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Natural product inspired scaffolds design: A closer look at mechanistically distinct proteasome inhibitors

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Natural products isolated from plant, animal or fermentation have long been the main source for compounds used in the chemotherapeutic intervention of cancer. However, in the later part of the 20th century, the advances of combinatorial chemistry have taken center stage in the drug discovery process and natural product synthesis took a temporary backseat for these new chemical processes. Combinatorial techniques and compound repurposing have resulted into large libraries in a very cost-efficient manner that can be screened for their biological activities against a desired target. Although cost-effective, these libraries suffer from a lack of diversity with respect to the structural complexity, stereochemistry and chemical space. In addition, the enforcement of restrictions of structural complexity and "drugability rules", further narrows the chemical space and thus limits the discovery of novel drug-target interactions. The goal of our program is to discover mechanistically distinct drug-target interactions by generating small libraries with high levels of structural diversity. Our approach is to simulate the structural complexity found in natural products and translate this into structurally diverse abridged scaffolds. Phenotypic screening of these abridged scaffold libraries followed by target identification resulted into two mechanistically distinct classes of proteasome inhibitors. In today's presentation, we will discuss this approach and the ability of these agents to overcome acquired drug resistance and effectively modify the onset of various diseases, such as multiple myeloma and rheumatoid arthritis, *in vivo*.

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Fabrication and properties of chitosan-hydrocortisone-silver nanoshells for drug delivery application

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Chitosan is a biopolymer that is usually produced from N-deacetylation of chitin which is extracted from crustacean. It is emerging substance as the promising bio-adaptable material that is harmless to human body. Many researchers have been interested in the chitosan for drug delivery system because of merits such as good absorptivity, biodegradability, and biocompatibility. Drug Delivery System (DDS) has been developed for the best control of drug releasing speed. It makes the drug to be delivered effectively and safely into the targeted living system. The drug used for the research was hydrocortisone, a steroid hormone. Hydrocortisone has been used to make allergic rhinitis medicine. This work was focused on the drug delivery through the nasal mucosa by using chitosan-hydrocortisone-silver nanoparticles. It was performed for an investigation in order to establish the optimal conditions, by changing concentration of hydrocortisone and reaction conditions. Silver nanoparticles have specific properties for the treatment of various diseases. Their extremely large surface area can collaborate with a vast number of ligands and prevent bacterial infections. The properties of silver nanoparticles applicable to patient treatments are under studying in many research groups and animal studies, assessing potential efficacy. In this research, the average size of chitosan-hydrocortisone-silver nanoshell was about 80 nm, was suitable as an drug carrier because maximum size of drug carrier in human body is 120 nm. UV-Vis spectra of chitosan-hydrocortisone-silver nanoshell show the characteristic peak of silver at 420 nm. Also, multi-layered silver nanoshell on the chitosan nanoparticles induced the red-shifted absorption peak and increased the intensity of absorption peak.