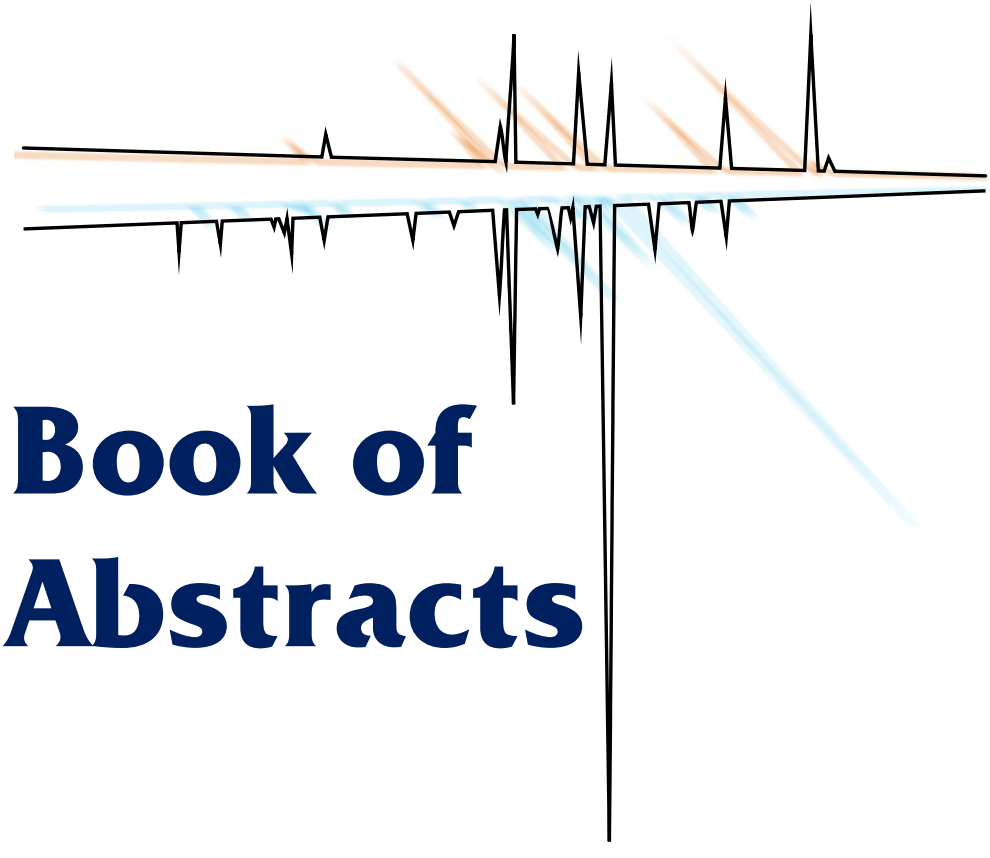
6th IAPC Meeting

Sixth World Conference on Physico-Chemical Methods in Drug Discovery

&

Third World Conference on ADMET and DMPK



Book of Abstracts

Zagreb, Croatia, September 4-7, 2017

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O 27

Measurements of plasma protein binding – variety of experimental techniques

Olivera S. Marković, Jelena M. Konstantinović*, Ilija N. Cvijetić**, Susana Amézqueta***, Klara Valko****, Clara Ràfols***, Natalija Đ. Polović*, Bogdan A. Šolaja*,*****, Tatjana Ž. Verbić*✉

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Drug molecules *in vivo* may be bound to proteins and lipids in plasma and/or in tissues, or free (unbound) in diffusion among the aqueous environment of the blood and tissues. Data from *in vitro* plasma protein binding experiments that determine the fraction of protein-bound drug are frequently used in drug discovery [1].

Human plasma proteins contain around 40 % albumin (HSA), α_1-acid glycoprotein (AGP) in much lower concentration (1-3 %) and immunoglobulins [2]. Methods used for drug – plasma protein binding (PPB) studies are numerous and can be divided into two main groups: separation methods (enabling the calculation of binding parameters, *i.e.* the number of binding sites and their respective affinity constants) and non-separation methods (describing predominantly qualitative parameters of the ligand-protein complex) [3]. Sometimes, results of PPB measurements obtained by different techniques are not consistent. High binding affinity to plasma proteins is not necessarily a crucial limiting factor for further delivery of compound to the target organ [1]. As an example, we show the study of the interactions between HSA/AGP and an "in-house" synthesized steroidal derivative that showed remarkable inhibitory potency against BoNT/A holotoxin in mouse embryonic stem cell derived motor neurons [4]. A variety of experimental techniques (ITC, HPLC, spectrofluorimetry, FTIR, and equilibrium dialysis) were used and the results were compared highlighting the advantages and disadvatages of various techniques.

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References:

[1] D.A. Smith, L. Di, E.H. Kerns, Nat. Rev. Drug Discov. 9 (2010) 929-939.
[2] K. Valko, Application of HPLC for the measurements of lipophilicity and bio-mimetic binding properties in drug discovery, in: Z. Mandić (Ed.), Physico-Chemical Methods in Drug Discovery and Development, IAPC Publishing, Zagreb, Croatia, 2012, pp. 61-119.
[3] J. Oravcova, B. Bohs, W. Lindner, J. Chromatogr. B 677 (1996) 1-28.
[4] J. Konstantinović, E. Kiris, J. Kugelman-Tonos, M. Videnović, L. Cazares, N. Terzić, T.Ž. Verbić, M. Zlatović, B. Andjelković, J. Srbljanović, A.J. Duplantier, S. Bavari, B.A. Šolaja, New Steroidal 4-Aminoquinolines Antagonize BoNT/A in Mouse Embryonic Stem Cell Derived Motor Neurons in Post-intoxication Model, manuscript in preparation as part of projected PhD thesis of J. Konstantinović.