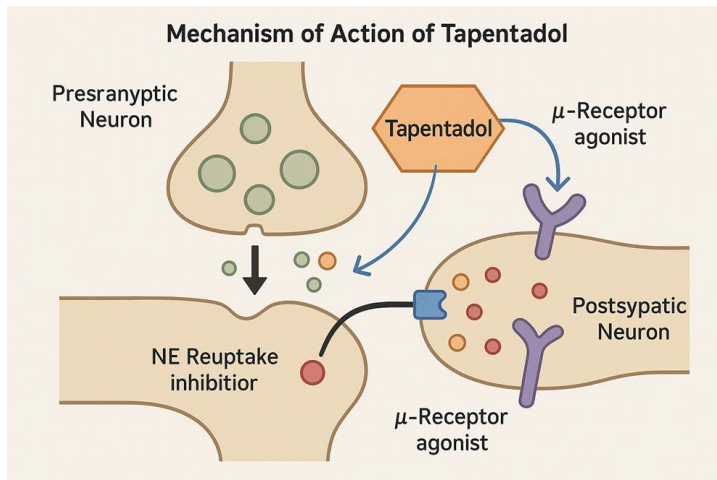




Supplementary Figure 1 Mechanism of action of Tapentadol. NE: Norepinephrine.

Supplementary Table 1 The studies on the preemptive analgesic effect of Tapentadol

Ref.	Surgery type	Tapentadol dose	VAS outcome	Rescue analgesia use	Notes
Yadav <i>et al</i> [12], 2016	Laparoscopic cholecystectomy	75 mg immediate-release	Reduced perioperative pain	Decreased	No orthopedic population; general surgery
Haeseler <i>et al</i> [9], 2017	Mixed ortho/trauma	50 mg extended-release	Non-inferior to oxycodone	Not significantly different	Heterogeneous surgeries; low dose; unblinded
Current study	TKA	100 mg sustained-release	VAS by 2.0 points at 24 hours	Significantly reduced	Homogeneous TKA cohort; placebo-controlled randomised controlled trial

TKA: Total knee arthroplasty; VAS: Visual analog scale.