

## A Slow Releasing Molecular Fentanyl Flask

**Introduction:** Intrathecal narcotics revolutionized pain relief during labor by providing analgesia without motor block. Can fentanyl analgesia be prolonged by storage in a slow release formulation suitable for subarachnoid delivery?

**Methods:** Cucurbiturils (CBs), barrel-shaped macrocycles possessing a hydrophobic cavity that is surrounded by electrostatically negative ureidyl carbonyl portals, have high affinity for diamines, tertiary, and quaternary amines. The binding constants of cucurbituril to fentanyl and methylnaloxone were determined using a micro calorimeter to solve the equation  $\ln K = (T\Delta s - \Delta H)/rT$ .

**Results:** CBs bind narcotics with affinity constants in the range of  $10^5/M$  (figure). This would allow a steady dissociation of fentanyl from its cucurbituril-macrocycle complex. This differs from very tight sugammadex binding of rocuronium which occurs at a  $K_a = 10^7/M$ . The order of binding to CB: diamine fentanyl > quaternary amine methylnaloxone, > naloxone. The latter two narcotic antagonists were used because a quaternary form of morphine is not available.

**Discussion:** Currently a slow release form of fentanyl is available as a matrix impregnated transdermal patch. Morphine, sequestered in liposomes, can be administered into the epidural space. Cucurbiturils can function as a sustained slow release intrathecal fentanyl delivery system.

