Hormesis Arising in a Simple Enzyme Kinetic Model

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Hormesis (also known as a biphasic dose response in pharmacokinetics) is a therapy response characterised by stimulation at low dose and inhibition at high dose. Its dose response has the shape of an inverted U-curve. This paradoxic phenomenon is observed in many situations ranging from therapy using antibiotic or antifungal drugs to kinase inhibitors in cancer treatment, but remains for the most part poorly understood.

A simple kinetic model of the action of a kinase inhibitor in the MAPK signalling pathway exhibits hormesis and demonstrates that the causes could be purely biochemical. The model also sheds light on why hormesis resulting in a simple regulatory mechanism could be masked in biochemical assays.

This is joint work with Ian Barrett and Claus Bendtsen (AstraZeneca, Cambridge, UK) and Ivana Gudelj (University of Exeter).

References

[1] P. Rashkov, I. Barrett, C. Bendtsen, I. Gudelj, preprint, 2016.