



Fig. 31.2 • The number of oral modified release patents granted from 1990 to 2010.

outcomes for a patient relative to an immediate-release medication. For example, a drug which is rapidly absorbed and eliminated can have a steep plasma profile in an immediate-release formulation. An extended-release formulation can keep the drug at therapeutic levels for longer (Fig. 31.3). For many chronic illnesses, symptom breakthrough can occur if the blood concentration falls below the minimum effective concentration e.g. in asthma or depressive illness. This minimum level can also be critical for control of pain, consequently drugs, such as opioid analgesics are often given as extended-release preparations.

Maintaining drug levels overnight. It is often not acceptable that patients be required to take medications during the night, with consequent loss of sleep. Overnight management of pain in terminally ill patients can be very important to maintain sleep.

Chronotherapy. Timing the drug release to coincide with when it is required is known as *chronotherapy*. For example, a modified-release dosage form may be tailored to enable drug release to occur in the morning around the time of waking, when symptoms of, for example, arthritis, asthma or allergies are often at their worst. A clinical study has shown that patients with arthritis had a better

reduction in morning joint stiffness when they received modified-release prednisolone rather than a conventional dosage form.

Reducing side effects. Immediate-release formulations can often have a high maximum concentration in the blood (C_{max}). If C_{max} is above the safety limit of the drug, adverse events may be more likely. Using modified-release formulations to reduce C_{max} can reduce the incidence and severity of the side effects of some drugs. Additionally, some drugs, such as potassium chloride can be irritating to the gastrointestinal tract if delivered in an immediate-release bolus. A slow, sustained release is required to minimize the build-up of irritant concentrations.

Improving compliance. A significant driver to developing a modified-release dosage form comes from trying to achieve once-daily dosing. Once-daily dosing is considered to be more convenient for patients and reduces the risk of missed doses throughout the day.

Treatment of local areas in the gastrointestinal tract. Some conditions such as inflammatory bowel disease require topical treatment (e.g. with steroids) at the inflamed intestinal surface. Site-specific drug targeting (e.g. to the colon) can deliver the drug directly to its site of action.