For application of this temperature-sensitive membrane to transdermal devices to thermoregulate drug release into the human body, the phase transition temperature of the liquid crystal embedded in the membrane must ideally be higher than the skin temperature of 32 °C,[44] preferably within 34-36 °C. A series of studies has found an optimal binary mixture of 36% COC and 64% cholesteryl nonanoate (CN) with a solid-cholesteric phase transition temperature of 35.1 °C,[45] which seemed proper to act as a model. The cellulose membrane entrapping such a binary mixture was also prepared by using a vacuum-filtration method. To verify the sensitivity, precision, compliance, and reproducibility of the temperature responsiveness of this binary mixture during the temperature change, isothermal FT-IR microscopy was used to repeatedly determine the thermal behavior of the binary mixture between 25 and 37 °C by simulating in vitro drug penetration through this thermo-responsive membrane. Once the binary mixture was determined continuously and repeatedly to alter the temperature between 25 and 37 °C for 8 cycles, the binary mixture did not change its IR spectral position and peak area ratio (Fig. 8),[46] implying a better temperature response in sensitivity, precision, compliance and reproducibility. In addition, the thermo-responsive efficacy of this binary liquid crystal-embedded membrane showed a well-controlled on-off pulsatile behavior in response to changes of body temperature (Fig. 9).[46] The present results also indicate the successful development of this binary COC-CN mixture-embedded cellulose membrane with rate-controlling and thermo- responsive functions.

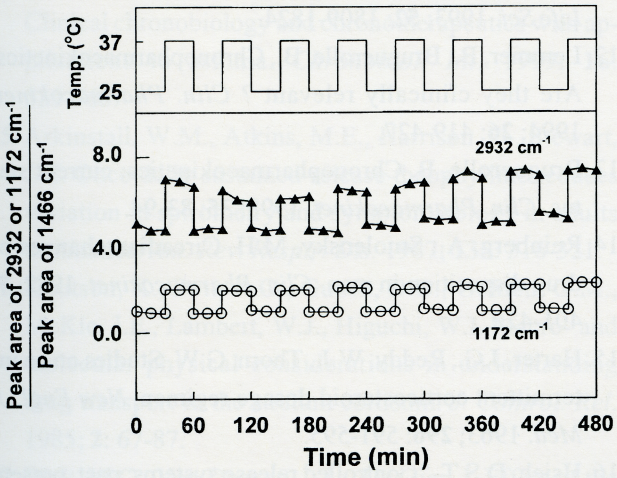

Fig. 8. Temperature-dependent changes in the IR peak area ratio of a binary mixture of 36% COC and 64% CN with repeated temperature cycles.[46]

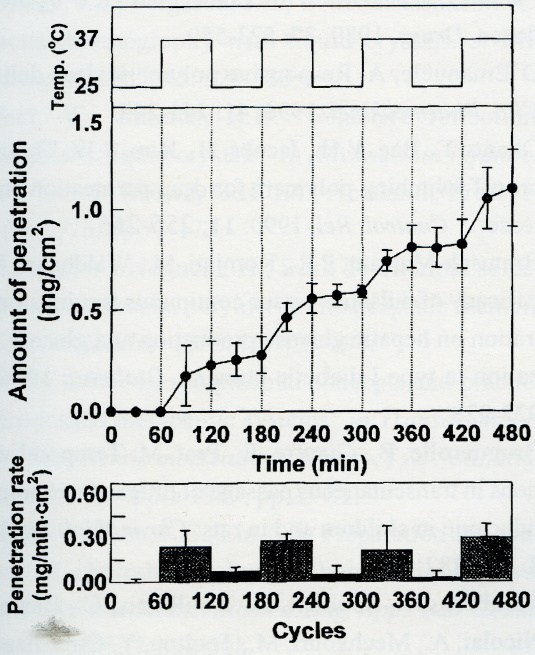

Fig. 9. In vitro penetration profile and rate of salbutamol sulfate across a binary 36% COC-64% CN mixture-embedded membrane in response to temperature exchange cycles.[46]

Future Perspectives

Circadian rhythms are well known to relate to almost all human functions and variables, particularly day-night variations in drug blood levels in patients. Since symptoms and onset of certain diseases predominate at certain times of the day, the choice of the timing for drug administration is very important to effectively achieve rational chronotherapeutics of drugs. In addition, a number of rhythmic variables influenced by environmental factors such as light, temperature, and social communication should also be taken into account. It is a future challenge to apply intelligent materials for new dosage designs to combine chronopharmacological concepts and novel preparation processes to design targeted DDSs with rate-control, site-control, and quantity-control functions