Macrophage-Stabilized drug crystals

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Biography

Gus R. Rosania, PhD is Professor of Pharmaceutical Sciences at the University of Michigan where he has been Principal Investigator of an NIH funded, internationally-recognized research group for the past fifteen years. At the forefront of pharmacokinetics research, his lab has performed pioneering research on the transport mechanisms governing the distribution of poorly soluble small molecule drugs, from cells to whole organisms. He has published over sixty original research articles and is inventor on six patents. He is a member of the editorial board of various pharmaceutical sciences journals and has received numerous awards for his scientific contributions at the interface of chemistry, biology and pharmaceutics.

Abstract

Poorly soluble drugs with slow rates of clearance are poised to precipitate in the organism following long term oral administration. In this context, my research group has been characterizing the intracellular crystal-like drug inclusions (CLDIs) that are formed by clofazimine, an antimycobacterial drugthat is FDA-approved for the treatment of leprosy, and part of the WHO list of essential medications. Using mice as a

model organism to study CLDI formation, we have employed X-ray diffraction and other physical methods to elucidate the molecular structure of CLDIs down to the atomic level. In addition, we have biochemically isolated CLDIs from the spleen and livers of drug-treated mice, and have studied the biological effects of CLDIs in relation to soluble clofazimine in vitro and in vivo, demonstrating that CLDIs possess potent anti-inflammatory activity. Using synthetic formulations of clofazimine that are designed to resemble CLDIs, we are exploring how biomimetic formulations of macrophage-stabilized drug crystals can be exploited as macrophage targeted, locally active, anti-inflammatory agents.

Audience take away

- New pharmacokinetic phenomena (insoluble drug complexes).
- New tools for studying drug transport from the whole organism down to molecular and atomic level.
- A new, revolutionary approach to formulation and drug delivery.