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Steroidal compounds of vegetable origin in treatment of circulatory disorders

Modern pharmacy pays a special attention to the development of vasoactive anti-inflammatory drugs free of unwanted side effects that characterize the majority of currently available corticosteroids and NSAIDs.

The presented study aimed to determine specific pharmacologic properties of spiro- and furostanol type steroidal glycosides obtained from the Butcher's broom (*Ruscus ponticus L.*) and estimate their possible mechanism of action.

Assessment of the specific anti-inflammatory activity of RE on "granuloma pouch" model revealed that it caused statistically significant ($p < 0.001$) difference both in exudate volume and mass of dried granuloma. Further investigation on the formalin-induced rat paw edema confirmed the anti-exudative activity of RE. As the observed effect can be conditioned by several reasons including the change in the diameter of blood vessels, stimulation of α-adrenoreceptors or blocking the release of histamine and bradykinin, more detailed study of the mechanism of action of RE, a series of experiments were conducted, using vital dyes Evans blue (EB) and sodium fluorescein (SF). In intact animals SF after intravenous administration rapidly permeates into all organ tissues in contrast with EB, which does not leave the blood vessels.

Subcutaneous administration of SF and EB on the background of adrenalin or histamine altered the shape of SF pharmacokinetic curve reflecting the vasotropic effects of the agents, whereas for EB it remains unchanged. RE does not change the Tmax of SF, but the concentration of the dye increases. No alterations are observed for EB.

In *in situ* experiments it was found RE causes the constriction of the mice mesenteric vessels along with increased blood flow. Moreover, RE neutralizes effects of histamine, probably due to stimulation of α1-adrenoceptors.

Finally, it was found, that both prazosin (α1-blocker) and diltiazem (Ca^{2+} channel blocker) decrease the contractility of isolated femoral vein rings caused by RE, suggesting that observed vasotropic effects of RE are mediated by stimulation of vascular adrenoreceptors along with the simultaneous increase of Ca^{2+} in vascular endothelium.

Assessment of safety of RE in chronic 90-day experiment revealed the absence of any toxic effects on major systems.

Summarizing the obtained data, it may be concluded that the studied RE can be considered as prospective candidate for the development of anti-inflammatory vasoactive remedy free of toxic/side effects.

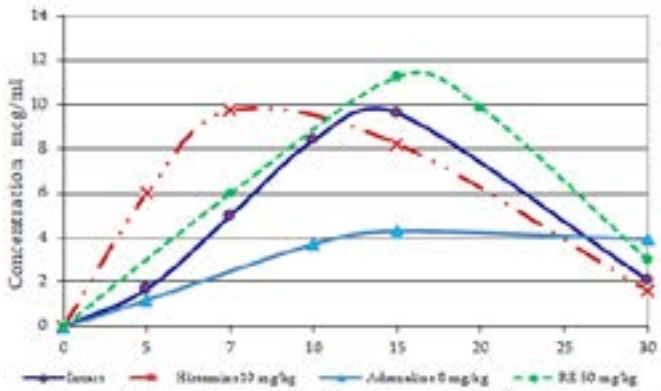

Figure: Pharmacokinetics of SF on the background of different vasotropic agents: x-axis - time (min)

Recent Publications

1. Khubulava S, Chichiveishvili N, Mulkijanyan K et al. (2019) Effect of high dose of selenium nanoparticles on alimentary tract in rodents. J Nanomed Nanotechnol, 10(2):531-537.
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3. Gokadze S, Mulkijanyan K et al (2017) Formulation and technology development of herbal phenolic biopolymer-containing films for burn treatment. Georgian Medical News, 6(267):119-124.
4. Taylor BJ, Mulkijanyan KG (2016) An overview of laboratory animal science in the nation of Georgia. Lab Animal 45(11):415-417.
5. Mulkijanyan K et al. (2015) Plant biopolymers from Boraginaceae family species and their synthetic derivatives: prospective pharmacological agents. Clinical & Experimental Pharmacology, 5(4):46.

Biography

Karen Mulkijanyan heads the Department of Preclinical Pharmacological Research at Tbilisi State Medical University Institute of Pharmacochemistry and is full Professor at Caucasus International University Faculty of Medicine. He holds MS in Biochemistry and PhD in Pharmacy. His research interests cover the experimental pharmacology; toxicology of natural products; analysis of structure-activity relationship (SAR) and prediction of bioactivity of natural, modified and synthesized compounds; IP protection; technology transfer and commercialization; use and care of laboratory animals. K. Mulkijanyan was a manager/key investigator of fundamental and applied research projects funded by CRDF Global/GRDF (2007-2014), STCU (2011), GNSF/SRSNF (2009-2018) and co-authored 120+ publications in peer-reviewed journals, 40+ presentations and 2 patents in pharmacology. As Organizing Committee Member, he arranged over 15 international events on pharmacology/toxicology. He is on the editorial boards of several journals in pharmacology/toxicology. In 2015 K. Mulkijanyan founded and is a President of the Georgian Association for Laboratory Animal Science.