Lemli, Lajos Szente, Dominik Bergmann, Hans-Ulrich Humpf, Miklós Poór. Interaction of the mycotoxin metabolite dihydrocitrinone with native and chemically modified cyclodextrins. ***4th Symposium on Weak Molecular Interactions*** (Matsue, Japan, May 17-19, 2019; oral presentation)

Miklós Poór, Eszter Fliszár-Nyúl, Violetta Mohos, **Zelma Faisal**, Beáta Lemli, Csaba Hetényi, Sándor Kunsági-Máté. Pharmacological/toxicological importance and investigation of albumin-ligand interactions. ***4th Symposium on Weak Molecular Interactions*** (Matsue, Japan, May 17-19, 2019; oral presentation)

Poór Miklós, **Faisal Zelma**, Fliszár-Nyúl Eszter. Mikotoxin-albumin kölcsönhatások vizsgálata és jelentőségük. ***TOX2019 Tudományos Konferencia*** (Szeged, Hungary, October 9-11, 2019; oral presentation)

Zelma Faisal, Virág Vörös, Beáta Lemli, Mónika Bálint, Csaba Hetényi, Rita Csepregi, Franziska Sueck, Benedikt Cramer, Hans-Ulrich Humpf, Miklós Poór. Interaction of *2'R*-ochratoxin A with serum albumins. ***40th Mycotoxin Workshop*** (Munich, Germany, June 11-13, 2018; poster)

Vörös Virág, **Faisal Zelma**, Derdák Diána, Lemli Beáta, Bálint Mónika, Hetényi Csaba, Csepregi Rita, Poór Miklós. Dihidrocitrinon kölcsönhatásának vizsgálata szérum albuminnal. ***TOX2018 Tudományos Konferencia*** (Lillafüred, Hungary, October 17-19, 2018; poster)

Zelma Faisal, Rita Csepregi, Tamás Kőszegi, Lajos Szente, Miklós Poór. Effects of native and chemically modified beta-cyclodextrins on the in vitro cytotoxicity of zearalenone. ***41th Mycotoxin Workshop*** (Lisbon, Portugal, May 6-8, 2019; poster)

Virág Vörös, **Zelma Faisal**, Rita Csepregi, Tamás Kőszegi, Miklós Poór. Testing the interactions of deoxynivalenol, patulin, and T-2 toxin with human serum albumin. ***41th Mycotoxin Workshop*** (Lisbon, Portugal, May 6-8, 2019; poster)

Garai Edina, **Faisal Zelma**, Bakos Katalin, Szente Lajos, Urbányi Béla, Poór Miklós, Csenki Zsolt, A béta-cyclodextrinek védőhatása a zearalenon által indukált toxicitásra TG(VTG1:MCHERRY) zebradánió embriókban. ***TOX2019 Tudományos Konferencia*** (Szeged, Hungary, October 9-11, 2019; poster)

Cumulative impact factor: 53.087
Number of independent citations: 32