Supplemental Material

Identification of the first marine-derived opioid receptor "balanced" agonist with a signaling profile that resembles the endorphins

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[Supporting Information]

Figure S1. Selected examples of major chemotypes that function as potent mu opioid receptor (μ-OR) agonists with significant analgesic activity.

Figure S2. ^{1}H NMR of aaptamine (400 MHz, d-DMSO)

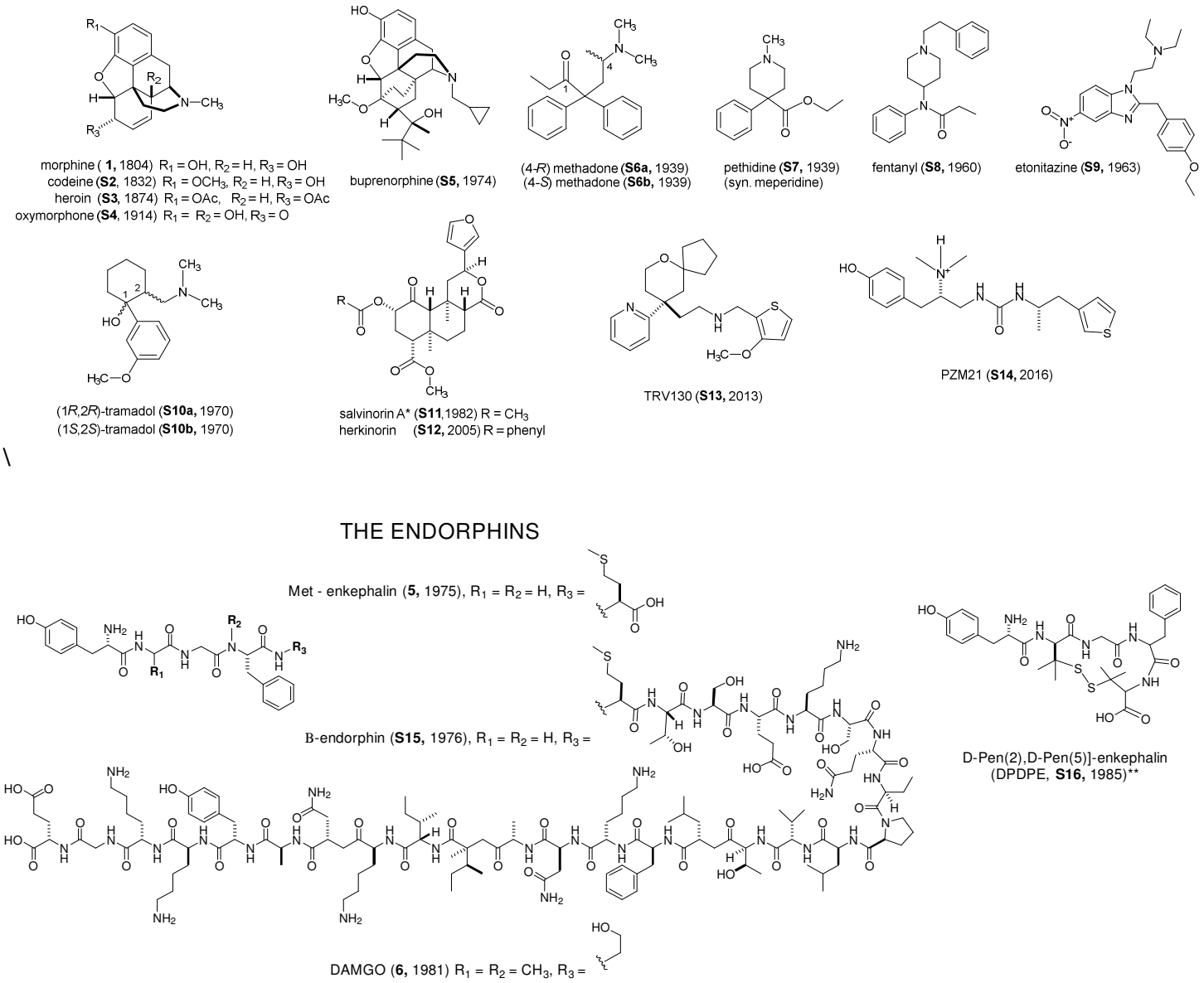

Figure S1. Selected examples of major chemotypes (discovery date in parenthesis), that function as potent mu opioid receptor (μ-OR) agonists with significant analgesic activity. *Salvinorin A is a potent and selective kappa opioid receptor (κ-OR) agonist, while herkinorin is a potent μ-OR agonist with analgesic activity. **D-Pen(2),D-Pen(5)]-enkephalin (DPDPE)* is a potent and selective δ-opioid receptor (δ-OR) agonist.

Figure S2. ^{1}H NMR spectrum of aaptamine, (400 MHz, DMSO) isolated from *A. aaptos.*