UNIVERSITY OF CHEMISTRY AND TECHNOLOGY, PRAGUE
Faculty of Chemical Technology
Department of Organic Technology

Reviewer's report for PhD thesis - Mgr. Chiazor Ugo Ogadah

The doctoral thesis **"Development of liquisolid systems for colon targeting"** submitted by Mgr. Chiazor Ugo Ogadah aims at formulating and evaluating liquisolid systems that will potentially allow for colon-specific drug delivery after oral administration and specifically a system to incorporating cyclosporine. This goal is being approached by pursuing research on choice of a suitable excipient for development of cyclosporine A dosage form with improved solubility and development of a mucoadhesive matrix core. Both particular objectives are addressed, and the thesis contribute to the technological development of intended drug delivery system. The discussion focus is product-oriented and it is made on the delivery system studied. Any generalization is provided in quite superficial comments, so that the main center point of this work remains in the model drug formulation for colon delivery, while the general methodology development is secondary.

The thesis spans over 130 pages, of which the regular text covers 106 pages with 19 pages of supplementary information, such as bibliography, research outputs, etc. The bibliography counts 137 references which are used not only for the introduction, but also throughout the discussion to support it. The bibliography is highly relevant to the topic, and it provides an evidence of the author's scientific involvement in the topic. At some places, I would recommend distributing references more specifically to individual data or claims rather than to whole paragraphs or tables.

The thesis is written as a standalone text. Some chapters are based on the published papers or conference proceedings. In such cases, the author contribution is thoroughly explained. The adoption of some results of the author's own papers does not interfere with the structure of the thesis, which is clear straightforward and follows the traditional structure of theory, methods, results and their discussion.

In my evaluation of the scientific quality of the work, I think two aspects must be considered. The thesis pursued a complex topic defined by a specific objective. In that aspect it involved two quite distinct research problems oriented on solubility improvement as well as on the formulation of a mucoadhesive matrix. The thesis addressed both objectives, used plethora of methods of experimental screening, and the results are persuasive for the system studied. Also the methods are thoroughly described and illustrated so that the readers can benefit from detailed information on non-widespread techniques. On the other hand, I find the discussion narrowly targeted, often neglecting the opportunities to make a more general discussion that would open new paradigms in LSS formulations.

The conclusions are provided separately for all sections as well as the concluding remarks are done for whole thesis. The conclusions are provided in quite elaborate manner for research sub-topics included, so that a way of summarizing is used rather than brief concluding remarks. I think this approach is appropriate for the thesis design and structure. The findings are clearly

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formulated and provide a concise overview of the results toward the research goal. From an engineer's perspective, I would welcome the if the purely phenomenological discussion of results was generalized using suitable material-independent dimensionless criteria, such as plotting the $AOS/AOS_{pure\ carrier}$ vs the pore saturation ratio, but I am aware of being rather off-topic with such desire.

The formal and language quality of the thesis is good. There are typographic errors, mainly when presenting the mathematical symbols, where the formatting does not follow standardized rules of technical literature (using italics for variables and normal text for constants in the very essence), small errors or imperfect references (e.g. 53 or 87), but they do not interfere with the clarity of delivered information. From an engineer's perspective, I would recommend taking greater care when defining the names of variables/quantities to reflect their actual dimensions (e.g. the "mucoadhesion force" is not in agreement with stated units mN/mm2 and either "mucoadhesion strength" or mN units should be used for compatibility, or cumulative frequency should be replaced by cumulative volume).

The presentation of data is of adequate quality, but in some instances, it suffers from extensive use of abbreviations, while not all of them are strictly defined, but some rely on the reader's imaginations (eg. NEU 0 – NEU 100 in Fig. 28).

Based on the evaluation above, **I can hereby recommend the thesis written by Mgr. Chiazor Ugo Ogadah for defense**. I have also several following points, where I am interested in further discussion, which may take place during the thesis defense:

1. Microcrystalline cellulose is listed on p. 25 as one of the pioneering LSS carriers. Standard MCC grades such as Avicel PH102 do not exhibit significant intraparticle porosity. Which was the liquid retention mechanism in such systems reported in the literature?

2. The thesis mentions the use of angle of slide as the preferred parameter for evaluating flow properties based on work of Spireas dating back to 1992. Can the state-of-the-art powder rheology measurements replace that method?

3. The particle porosity is mentioned as one of the key factors affecting the liquid retention. Internal/external surface ratio and the particle size will be also the relevant factors. Was the porosity of particles measured (e.g. using He pycnometry)? If no, why? If yes, is the angle of slide correlated to pore saturation ratio (How would the Fig. 6 look like if the pore saturation was used on x-axis)? Is it possible to specify general material-independent requirements on the carrier system based on the obtained results?

4. The SSA decrease after milling for NEU and also for FCC is quite counterintuitive. It may be caused by a complete destruction of porous structure and formation of agglomerates. Is it possible to provide any quantitative analysis based on the theoretical external specific surface area of the milled particles to fully understand the change?

5. The dissolution profiles of LSS presented on Fig. 17 (and others) reach “plateau” after releasing no more than 25 % of the drug. Is the whole content of the drug releasable? Was it proved by some infinity dissolution measurement?

6. Fig. 28 A shows a swelling behavior for pure Neusilin (NEU 100). Given the magnesium aluminosilicate nature of the material, any swelling is highly unlikely. Can the results be explained ?

In Prague, March 11th 2024

prof. Ing. Petr Zámostný, Ph.D.