

**Review of diploma thesis**

Student: **Jana Kubačková**

Mentor of the thesis: PharmDr. Ondřej Holas, Ph.D.,

Year of the defence:

Reviewer of the thesis: Dr. Georgios Paraskevopoulos,  
Ph.D.

2016

Title of diploma thesis:

**Polymeric stabilizers maintaining the saturation solubility of itraconazole  
nanocrystals after dissolution process**

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Formal comments: number of pages: 65, number of graphs: 0, number of figures: 16,  
number of tables: 10, number of references: 73

Type of work: Experimental

- a) Aim of the thesis is: Fulfilled
- b) Language and graphic level: Very good
- c) Processing of theory: Excellent
- d) Methods description: Very good
- e) Results description: Very good
- f) Discussion and conclusions: Very good

Reviewer comments: The aforementioned diploma thesis deals with the potential synergistic effect of different polymeric stabilizers on maintaining the supersaturated state of nanocrystalline itraconazole.

The used language is generally adequate with minor grammatical, syntactic and typing errors. Some of the tables were difficult to follow due to non-specific ordering of results. Some of the experimental procedures needed to be described in more details in order to avoid potential misunderstandings.

Overall, the conducted experimental work allows enough evidence for useful conclusions regarding the effect and use of specific polymeric stabilizers at the saturation solubility of a poorly water soluble drug and opens further potential directions.

Questions:

- 1) Page 4, lines 19-20: "As a weak base, the solubility (of itraconazole) decreases with reduced gastric acidity". Why itraconazole is considered a weak base and how the gastric environment affects its solubility?
- 2) Page 20, lines 2-3: "The aqueous solubility (of Poloxamer F127) depends on temperature, with rising temperature solubility diminishes". Why the solubility of Poloxamer F127 "diminishes" when the temperature of the aqueous solution is higher?
- 3) Paragraph 4.2.4: The experimental procedure of solubility and supersaturation testing describes measurement of itraconazole's concentration in different hydrochloric acid buffer solutions (pH=1,2) using UV spectroscopic method. On the other hand, the calibration curve

was measured using methanolic solutions of itraconazole. Why hasn't been used the same solvent in both cases?

4) Paragraph 4.2.4: The experimental procedure of solubility and supersaturation testing describes addition of hydrochloric acid buffer (3mL) to dissolution flask after sampling in order to maintain the volume of the medium. Doesn't this affect the next measured concentration?

**Evaluation of diploma thesis: Very good, to defense: Recommended**

In Hradec Kralove 24.05.2016

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