Synthesis, physicochemical characterisation and bio-activity of new amoxicillin and pyrazole-based complex compounds

David Kočović[1,*], Željko Jaćimović[2]

[1]Institute for Medicines and Medical Devices of Montenegro, Laboratory, Bulevar Ivana Crnojevica 64A. Podgorica, Montenegro

[2]University of Montenegro, MARDS Department, Cetinjski put b.b. Podgorica, Montenegro

Abstract. This research aims to synthesise new amoxicillin and pyrazole-based complex compounds using metal ions with ligand-metal structures, structurally characterise them and check for their bio-activity on microorganisms. The structure of the newly synthesised compounds is to be confirmed based on analytical and spectral data. Some of the prepared compounds are to be evaluated for their in vitro activity on different bacterial strains. The reaction of pharmaceutically active compounds, such as pyrazoles and amoxicillin, with metal ions that are high-potential bioactivity stimulators is supposed to produce a superior compound by a proper structural organisation of these compounds.

1 Problem definition, background, research methodology and our progress

Antimicrobial resistance in bacterial pathogens poses a challenge in treating both Gram-positive and -negative bacteria. The diseases that result from these phenomena are difficult to treat and may even be untreatable with conventional antibiotics. As there is a shortage of effective therapies and very few new antibiotics, creating new, complex compounds could potentially help or solve the problem of antibiotic resistance.

Amoxicillin is one of the most commonly used antibiotics. It is an amino-penicillin produced by adding an extra amino group to penicillin to battle antibiotic resistance.

Pyrazole and its derivatives are potent medicinal platforms and exhibit a full spectrum of biological activities. Three different pyrazole compounds will be used as bases on which other complex compounds will be created.

As the principle of this synthesis is the relation between metals and ligands, metal was chosen on the basis of health activity. The metals to be used are Pd, Ru, Pt, Zn, Co, and Cu.

The workflow is organised in three parts: synthesis, physicochemical characterisation and bio-activity study. Thus far, all the materials have been prepared for the first stage of our work – synthesis.

2 Future work and Conclusions

The aforementioned first stage of our work should be finalised during September, with the possible addition of new syntheses in the later stages of the work. The second – physicochemical characterisation phase is planned to finish by June 2023 and will consist of characterisations via XRD, XRF, IR, UV/VIS, CHNS, and other instrumental and analytical analyses, while the final phase should be concluded in September 2023.

As pyrazole derivatives are found to be pharmacologically more potent, their synthesis is a potential area of scientific research. In combining amoxicillin and pyrazole derivatives with stated metals, new complex compounds could be superior in their effectiveness and safety in treating different health conditions and/or express completely different spectra of activity. It will be interesting to observe what these modifications can do to the activity of newly developed complexes, as some of them could show the potential of potent therapeutic agents in the future.

Acknowledgements

We would like to thank the MARDS department for enabling our research and for all the support provided.

References

[1] A. Abdelghany, M. A. El-Desouky, and M. Shemis, “Synthesis and characterization of amoxicillin-loaded polymeric nanocapsules as a drug delivery system targeting Helicobacter pylori,” Arab Journal of Gastroenterology, vol. 22, no. 4, pp. 278–284, Dec. 2021, doi: 10.1016/j.ajg.2021.06.002.

[2] A. Reiss, A. Samide, G. Ciobanu, and I. Dabuleanu, “SYNTHESIS, SPECTRAL CHARACTERIZATION AND THERMAL BEHAVIOUR OF NEW METAL(II) COMPLEXES WITH SCHIFF BASE DERIVED FROM AMOXICILLIN,” Journal of the Chilean Chemical Society, vol. 60, no. 3, pp. 3074–3079, Sep. 2015, doi: 10.4067/S0717-97072015000300021.

[3] N. E. A. El-Gamel, “Metal chelates of ampicillin versus amoxicillin: synthesis, structural investigation, and biological studies,” Journal of Coordination Chemistry, vol. 63, no. 3, pp. 534–543, Dec. 2009, doi: 10.1080/00958970903494157.

[4] J. R. Anacona, K. Mago, and J. Camus, “Antibacterial activity of transition metal complexes with a tridentate NNO amoxicillin derived Schiff base. Synthesis and characterization,” Applied Organometallic Chemistry, vol. 32, no. 7, p. e4374, Apr. 2018, doi: 10.1002/aoc.4374.

[5] Y. Junejo, A. Güner, and A. Baykal, “Synthesis and characterization of amoxicillin derived silver nanoparticles: Its catalytic effect on degradation of some pharmaceutical antibiotics,” Applied Surface Science, vol. 317, pp. 914–922, Oct. 2014, doi: 10.1016/j.apsusc.2014.08.133.

David Kočović obtained his MSc degree from the University of Donja Gorica in Food technology.

Master of Science in Food Technology

Date of birth: 17/06/1996

Address: Vijenci Danila Kisa 3/71, 81 000 Podgorica

Tel.:+38269335545

Email: david.kocovic@cinmed.me

Work experience:

- 2022 - (April-ongoing) – Head of Laboratory at the Institute for Medicines and Medical Devices of Montenegro – Podgorica, Montenegro (Techniques – XRPD and XRF)
- 2020 – 2022. (December-April) – Expert in instrumental methods and equipment qualification at the Institute for Medicines and Medical Devices of Montenegro – Podgorica, Montenegro (Techniques – XRPD and XRF)
- 2020 – 2020. (July-December) – Associate for development of laboratory system at the Institute for Medicines and Medical Devices of Montenegro – Podgorica, Montenegro (Techniques – XRPD and XRF)
- 2019 – 2020. (October-July) – Associate in laboratories for liquid and gas chromatography at the Centre for Ecotoxicological Research – Podgorica, Montenegro (Techniques – LC-MS/MS, GC-MS, GC-ECD, GC-FID)
- 2019 – 2019. (January-October) – Associate in the laboratory for liquid chromatography at the Institute for Public Health – Podgorica, Montenegro (Technique - HPLC-UV/VIS)

Projects and additional memberships:

- 2022. Sci paper : Adamov, I., Stanojević, G., Medarević, D., Ivković, B., Kočović, D., Mirković, D., & Ibrić, S. (2022). Formulation and characterisation of immediate-release oral dosage forms with zolpidem tartrate fabricated by digital light processing (DLP) 3D printing technique. International Journal of Pharmaceutics, 122046.
- 2022 - (April-ongoing) – Member of a Committee of Experts on Minimising Public Health Risks Posed by Counterfeit Medicinal Products and Similar Crimes (CD-P-PH/CMED) – EDQM (European Directorate for the Quality of Medicines and HealthCare)
- 2022 - (April-ongoing) – Chairperson of a Team for monitoring and implementation of activities in the suppression of the sale of counterfeit medicines, formed by the Ministry of Health – Podgorica, Montenegro
- 2022 - (April-ongoing) – Expert/researcher/ trainer for MEDI-THEFT project – by Italian Medicines Agency
- 2022- (March-ongoing) – Chairman for WHO's working group "Detection Technologies"
- 2020 – (October-ongoing) – National Focal Point for Member State Mechanism on Substandard and Falsified (SF) Medical Products of World Health Organization
- 2019 – 2019. (January-December) Associate in Erasmus + project ,,BUGI - Western Balkans Urban Agriculture Initiative" (development of study materials, preparation of documentation for study programme accreditation, working od tender documentation and procedures for purchase of study greenhouse)
- 2016. 3rd place award, international competition "Zero Hackathon", Romun SIOI Rome-Italy

Education:

- 2021 – (November-ongoing) – University of Montenegro, Montenegro

PhD studies in Sustainable Development

- 2022 – 2022. (March-June) –Guest scientist at German Federal Institute for Risk Assessment (Technique – LC-MS/MS qtof)
- 2019 – 2020. University of DonjaGorica, Montenegro

Master course on Faculty for Food Technology – Master of Science in Food Technology – Technology of Food of Plant Origin

- 2018 – 2019. University of DonjaGorica, Montenegro

Specialisation course on Faculty for Food Technology – Specialization in Food Technology – Technology of Food of Plant Origin

- 2015 – 2018. University of DonjaGorica, Montenegro

Faculty for Food Technology, Food Safety and Ecology

- 2011-2015. High school gymnasium “Slobodan Škerovic”, Podgorica, Montenegro

Languages:

- English: fluent (speaking and writing)
- Italian: intermediate (speaking and writing)
- Montenegrin: native language