

21<sup>st</sup> Scientific Symposium of the Austrian Pharmacological Society:  
Joint Meeting with the British Pharmacological Society and the  
Pharmacological Societies of Croatia, Serbia and Slovenia  
Graz, 16–18 September 2015

MEETING ABSTRACT

A4.3

**The relaxation of myometrium by the natural polyphenols  
resveratrol and naringenin**

Radmila B. NOVAKOVIĆ<sup>1,\*</sup>, Jovana RAJKOVIĆ<sup>1</sup>, Sanja ČIROVIĆ<sup>2</sup>,  
Jasmina MARKOVIĆ-LIPKOVSKI<sup>2</sup>, Nebojša V. RADUNOVIĆ<sup>3</sup>,  
Vladimir ĐOKIĆ<sup>1</sup>, Helmut HEINLE<sup>4</sup>, Vladimir ŽIVANOVIĆ<sup>5</sup> and  
Ljiljana C. GOJKOVIĆ-BUKARICA<sup>1</sup>

<sup>1</sup>*Institute of Clinical Pharmacology, Pharmacology and Toxicology,  
Faculty of Medicine, University of Belgrade, Serbia;* <sup>2</sup>*Institute of  
Pathology, Faculty of Medicine, University of Belgrade, Serbia;*  
<sup>3</sup>*Institute of Gynecology and Obstetrics, Clinical Center of Serbia,  
Belgrade, Serbia;* <sup>4</sup>*Institute of Physiology, University of Tübingen,  
Germany;* <sup>5</sup>*University Clinical Hospital Center "Dr Dragiša Mišović  
– Dedinje", University of Belgrade, Serbia*

**Background:** Natural polyphenols are present in a large number of plant species. Special sources of resveratrol are grapes and wine, as well as its products, but also for naringenin grapefruits, its juice, hop and beer. During the last decade, resveratrol was in the focus of the scientific and wider public as a substance that slows aging or has anti-cancer, anti-inflammatory and cardioprotective properties. A large number of cellular structures have been shown as possible sites of action, thus resveratrol is labeled as "one molecule – many targets". Unlike resveratrol, naringenin belongs to a group being studied less, flavonoids. Its mechanism of inhibition of the contraction of uterine smooth muscle has not been studied. The aims of this study were to investigate the possible inhibitory effect of polyphenols in several experimental models of pregnant and non-pregnant uterus.

**Methods:** The animals used in the experiments were virgin female Wistar rats. Myometrial samples were obtained from non-laboring women (37–39 weeks of gestation) undergoing elective cesarean sections. Samples were mounted into organ baths for recording isometric tension. Resveratrol (1  $\mu$ M – 100  $\mu$ M) and naringenin (1  $\mu$ M – 1 mM) were added cumulatively to the bath for isolated organs. The effects of polyphenols were investigated on the spontaneous rhythmic contractions, oxytocin-induced phasic (0.2 nM) and tonic (20 nM) contractions of rat uterus and oxytocin-induced (2 nM) contractions of human uterus. The effects of synthetic openers of K<sup>+</sup> channels, pinacidil and NS1619, were tested and compared to the effects of polyphenols.

**Results:** The results show that resveratrol exerts potent inhibitory effect on spontaneous and induced contractions of non-pregnant rat uterus and human pregnant myometrium. Naringenin inhibited contractions of animal and human myometrium in a concentration-dependent manner. Resveratrol showed a statistically significantly higher potency than naringenin in all contraction models. Mean effective concentrations of naringenin were similar for all models, which was not the case for resveratrol.

**Discussion:** Based on the results presented in this work, it is acceptable to conclude that resveratrol and naringenin have great potential to be used in the prevention and treatment of abnormal and undesirable uterine contractility, as in the case of dysmenorrhea and premature births.

**Acknowledgements:** Our work has been supported by scientific research grant no. 31020 from the Ministry of Education, Science and Technological Development of the Republic of Serbia.

\*Corresponding author e-mail: [novakovicr@yahoo.com](mailto:novakovicr@yahoo.com)