

Investigations on the Drug Releasing Mechanism from an Asymmetric Membrane-Coated Capsule with an in-situ Formed Delivery Orifice,

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Abstract

Asymmetric membrane-coated capsules with in situ formation of a delivery orifice were examined for their improved osmotic effects. The release mechanisms were investigated for drugs with both moderate to high water solubility and those with poor water solubility. The capsule wall membrane was produced by a phase-inversion process, in which an asymmetric membrane was formed on stainless steel mold pins by dipping the mold pins into a coating solution containing a polymeric material followed by dipping into a quenching solution. In situ formation of a delivery orifice in the thin membrane was proven by visualization of a jet stream of chlorophyll being released from the capsule. The release mechanism for drugs with moderate to high water solubility was mainly controlled by the osmotic effect, which is a function of the drug's solubility. Permeability across the asymmetric membrane of the capsule was determined to be 4.28×10^{-6} cm²/h-atm at 37 degrees C for drugs with water solubilities in a moderate to high range. Accordingly, the poorly water-soluble drug, nifedipine, was unable to create enough of an osmotic effect to activate drug release. Solubilization either by the addition of the solubility enhancer, SLS, or by a solid dispersion with HPMC could increase the solubility of nifedipine to a sufficient extent to activate drug release. It was found that the suspending ability induced by the viscous nature of HPMC further interacted with SLS to synergistically increase the maximal percent release and the release rate of nifedipine. The osmotic effect of this suspension ability was proposed as the underlying mechanism responsible for the release of poorly water-soluble drugs, i.e. nifedipine, from this system.