



FACULTY OF PHARMACY

UNIVERSITY OF VETERINARY AND PHARMACEUTICAL
SCIENCES BRNO

Faculty of Pharmacy, Department of Natural Drugs

Palackého třída 1946/1, 612 42 Brno, Česká republika

In Brno

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Habilitation thesis review

Pavel Babica

**GAP JUNCTIONAL INTERCELLULAR COMMUNICATIONS: *In vitro* assessment of
hazardous and beneficial effects of chemicals**

The evaluated habilitation thesis written by Dr. Pavel Babica comprises a comprehensive review of the very current topic of gap junctional intercellular communications and possibilities of their general studies, an interaction of different chemicals with gap junctions and also the possible importance of an affecting of intercellular communication in development of certain diseases or toxicity. It summarizes the overall knowledge of author on the topic of GJIC and includes his own experimental works on this topic.

Different *in vitro* models became very integral part of toxicological and pharmacological evaluation of various chemical substances due to some practical, economical and also ethical reasons. *In vitro* models are relatively rapid, sensitive, effective and cheap alternative to *in vivo* studies, and can be used not only to simply evaluate the endpoint effect of a single chemical, but to study in the detail kinetics of different procedures and mechanisms of action. With the gaining of knowledge of GJIC importance for both the physiological and pathophysiologic processes in cells and further continuous improvement of methodology useful for intercellular communication evaluation, the testing of effects of various chemicals on GJIC is shown to be important for the understanding and prediction of effects on human health and also effect on surrounding environment.

The work is classically composed of the theoretical introduction summarizing and giving the overall information about gap junctions, connexins, about their composition, formation and regulation of expression, and explains the importance of cellular communication for the maintenance of homeostasis. A chapter is focused on connection of connexins and GJIC with



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development of human diseases, including various inflammations, problems with the immune system and also the cancer. The comprehensive chapter is dedicated to *in vitro* assessment of GJIC in toxicology and pharmacology, showing methods for electrophysiological measurements, endogenous metabolite transfer and various dye transfer assays. These introductory chapters are very well illustrated by well-arranged schemes and pictures and give a perfect insight into problem, especially for person who is not fully oriented in gap junction topic. I appreciate the scope of recent literature used for construction of introduction.

Next, results of 15 experimental papers generally on GJIC are summarized and commented in light of recent knowledge. These papers were published in reputable peer-reviewed journals and there is no doubt about their quality. They show the use of GJIC assays for identification and characterisation of new chemical hazards, confirm the variability of the effect of different compounds in connection with structural variance, cell type and mechanism of effect. Some results show and the author later discusses the relevance of GJIC *in vitro* assays to *in vivo*. Several sub-chapters are dedicated to usage of GJIC to analyse effect of complex mixtures, with possibility to identify new effect-responsible substances, and also the application of these methods in the evaluation of water treatment procedures. Last, but not the least is mentioned the possibility of different chemicals (including drugs and phytochemicals), therapeutical methods or products of the nanotechnology for drug delivery to affect GJIC, with possibility of restoration of their function, and so-called chemo-protection activity.

The body of habilitation thesis incorporates the full-texts of commented papers, list of more than 270 used literature sources, and *curriculum vitae* of author, research experience, ability to supervise students of both undergraduate and postgraduate programs, the ability of the author to prepare a research project and to be successful principal investigator and co-investigator, and also the work is showing also an outstanding record of further publications (majority in category Q1 and Q2 journals).

My overall impression from the habilitation is very good, as I did not find almost no un-logic statements and mistakes. The general performance of thesis is on the very high level. Rising from my personal interests and expertise, I have only general questions on the author:



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- 1) Besides the mentioned phytochemicals, are there other signs or supports of the effect of natural compounds on GJIC?
- 2) What do you think about the so-called “chemo-protectives or chemo-preventives” and GJIC, are there any clinical support of their effectiveness?

According to my expertise and my opinion, this habilitation thesis fulfil the requirements for the habilitation at habilitation field Ecotoxicology at Faculty of Science, Masaryk University. It brings an overview of original results from the area of interaction of chemicals with environment and resulting possible effect on human health.

Based on this evaluated thesis, I fully recommend to award Dr. Pavel Babica the title *Associated professor in Ecotoxicology*.


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