

موم طبيقية درعية

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Opioids and Derivatives

- **HISTORY AND CLASSIFICATION**
- From the introduction of opium into China in the seventeenth century, resulting in the undermining of its organized system, to the modern-day pharmaceutical production of synthetic narcotic analgesics, these compounds have infiltrated urban and rural societies alike.
- Today, narcotic addiction permeates all socio-economic classes, from economically underserved communities, to affluent neighborhoods, to the U.S. armed forces.

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Opioid analgesics are readily and easily available.

- These compounds are not necessarily obtained only through illicit drug dealing (street drugs), but their supply is also abundant through fraudulent and illegitimate prescriptions, as well as in the course of over prescribing practices.
- Health care professionals are also particularly vulnerable to the addictive potential of narcotics, principally due to easy accessibility.

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- **The variety of opioid derivatives encountered in the twentieth century reflects the cyclical appearance and disappearance of individual compounds, mostly because of popularity among users and availability .**
- **In the 1980s, opioid addicts inadvertently ingested what they thought was a designer derivative of meperidine (4'-methyl- α -pyrrolidinopropiophenone, MPPP).**

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- **Instead, synthesis and contamination with 1- methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) lead to the development of an idiopathic Parkinson-like state in these patients.**
- **In the same decade, a new more potent form of heroin from Mexico (Black tar heroin) made its appearance, resulting in an increase in acute overdose fatalities.**

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- **Simultaneously during this period, heroin usage began to wane, only to be replaced with the more versatile forms of cocaine.**
- **Despite the counter-effects of narcotic law enforcement efforts to remove or dissuade its non therapeutic use, opioid use is still a major public health problem.**
- **Initial narcotic ingestion is often an unpleasant experience. Patients usually complain of nausea, dizziness, and muscular weakness.**

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- **With continued use, individuals build tolerance to the unpleasant adverse reactions in preference to the euphoric effects.**
- **Opioid compounds are ingested orally in tablet or capsule form, the most common method of administration (considering both therapeutic and illicit drug use).**

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- **As greater tolerance develops, ingesting the same amount of drug does not produce euphoria as initially experienced, necessitating either higher doses or an alternate, more immediate method of administration.**
- **This includes rendering the tablets to a powder, or using a preformulated powder form, for nasal insufflation (*snorting*), for injection subcutaneously (*skin popping*) or intravenously (*mainlining*).**

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CLASSIFICATION

- **By definition opioids, as a class, exert their pharmacological effects at opioid receptors, whereas opiates are alkaloid extracts of the opium poppy.**
- **The opioids are traditionally classified according to their source, as summarized in Table 12.1.**
- **Opium, the parent crude form of the naturally-occurring compounds, is derived from the milky exudates of the unripe capsule of *Papaver somniferum* L. (opium poppy).**

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- **The plant is cultivated in the Mediterranean and Middle East regions, India, and China.**
- **About two dozen alkaloids, of which morphine occupies about 10%, are formed primarily in various cells of the poppy plant and excreted into the lactiferous ducts.**
- **Depending on diurnal variations, the isolated latex undergoes alkaloid biosynthesis and metabolic destruction, which contribute to the variability in alkaloid composition of crude opium samples.**

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The narcotic, antispasmodic, sedative, hypnotic, and analgesic properties of the extract have been recognized for centuries.

- **Interestingly, the numerous and very small seeds of the plant do not contain opium.**
- **Few pharmacological and toxicological differences exist between the classes.**
- **Some pharmacokinetic properties, however, distinguish the compounds, especially among the many narcotic derivatives (listed below).**

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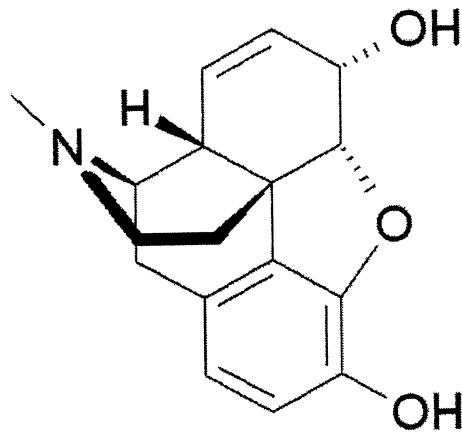
MEDICINAL CHEMISTRY

- The opioids are composed of six-membered saturated heterocyclic rings forming the **phenanthrene nucleus** (in bold) to which is attached a piperidine ring.
- The structure represents the prototype for all opioids except methadone and meperidine .
- Although the more important opiate alkaloids exhibit a phenanthrene nucleus, the majority of the derivatives have the isoquinoline ring structure

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