MUNI
PHARM

DOCTORAL THESIS REVIEW

"Development of liquisolid systems for colon targeting "

Applicant:	**Mgr. Chiazor Ugo Ogadah**
Supervisors:	Assoc. Prof. PharmDr. Barbora Vraníková, Ph.D.
	Assoc. Prof. PharmDr. Zdeňka Šklubalová, Ph.D.
Doctoral degree program:	Pharmaceutical Technology
Institution:	Department of Pharmaceutical Technology
	Faculty of Pharmacy in Hradec Králové
	Charles University

Reviewer: Assoc. Prof. PharmDr. Jan Gajdziok, Ph.D.
Department of Pharmaceutical Technology, Faculty of Pharmacy, MU

Relevance of the issue addressed:

The highly actual topic of developing a delivery system capable of targeting a poorly water-soluble drug, cyclosporine A (CyA), to the colon was chosen for this doctoral thesis.

During the first phase of experiments, the preformulation study related to improving the solubility and dissolution rate of the CyA by formulating liquisolid systems (LSS) or interactive mixtures by co-milling was performed. It included selecting a suitable carrier, evaluating excipient milling properties, and selecting a non-volatile solvent for the solubilization of CyA. Neusilin US2 was evaluated as the most suitable carrier, and Transcutol HP as the solvent. LSS formulations showed better results than co-milling technology. The second part of the experiment focuses on optimizing the composition of the hydrophilic mucoadhesive matrix system for colon delivery of the drug. HPMC and GG were evaluated as the best candidates due to their suitable swelling, drug release modification, and mucoadhesive properties necessary for the matrix core with prolonged release.

The chosen topic, as well as the overall design of the thesis, undoubtedly represents one of the current trends in drug formulations with subsequent practical potential.

Characterization of the doctoral work:

The submitted dissertation is written in English. It has a common structure of this type of work, consisting of an introduction, which includes the objectives of the work, and a theoretical part based on a literature review dedicated to specific issues solved during the experiment – colon delivery and solubility increasing. *The theoretical part of the thesis is adequate in scope and provides a basic overview of the problems treated. The theoretical part is written logically, confirming the applicant's erudition in the given problem.*

The experimental part of the thesis is then divided into the usual chapters devoted to methodology and materials, as well as parts focused on the presentation and discussion of results obtained during the experimental activities of the applicant. These include areas of development of the dosage system to improve the solubility of CyA and mucoadhesive matrix core development. The author's literature outputs complement the presented data. Finally, the thesis is completed with conclusions and the obligatory chapter of used references.

The experimental chapters have the proper requisites and are well-prepared and written. The applicant has covered a range of skills in the experimental activities during the DSP. Overall, many results were obtained during the experimental activity, and the objectives of the dissertation were met.

Questions, comments, and topics for discussion:

- Translation of Abstract into Czech sounds artificially.
- Some theoretical chapters are brief and superficial. Recent studies and their conclusions should be discussed.
- Not only physiological pH ranges (chapter 6.2, p. 18) are important for oral drug delivery, but also pathologically altered, e.g., by IBD, transit times, and microbial activity. Can you please provide a summary of these parameters?
- Which approach for colon delivery referred to in theoretical chapters works best or is used most often in clinical practice? Please discuss.
- Is CyA a model drug? In my opinion, it is not. It is a real drug that has therapeutic potential in the optimized formulation.
- The volume of used dissolution media was high (900 mL) for CyA release studies. Wouldn't it be beneficial to decrease the amount of used media to physiological conditions?
- Mucoadhesivness is comparable in all three conditions (p. 94). How do you want to prevent sticking the tablet to the mucosa of other parts of GIT, where the mucus layer is more pronounced than the colon?
- Why was theophylline used? I understand it is a model well-soluble drug, but CyA should also be incorporated into the system to merge both parts of the work and complete it.

CONCLUSIONS

Mgr. Chiazor Ugo Ogadah developed a doctoral work based on a well-organized theoretical review and extensive experimental scientific work. The applicant has supported the dissertation with publications in journals with IF (2 publications listed in the WoS; 1 main author, 1 co-authors). Applicant's scientific competence is also evidenced by participation in grant projects and conference presentations. The applicant has fulfilled the thesis objectives, as evidenced by the well-described summary. I positively evaluate the number of experiments, the large volume of work, and the clarity and logical structure of the work. The thesis expands the knowledge in the research area of solubility improvement of poorly soluble drug cyclosporine A (CyA) by the preparation of a liquisolid system (LSS), specifically aimed at the colon-targeted drug delivery in combination with a swellable, mucoadhesive matrix core. *The applicant demonstrated the ability to work with scientific literature, use the information for independent scientific activity, evaluate the results, and interpret them into adequate conclusions. From the above, I believe that the candidate has sufficiently demonstrated creative and scientific research abilities, and the submitted doctoral work meets the requirements for a thesis of this type. Based on the above, I recommend that the submitted work of Mgr. Chiazor Ugo Ogadah can be accepted for defense, and that applicant can be awarded the Ph.D. degree after successful defense and fulfillment of all prescribed obligations.*

Brno, 21/3/2024 Assoc. Prof. PharmDr. Jan Gajdziok, Ph.D.