29【C】11100

Current Trends in New Drug Discovery & Development Based on Natural Product Leads

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Useful drugs have and continue to be developed from natural compounds contained in medicinal plants. In the drug discovery and development program at the Natural Products Laboratory (NPL), UNC-CH, we use three main research approaches to identify bioactive lead compounds: (a) bioactivity- or mechanism of action-directed isolation and characterization of active compounds, (b) rational drug design-based modification and analog synthesis, and (c) mechanism of action studies. Four types of studies then help refine the most promising drug development targets: (a) structure-activity relationship (SAR) studies including qualitative and quantitative SAR, (b) mechanism of action studies including drug receptor interactions and specific enzyme inhibitions, (c) drug metabolism studies including identification of bioactive metabolites and blocking of metabolic inactivation, and (d) molecular modeling studies including determination of 3D pharmacophores. Highlights of the research include development of anticancer etoposide analogs, such as GL-331 and related compounds, as well as anti-HIV triterpenes and coumarins, such as DSB and DCK, respectively.

Dr. K. H. Lee, Kenan Professor and Director, applies modern medicinal chemistry to discover and develop new, improved chemotherapeutic agents based on natural products models. He recently received the Taiwanese-American Foundation Achievement Award in Science & Engineering (2003).