TARGETING MULTIFACTORIAL DISEASES WITH PLEIOTROPIC ACTING MOLECULES

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Many diseases called "multifactorial" or "complex" are highly heterogeneous in nature presenting an extremely complex etiopathology concerning two or more pathophysiological indications, involving multiple organ systems, tissues and potential targets. These include Alzheimer's diseases (AD), asthma, atherosclerosis, metabolic syndrome, rheumatoid arthritis, osteoarthritis, diabetic complications, malaria, tuberculosis, cancer, CNS disorders and multiple sclerosis etc.
Based on the above it is clear that a multidisciplinary approach will be useful for the treatment of multifactorial diseases. The traditional therapeutic approach, "single drug against one target", has proved to be insufficient. Different strategies have evolved for efficient and safe treatment of such diseases including complex drug therapy or drug cocktails (independent dosage of the drugs) and combined drugs (fixed combinations of two or more drugs in one dosage form) bearing major drawbacks and including poor patient compliance and possible severe side effects.
Over the last decades, the treatment of multi-factorial diseases was based on multi-target-directed-ligand practices. The multifunctional compounds (MFCs) are broadly classified as hybrid drugs and chimeric drugs. The combination of two or more pharmacophore groups on the same scaffold leads to the rational design of new "smart" molecules maintaining pre-selected characteristics of the original templates, illustrating some benefits as well, e.g., reduced risk of toxicity and adverse reactions, additive effects, reduced financial burden, improved quality of life for patient and carers.
Most of the above-mentioned diseases are associated with the inflammatory processes and oxidative stress. Recent findings suggest the important role of inadequate or chronic inflammation in the progression of multifactorial chronic diseases and pathological conditions. Additionally, inflammatory process induces oxidative stress and reduces cellular antioxidant capacity.
In recent years, there has been ongoing research into the discovery of novel potential anti-inflammatory and antioxidant "smart" molecules. Based on previous findings of our laboratory novel series of chimeric and hybrid molecules derived from the appropriate substituted chalcones, dibenzacetones and cinnamic acids with different pharmacophores have been designed, synthesized, and evaluated for their antioxidant activity and lipoxygenase inhibition. Their interactions with the enzyme have been studied using molecular docking.