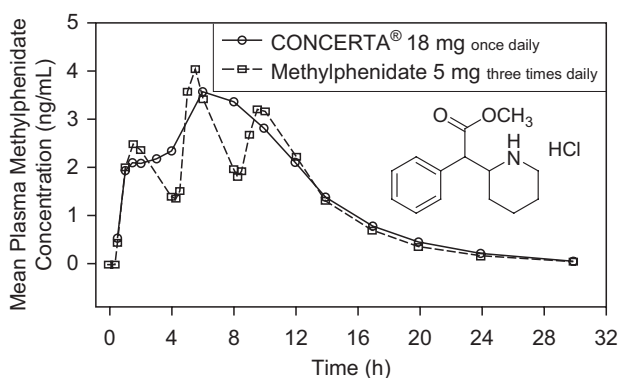


and attention deficit hyperactivity disorder (ADHD). It is considered the standard of care for children with ADD or ADHD and has been successfully used for this purpose for over 50 years.<sup>51</sup>

Despite its commercial success under the name Ritalin<sup>®</sup>, it was not a perfect drug for the treatment of children. Its safety profile and efficacy profile were not an issue, but the three times daily administration was viewed as a problem by some. Although this may not seem like a significant issue to many, ask any parent about the difficulties of giving their child medicine and they will tell you how challenging this can be. Add the complication of ADD or ADHD to the picture, and the difficulty only increases. The dosing regimen is, of course, a result of methylphenidate's PK profile (Figure 13.20), which produces peak



**FIGURE 13.20** Comparison of the mean plasma concentration of drug observed with immediate release methylphenidate and Concerta<sup>®</sup> extended release formulation. *Source: Reproduced with the permission of Janssen Pharmaceuticals, Inc.*

plasma concentrations approximately 2 h after ingestion of immediate release tablets (Ritalin<sup>®</sup>). Plasma concentration of the drug then falls, and additional doses are required to maintain efficacy during day time hours (Night time coverage is generally not necessary). Scientists at Janssen Pharmaceuticals recognized the opportunity to improve the utility of methylphenidate by developing an alternative formulation of this important drug. They designed an extended release delivery system that delivered efficacious plasma concentrations of the drug over a 12-h period, enabling once-daily dosing (Figure 13.20).<sup>52</sup> Their product was approved by the FDA in 2000 and marketed as Concerta<sup>®</sup>. Safety and efficacy were essentially the same as the original formulation, but the once-a-day dosing system greatly simplified the lives of children receiving the medication and their caregivers. In this case, improved performance generated by a change in formulation provided Janssen Pharmaceuticals with a blockbuster product based on an old