

Accepted Abstracts



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Functional proteomics ties calreticulin with the Anti-Angiogenic Properties of the Pyrazolyl-Urea GeGe-3

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In the last twenty years, 5-pyrazolyl-ureas have been largely investigated for their poly-pharmacological outline. In this scenario, ethyl 1-(2-hydroxypentyl)-5-(3-(3-(trifluoromethyl)-phenyl)-ureido)-1H-pyrazole-4-carboxylate (i.e., GeGe-3) emerged as a promising anti-angiogenic compound, inhibiting Human Umbilical Vein Endothelial cells (HUVECs) proliferation and endothelial tube formation, and blocking angiogenesis in mice and tumor growth in transplanted subcutaneous Lewis Lung Carcinomas¹. Regrettably, although different primary targets implicated in cell division and/or calcium homeostasis have been hypothesized for this compound, all the performed tests gave negative results. Thus, to link GeGe-3 anti-angiogenic potential to a suitable protein partner, the molecule interactome has been inspected in HUVECs, through a label-free functional proteomics platform^{2,3} comprising Drug Affinity Responsive Target Stability (DARTS)⁴ and targeted Limited Proteolysis-Multiple Reaction Monitoring mass spectrometry (t-LiP-MRM)⁵. These techniques share the principle that, interacting with a molecule, a protein undergoes conformational changes that result in its altered sensitivity to limited proteolysis, when performed in native conditions. Thus, in a first step, pairing DARTS with high-resolution mass spectrometry allowed the identification of GeGe-3 most reliable interacting protein, calreticulin, as later on validated by Western Blotting. Subsequently t-LiP-MRM served the purpose of pinpointing calreticulin regions directly or distally involved in the interaction with the compound. Calreticulin is a major Ca²⁺ binding protein involved in intracellular Ca²⁺ homeostasis and uptake/release within the endoplasmic reticulum and mitochondria, cells adhesion, migration, proliferation, differentiation, and apoptosis, as well as in cell-cell interactions. Thus, to shed light on the biological consequences of GeGe-3 interaction with calreticulin, in cell assays have been performed. The obtained results disclosed GeGe-3 potential anti-angiogenic mechanism: as demonstrated by cytofluorimetry, the molecule alters Ca²⁺ intracellular shift in HUVECs and, as highlighted through confocal microscopy, induces F-actin to acquire a cortical localization, totally in line with cells showing a less motile phenotype.

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Herbal Medicines - The Evidence Base

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The use of herbal medicines expanded globally during the last decade in national health care systems in developing and developed countries. A survey conducted by Eisenberg et al, in 1998 involving 1,539 adults showed that 34% used at least one unconventional therapy in the past year and a third of these saw providers for unconventional therapy. Greatest use was among patients 25-49 year olds, with higher education and higher income. Patients used herbs for chronic and life threatening problems. Of those who used unconventional care for life threatening conditions, 83% also consulted a medical doctor. 72% of the unconventional medicine users did not advise their medical doctor. One third of them had adverse effects ranged from mild to severe. Studies indicated that the majority of herbal medicines are subjected to limited efficacy and safety testing. The quality of these products is also of a concern. A study published in JAMA (2004) showed that 20% of the herbal medicine products from south Asia contained potentially harmful levels of lead, mercury and/or arsenic as measured by X-ray fluorescence spectroscopy. Most physicians do not receive formal education on herbal medicine therapies, which necessitates the developing of appropriate training programs. This presentation summarizes an evidence-based approach to understand the safety, efficacy and quality of herbal medicines in clinical practice.

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Post COVID-19 rehabilitation and immunity through yoga and ayurveda

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The COVID-19 pandemic has created a worldwide health crisis. Many People who have survived this disease suffer their physical and mental health. Rehabilitation of these Patients is an immense need. A holistic and multi-disciplinary rehabilitation is needed to boost the immunity and to restore the health status of these patients. The governments of India, China and many other countries are actively promoting traditional treatments for post Covid-19 rehabilitation. WHO also supports for Rehabilitation Self-Management after COVID-19- Related Illness.

Ayurveda and Yoga can certainly play a pivotal role in the rehabilitation to boost the immunity. Regular Yoga practice revives the exhausted body, soothes the troubled mind, and brings back confidence and positivity in life. It is well accepted that COVID rehabilitation must focus on breathing exercises. Yogic techniques such as the Asanas (body positions) and Pranayama (controlled breathing) facilitate body stretching and help to boost the immunity and strengthen the lungs. Regular meditation relaxes the troubled mind in a highly effective manner, by bringing back confidence and positivity.

According to Ayurveda concepts, there will be Agnimandya (improper digestion) and DhatuKshaya (depletion of body tissues) in post COVID 19 infection. Diet has a very important role in the management of Post COVID-19 and it should be for all six tastes and may include ginger, turmeric, pepper, cinnamon and mint in their diet, to boost the digestion. Various herbs and herbo mineral drugs, including Rasayana drugs play a vital role to improve the body tissues and boost the immunity in post COVID-19.

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