Natural Multi-targets: Advances and Applications

The basic principle of action of a drug is based on the model of lock and key, where the drug is considered desirable if it has the highest possible affinity for a target and it causes little to no side effects. For many years, ‘one drug for one target and for one disease’ has been valued; however, the researchers have observed that complex diseases are best addressed when treated with multi-target drugs. In recent years, the researchers have been trying to find polypharmacology drugs that act on multiple rather than single targets against several diseases [1-11].

Natural products often result from an optimized evolutionary process in which chemicals have been under the selective forces of coevolution, i.e., organisms producing substances in the presence of their predators. These natural compounds have been utilized by humans since ancient times to treat and cure different diseases. Of the existing plants in the world, most of which are unknown from a scientific point of view, only about 5% of the approximately 250-500 thousand species have been biologically studied and evaluated. Natural products include phenolic compounds, flavonoids, alkaloids, or terpenes, as well as secondary plant metabolites that may provide several benefits for our health [9-11].

This issue reports researches focused on new natural multi-target compounds.

The drugs currently available for the treatment of anxiety and depression act through modulation of the neurotransmission systems involved in the neurobiology of the disorder, yet they often present side effects, which can impair patient adherence to treatment. This has driven the search for new molecules with anxiolytic and antidepressant potential. Aromatic plants are rich in essential oils, and their chemical constituents, such as monoterpenes, are being studied for these disorders. Our work, a review with unpublished results entitled Anxiolytic and Antidepressant-like Effects of Monoterpane Tetrahydrolinalool and In silico Approach of New Potential Targets aims to evaluate the anxiolytic and antidepressant-like potential of the monoterpene tetrahydrolinalool in vitro animal models, and review pharmacological targets with validation through molecular docking. Male Swiss mice (Mus musculus) were treated with THL (37.5-600 mg kg-1 p.o.) and subjected to the elevated plus-maze, open-field, rotarod, and forced swim tests. In the elevated plus-maze, THL at doses of 37.5 and 75 mg kg-1 induced a significant increase in the percentage of entries (72.7 and 64.3%, respectively) and lengths of stay (80.3 and 76.8%, respectively) in the open arm test. These doses did not compromise locomotor activity or motor coordination in the animals. In the open field, rotarod tests, and the forced swimming model, treatment with THL significantly reduced immobility times at doses of 150, 300, and 600 mg kg-1, and by respective percentages of 69.3, 60.9 and 68.7%. In the molecular docking assay, which investigated potential targets, THL presented satisfactory energy values for nNOS, SGC, IL-6, 5-HT1A, NMDAr, and D1. These demonstrate the potential of THL (a derivative of natural origin) in vitro and in silico models, making it a drug candidate.

Phenolic acids being moietyes or leads are much versatile in nature as they possess a wide range of biological activities, like antimicrobial, antioxidant, antiviral, antilucre, anti-inflammatory, antidiabetic, anticancer, and many more, enabling researchers to explore more about these or many untapped benefits in the medicinal field. Medicinal uses of natural phenolic acids and their synthetic derivatives have been extensively explored in recent years. Phenolic acids are chemically defined secondary plant metabolites; which serve as moietyes or leads for drugs; they are much versatile in nature and possess a wide scope of biological activities, which have attracted the attention of researchers across the world to synthesize different derivatives of phenolic acids and screen them for their various biological properties. These compounds are of meticulous interest due to the properties they possess and their occurrence. Based on the convincing evidence reported in the literature, it is suggested that phenolic acids and their derivatives are promising molecules and can be lead drug candidates. The review article by Dr. Sehrawat and co-workers, Phenolic Acids - Versatile Natural Moiety with Numerous Biological Applications, aims to bring together the information on the biosynthesis, metabolism, and sources of phenolic acids and emphasizes the therapeutic potential of phenolic acid and its synthetic derivatives to comprehensively portray the current scenario for researchers interested in designing the drugs for different diseases.

P-coumaric acid is present in common dietary polyphenols distributed in fruits, vegetables and cereals in associated or free form. It has less toxicity and exhibits many pharmacological actions (antihypertensive, anti-inflammatory, anticancer, antimicrobial activity, antidiabetic, anticancer, and antioxidant effect). P-coumaric acid also acts as a scavenger of free radicals and inhibits enzymes that generate free radicals. It is also used as the raw material for the preparation of preservatives and vanillin, as an ingredient in sports foods and skin defense agents, and as a cross-linker for the formation of edible films and food gels. The work by Drs. Malik and Dhiman, New Approaches and Advancement in Drug Development from Phenolic p-coumaric Acid, is based on biological effectiveness, molecular docking, SAR, and sources of p-coumaric acid and related derivatives.

Influenza viruses (INFV), the Orthomyxoviridae family, are mainly transmitted among humans via aerosols or droplets from respiratory secretions. However, fomites could be a potential transmission pathway. Annually, seasonal INFV infections
account for 290-650 thousand deaths worldwide. Currently, there are two classes of approved drugs to treat INFV infections, neuraminidase (NA) inhibitors and blockers of matrix-2 (M2) ion channel. However, cases of resistance have been observed for both chemical classes, reducing the efficacy of treatment. The emergence of influenza outbreaks and pandemics calls for new antiviral molecules that are more effective and that could overcome the current resistance to anti-influenza drugs. In this context, polyphenolic compounds are found in various plants, and these have displayed different multi-target approaches against diverse pathogens. Among these, green tea (Camellia sinensis) catechins, specifically epigallocatechin-3-O-gallate (EGCG), have demonstrated significant activities against the two most relevant human INFV, subtypes A and lineages B. In this sense, EGCG has been found to be a promising multi-target agent against INFV since it can act by inhibiting NA, hemagglutination (HA), RNA-dependent RNA polymerase (RdRp), and viral entry/adsorption. In general, the lack of knowledge regarding potential multi-target natural products prevents an adequate exploration of them, increasing the time for developing multi-target drugs. The review by Drs. Silva & Silva-Júnior entitled Multi-Target Approaches of Epigallocatechin-3-O-gallate (EGCG) and its Derivatives against Influenza Viruses aimed to compile the most relevant studies showing the anti-INFV effects of EGCG and its derivatives, which could become antiviral drug prototypes in the future.

Caralluma edulis is a well-known species of the genus Caralluma from Apocynaceae, commonly known as chunga. Caralluma species are mostly succulent perennial herbs, several of which are edible species. The plant has an outstanding therapeutic background in the traditional system of treatment. It has been recommended for the treatment of a number of medical disorders, such as hypertension, Alzheimer’s disease, rheumatism, gastric problems and leprosy. Traditionally, the stem was boiled in water, and this extract was then used to cure diabetes. The pharmacological effects of C. edulis have also been explored in various in vitro and in vivo experiments. In this regard, the extract of the plant exhibited strong antioxidant and analgesic activity against inflammation as well as xylene-mediated ear edema. The significant anti-hyperlipidemic effect of the plant extract is also reported. However, the extract was found insignificant for the reversal of alloxan-induced diabetes in the rabbit model at test doses. These pharmacological effects are strongly supported by the presence of different bioactive phytochemicals in the plant. These groups of compounds include sterols, terpenoids, flavonoids, and pregnane glycosides. C. edulis is a very potential member of the genus Caralluma with strong traditional history, phytochemistry and phytopharmacology, needing further exploration for clinically used lead compounds. In the review written by Dr. Ansari et al. entitled Caralluma edulis (Apocynaceae): A Comprehensive Review on its Traditional Uses, Phytochemical Profile and Pharmacological Effects combined different reported data on the traditional uses of the plant, phytochemical profile and pharmacological effects in different experimental assays and subsequent future prospects.

Cancer is a fatal disease with a collection of related diseases in various body parts. The conventional therapies cannot show the desired treatment results due to their imprecise targeting, deprived drug delivery, and side effects. Therefore, it is required to engineer the drug in such a way that it can target only cancerous cells and can inhibit their growth and proliferation. Nanotechnology is a technology that can target and differentiate between cancerous cells and the normal cells of the body. Silver itself is a good anticancer and antibacterial agent, and employing it with phytochemicals having anticancer properties and nanotechnology can provide the best approach for the treatment. The synthesis of silver nanoparticles using plant extracts is an economical, energy-efficient, low-cost approach, and it does not need any hazardous chemicals. In the review, A Review on Green Synthesis of Silver Nanoparticles and their Role against Cancer, Dr Rani et al. have discussed different methods of synthesis of silver nanoparticles using herbal extracts and their role in cancer therapy along with the synergistic role of silver and plant extracts against cancer.

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 Natural Multi-targets: Advances and Applications.

REFERENCES


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