Recent Medicinal Chemistry Studies for Multitarget Agents-Part I

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The basic principle of action of a drug is based on model lock and key, where is desirable the highest possible affinity for a target avoiding no side effects. For many years it was desirable ‘one drug for one target for one disease’, however the researchers observed that complex diseases are best addressed when treated with drugs multi-targets. However, in the recent years the researches try find polypharmacology- drugs that act on multiple rather than single targets against complex diseases, such as oncology, psychiatry and anti-infectives. Examples are: the fluoroquinone that inhibits two of the multiple penicillin-binding proteins to induce cell death; anti-psychotic drugs exhibit activities in serotonin and dopamine receptors; the protein kinase inhibitors, including sunitin (Sutent) and imatin (Gleevec) against cancer. In the searches, new drugs against a specific target of one disease have been found to be active against another target of a different disease and/or reduce the resistance. All additional activities of these drugs should be explored in repositioning them for new therapeutic applications. This special issue was dedicated to multi-target chemicals (drugs, organic compounds, nanoparticles), including (but limited to) those with dual (or multiple) mechanisms of action [1-10].

Our manuscript entitled In silico study examining new phenylpropanoids targets with antidepressant activity, conducted a brief review of new important targets for antidepressant activity, to select potentially active phenylpropanoids, using Molegro Virtual Docker and Ossis Data Warris, and thus, to verify which substance is more promising for antidepressant activity.

Curcumin, a major active principle of Curcuma longa. There are more than 1700 citations in the Medline reflecting various biological effects of curcumin. Most of these biological activities are associated to the antioxidant, anti-inflammatory and anti-tumor activity of the molecule. Several reports suggest various targets of natural curcumin that includes growth factors, growth factor receptor, cytokines, enzymes and gene regulators of apoptosis. This review focuses on the improved curcumin derivatives that targets the cancer and inflammation. The detailed analysis of structure activity relationship (SAR) and common synthesis of curcumin-based derivatives are discussed in review of Dr Veena et al, Design of New Improved Curcumin Derivatives to Multi-targets of Cancer and Inflammation. Utilising the predictions of in silico coupled with validation reports of in vitro and in vivo studies have concluded many targets for curcumin. Among them, cancer related inflammation genes regulating curcumin-based molecules are very promising target to overcome hurdle in the multimodality therapy of cancer. Physcion and physcion 8-O-β-D-glucopyranoside (PG) are bioactive natural anthraquinones which exert anti-inflammatory and anti-cancer properties with minimum or no adverse effects, this is the study of Dr Shah et al, entitled Physcion and Physcion 8-O-β-D-glucopyranoside: Natural Anthraquinones with Potential Anti-cancer Activities.

Plant-derived compounds such as gallic acid and tannic acid are effective potentiators of various antibiotics including novobiocin, chlorobiocin, coumermycin, fusidic acid, and rifampicin, resulting in a 4-fold increase in the potencies of these antibiotics. Several lines of research, as discussed in the review Antibiotic potentiating of natural products: A promising target to be an ongoing fight pathogenic bacteria, of Drs Mahomoodally & Sadeer. For this reason, the search for more efficient combinations should be an ongoing process with the aim to extend the life of the ones that we have and maybe preserve the life for the ones that is yet to come.

The study of Dr Tarannum et al entitled To Explore the Potential Targets and Current Structure-based Design Strategies Utilizing co-crystallized Ligand to Combat HCV explored the various targets of HCV involved in the mechanism(s) of the disease initiation and progression and to focus on the mode of binding of ligands, which are co-crystallized at the active cavity of different HCV targets.

Dr Piolla and co-workers discussed therapeutic targets involved in Alzheimer’s disease (AD) as well as the available drugs and their synthetic routes. Bioactive com-pounds under development are also exploited to illustrate some recent research advances on the medicinal chemistry of AD, including structure-activity relationships for some targets. The importance of multi-target approaches, including some examples from our research projects, guides new perspectives in the search of more effective drug candidates. Their review, Alzheimer’s Disease: Related Targets, Synthesis of Available Drugs, Bioactive Compounds Under Development, and Promising Results Obtained from Multi-target Approaches, comprises the period between 2001 and
early 2020. The neuroprotective effects exhibited by natural products are mainly due to their ability to increase dopamine levels in the striatum, manage oxidative stress, mitochondrial dysfunction, glutathione levels, clear the aggregation of α-synuclein, induce the autophagy and decrease the pro-inflammatory cytokines and lipid peroxidation.

We, the Guest-Editors, would like to express our gratitude to the many authors who contributed to this special issue, reporting investigations in various aspects of Recent Medicinal Chemistry Studies for Multitarget Agents-Part I.

REFERENCES


