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Chronopharmacology: Recent Advancements

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ABSTRACT:

Most aspects of mammalian physiology and behavior vary according to time-of-day thanks to an endogenous “circadian” clock. Therefore, it is not unforeseen that many aspects of pharmacology and toxicology also oscillate according to the same 24-hour clocks. Daily fluctuations in abundance of proteins necessary for either drug absorption or metabolism outcome in circadian pharmacokinetics; and oscillations in the physiological systems embattled by these drugs result in circadian pharmacodynamics. These clocks are existing in most cells of the body, but systematized in hierarchical fashion. Fascinatingly, some aspects of physiology and behavior are controlled directly via a “master clock” in the suprachiasmatic nuclei of the hypothalamus, while others are organized by “slave” oscillators in separate brain regions or body tissues. Recent research displays that these clocks can respond to different cues, and thereby display different phase relationships. Therefore, full calculation of chronopharmacology in pathological contexts will likely require a systems biology approach considering “chrono-interactions” among dissimilar clock-regulated systems.

Keywords: chronotherapy; cancer; circadian rhythms; drug metabolism; peripheral oscillators

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