immune system in upper respiratory tract, and certain pectic polysaccharides were identified to involve in potentiation of the immune response. It was also clarified that synergic action of two stereoisomers are required for the oral adjuvant activity of Shoseiryuto (SST: Xiao-Qing-Long-Tang). Like examples of the studies of Kososan (KS: Xiao-Su-San) and SST, proteomic analysis of disease model animals using agarose 2-DE is also useful another approach to find target protein candidates. These accumulated comprehensive results may contribute for more evidence-based clinical application.

Key words: Kampo medicines; mucosal immune system; polysaccharides; adjuvant; depression; proteomic analysis

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Targeting K-ras with semisynthetic andrographolide derivatives: A valid approach in the discovery of potential anticancer drug leads

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Abstract: We embarked on the discovery of anticancer agents from andrographolide nearly 15 years ago. Thus far, a few lead semisynthetic compounds have been identified, but only recently we managed to pinpoint their potential molecular target. Through *in silico* and cell-based studies, these lead molecules have been found to bind K-ras oncoprotein and disrupt its function. Further molecular docking analysis suggested the compounds targeted both wild-type and oncogenic mutant K-ras. However, the binding affinity was greater for the oncogenic protein. Low binding energies to wild-type K-ras protein suggested transient binding and inhibition. The compounds showed stronger binding interactions to all three mutant K-ras proteins (G12V, G12C and G12D) with average free energies (ΔG_{bind}) of -82 kcal·mol^{-1} as compared with -61 kcal·mol^{-1} for the wild-type protein. It is noteworthy that the binding pocket in wild-type K-ras protein, however, is different from that of the mutant proteins. SRJ23, one of the lead compounds, showed the strongest binding interactions to all three mutant K-ras proteins. Stronger binding to the mutant proteins could lead to more targeted and prolonged inhibition. Investigation into the effect of the compounds on RAS-MAPK pathway showed this pathway was disrupted in colon, breast and prostate cancer cells. *In vivo* studies revealed the compounds retarded the growth of human colon (HCT-116) and prostate (PC-3) cancer xenografts in mice. All of the above prompted us to synthesise derivatives of the lead compounds for improvement of binding affinity for the oncogenic K-ras. A preliminary *in silico* exploration found some compounds with such property and these compounds are presently undergoing extensive pharmacological investigations.

Key words: anticancer drugs; andrographolide derivatives; K-ras protein

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Trends in the exploration of medicinal plants and their clinical uses

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Abstract: Plant biodiversity has been source of myriad forms of natural substances utilized in simi-

larly multiple ways. The history of medicinal and aromatic plant (MAP) utilization dates back to the beginnings of mankind. Our forefathers used plants they could find in nature, to ease, cure their sufferings, illnesses, or heal their wounds. This type of approach has survived in the traditional medicinal (TM) uses, until today, since nearly 80% of the world population still relies on MAPs in their medications (Akerele, 1992). Especially rich are the traditions in China and India, where TMs have been used for thousands of years. The use of TM, however, goes well beyond these countries. It has been estimated that more than 1.5 billion people all over the world are trusting in the efficacy and safety of Chinese medicine (Wang and Franz, 2014). The renaissance of MAP-use in the high-income countries has brought about different types of use i.e.: in the form of Herbal Medicines (CAM=Complementary and Alternative Medicine). MAPs have become "industrial products" with versatile and innovative new concepts in phytotherapy and veterinary medicine, aromatherapy, nutraceuticals, cosmeceuticals, animal welfare, etc. New, innovative, value added applications include MAP use in functional foods, animal husbandry, as well as plant protection in agriculture. The versatile utilization of essential oils is most promising. MAPs are sourced from both wild-crafting and cultivation, where quality is primarily determined by the genotype, the environment and the conditions during the life cycle of the plant. Processing to preserve/isolate their active principles is an additional precondition for the safety and efficacy in use. Current areas of utilization constitute powerful drivers for the exploitation of these natural resources. Increasing demands, coupled with the already limited availability and potential exhaustion of natural resources, make it necessary to take stock of both our resources and our knowledge regarding research and development, production, trade and utilization, especially in view of sustainability National/international regulatory authorities have elaborated guidelines (GACP, GMP and GLP) to be included in quality assurance systems. The entire production system should observe these practices and this fact should be continuously documented, certified. Modern approaches in production and use have called attention to the importance of quality, safety and efficacy of both MAPs and their produce. There is also a need to ensure the quality of medicinal plant products by using modern sample preparation and control techniques as well as suitable standards.In Europe,this regards also the quality of TCM herbals. Their quality assurance systems should guarantee that they can be freely imported into the European Union and other Western European Countries (Wang and Franz, 2014). A new aspect in quality assurance is the trend for the protection of 'geographical indication'(GI) botanicals in the context of intellectual property rights. MAPs will also maintain their importance in the search for new, valuable sources of drugs and lead compounds. The ultimate aim would be to use MAPs with well-defined and constant composition. There is a need to ensure the quality of medicinal plant products by using modern sample preparation and control techniques. Thepharmacological effects of herbs are caused by the interaction several biologically active principles, therefore, the present clinical testsaimed at single chemicals, are also not really adequate. Todate, the lesson worthily worded by the Chiang Mai Declaration (1988) is more than valid: "Let us save plants that Save Lives".

Key words: medicinal plants; clinical uses

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Developing programmable biological functionalities for autonomous microbial factories

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Abstract: Synthetic biology aims to engineer genetically modified biological systems that perform novel functions that do not exist in nature, with reusable, standard interchangeable biological parts. The use of these standard biological parts enables the exploitation of common engineering principles such as standardization, decoupling, and abstraction for synthetic biology. With this framework in place, synthet-