Chronopharmaceutics and molecular clock mechanisms

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Mammalians circadian pacemaker resides in the paired suprachiasmatic nuclei (SCN) and influences a multitude of biological processes, including the sleep-wake rhythm. Clock genes are the genes that control the circadian rhythms in physiology and behavior. The effectiveness and toxicity of many drugs vary depending on dosing time associated with 24 hr rhythms of biochemical, physiological and behavioral processes under the control of circadian clock. Such chronopharmacological phenomena are influenced by not only the pharmacokinetics but also pharmacodynamics of medications. Identification of a rhythmic marker for selecting dosing time will lead to improved progress and diffusion of chronopharmacotherapy. The mechanisms underlying chronopharmacological findings should be clarified from viewpoint of clock genes. On the other hand, several drugs have an effect on circadian clock. The knowledge of interactions between circadian clock and drug should be very useful for the clinical practice. Recently, we clarified the regulatory mechanisms underlying the rhythmicity of CYP and transporter transcription. Therefore, I introduce the regulatory system of biological rhythm from viewpoints of clock genes and the possibility of pharmaceutics based on clock genes.