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Comfrey based remedies: Past, present and future

History of Comfrey (*Symphytum L.*) remedies clearly illustrates that despite plant extracts are still among most attractive sources for drug development as they are considered relatively safe for use in humans, many of their chemical constituents represent serious risks to the human health and it is important to justify biological effects that the vegetal products obtained from medicinal plants can present. For ages, folk remedies on the basis of extracts of various comfrey species were used both internally and externally to treat different disorders, but nowadays internal usage is banned due to the presence of hepatotoxic and carcinogenic pyrrolizidine alkaloids (PAs) - symphytine, echimidine and lasiocarpine. When determining principal constituents responsible for diverse curative properties of comfrey, a novel biopolymer poly[3-(3,4-dihydroxyphenyl) glyceric acid] (PDGA) was isolated from PAs- and allantoin-free high molecular fractions from *S. asperum*, *S. caucasicum* and its monomer 3-(3,4-dihydroxyphenyl) glyceric acid (MDGA) was synthesized at I. Kutateladze Institute of Pharmacochemistry. Pharmacological properties of PDGA and MDGA were studied both *in vitro* and *in vivo* experiments. The obtained results revealed: *in vitro* i) abrogation of melanoma cells adhesion to tumor-conditioned medium- and VEGF-activated endothelial cells as well as ii) strong inhibition of human prostate cancer (PCA) cells growth. Consistent with *in vitro* results, *in vivo*

study showed iii) efficacy against PCA 22Rv1 tumors; iv) anti-inflammatory activity in formalin- and carrageenan induced edemas; v) rapid burn and wound healing (fourfold superior to that of allantoin – substance claimed to be comfrey's most active ingredient) due to the shortening of the second phase of wound healing - the inflammatory response; vi) significant stimulation of leucopoiesis in mice drug-induced leukopenia; vii) promising results in prevention of ethanol- and NSAID-induced gastric ulcers. Importantly, all observed effects were accompanied with no or minor side effects, suggesting high therapeutic potential of novel API from comfrey.

Speaker Biography

Karen Mulkijanyan is the Head of the Department of Preclinical Pharmacological Research at Tbilisi State Medical University Institute of Pharmacochemistry. He has obtained his MS in Biochemistry in 1981 and PhD in Pharmacy in 2005. His research areas include pharmacology of anti-inflammatory, ulcer preventing, wound healing and vasoactive drugs; analysis of SAR and prediction of bioactivity of natural, modified and synthesized compounds. He is also an expert in IP protection and technology commercialization. He was the Manager/Key Investigator of fundamental and applied research projects funded by CRDF Global/GRDF (2007-2014), STCU (2011), GNSF/SRSNF (2009-2016). As Organizing Committee Member, he arranged about 10 international congresses and conferences on Pharmacology and Pharmacy. He is the author and co-author of more than 100 papers in peer-reviewed journals, about 40 presentations at national and international scientific meetings

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