
19 Opioid and Cannabinoid Receptors

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CONTENTS

19.1 Opioid Receptors	329
19.1.1 Opioid Receptor Subtypes and Effector Mechanism	330
19.1.2 Endogenous Opioid Receptor Ligands	330
19.1.3 Nonendogenous Opioid Receptor Ligands	333
19.1.4 Therapeutic Applications and Prospects	337
19.2 Cannabinoid Receptors	338
19.2.1 Endocannabinoid System	339
19.2.2 Cannabinoid Receptor 1	341
19.2.3 Cannabinoid Receptor 2	341
19.2.4 Other Cannabinoid Receptors?	342
19.2.5 Therapeutic Use and Potential	342
19.2.6 FAAH Inhibitors and Anandamide Uptake Inhibitors	342
19.2.7 CB ₁ -Receptor Agonist/Antagonist	343
19.2.8 CB ₂ -Receptor Agonist/Antagonist	343
19.2.9 Diacylglycerol Lipase Inhibitors	343
19.2.10 Monoacylglycerol Lipase Inhibitors	345
Further Reading	345

19.1 OPIOID RECEPTORS

Presently she cast a drug into the wine of which they drank to lull all pain and anger and bring forgetfulness of every sorrow.

The Odyssey, Homer (ninth century BC)

The history of opioids and its receptors span several millennia. The first evidence of uses of the seed pods of *Papaver somniferum* dates back to 4200 BC, and numerous findings and descriptions up through history witness the use of different parts of this plant for food, anesthesia, and ritual purposes. Opium (from *opos*, the Greek word for juice) refers to the liquid that appears on the unripe seed capsule when it is notched. This liquid contains as much as 16% of morphine, a compound that was isolated already in 1806 as the major active ingredient in opium. A few years later, codeine was also isolated. Morphine can now be produced and applied in its pure form for the treatment of pain and as an adjunct to general anesthetics, but it was quickly realized that morphine had the same potential of abuse as opium. In 1898, heroin was synthesized and claimed to be a safer, more efficacious, nonaddicting opiate as were several other analogs around that time; however, later they all proved to be unsafe. Heroin is an early example of a prodrug since the highly potent analgesic properties can be attributed to the rapid metabolism to 6-monoacetylmorphine and morphine, combined with higher blood–brain barrier penetration due to better lipid solubility compared to morphine (Figure 19.1).