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Biorhythmic Approaches to the Design of Thermo-responsive Membranes for Drug Delivery

Key Words

Biological rhythm
Chronopharmacology
Chronokinetics
Pulsatile release
Thermo-responsive membrane

ABSTRACT

In this review, the concept of chronopharmacology is introduced into rational drug therapy, in which the regimen of drug administration plays an important role. Thus there is the need to consider chronopharmacology in drug delivery system design. Based on the above consideration, our laboratory has developed a thermo-responsive membrane entrapping a single or binary liquid crystal which exhibits pulsatile on-off drug release behavior simulated by the biological rhythms in the human body. (N. Taipei J. Med. 2001; 3:83-92)

Living organisms in the process of growing may develop various endogenous rhythms ranging in time from seconds to years.^{1,2} This means that almost all organisms have a biologically controlled clock, i.e., biological rhythms. The science concerned with the phenomenon of rhythmicity in organisms is called chronobiology,^{3,4} which presumes that bioprocesses and functions exhibit predictable variability in time for every living organism. In fact, all organisms are influenced by day-night and seasonal rhythms. The best-known rhythm is the circadian (*circa diem* meaning 24 h) rhythm.⁵ Human beings vary greatly in their physiological and biochemical status over 24 h due to circadian rhythms. The phenomenon of circadian rhythms in the human body is expressed by sleep-wakefulness, changes in body temperature, performance, cell division, and heart rate.^{1,2}

Medical Chronobiology

Medical chronobiology in human beings contains 2 predominant concepts: chronopharmacology and chronotherapy, and is also concerned with biological rhythms and other bioperiodic influences on human diseases during medication.^{4,6} Chronopharmacology is the study of how the effects of drugs vary with biological rhythms and endogenous periodicities.^{7,8} As a matter of fact, time-related differences in drug effects depend heavily on circadian rhythms. The influence of physiological rhythmicity on drug disposition and response is the major goal of chronopharmacology, which is now subdivided into chronoeffectiveness, chronokinetics, chronotoxicity, chronoesthesia, chronotolerance, etc. (Fig. 1). Clinical chronopharmacology involves the application of the knowledge of chronobiology to provide optimal drug treatment in a

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