Adrenergic $\alpha_{2A}$ and $\alpha_{2B}$ Receptors Mediate Antinociceptive Effect of Centhaquin Citrate in Mice

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Purpose
The use of clonidine as a primary and adjuvant analgesic is well-documented. It is known that imidazoline and $\alpha_2$-adrenergic receptors are involved in clonidine antinociception. Clonidine also produces antihypertensive actions mediated through the central nervous system. We have reported that centhaquin, a centrally acting anti-hypertensive drug, produces its hypotensive effect through a mechanism similar to that of clonidine. Centhaquin has also been shown to possess significant antinociceptive activity which is partially blocked by yohimbine, idazoxan, and naloxone. However, the involvement of specific adrenergic receptor subtypes ($\alpha_{2A}$, $\alpha_{2B}$, or $\alpha_{2C}$) in centhaquin antinociception is unknown. The present study was conducted to determine antinociceptive properties of centhaquin citrate, a water soluble salt of centhaquin, and involvement of $\alpha_{2A}$-, $\alpha_{2B}$-, or $\alpha_{2C}$-adrenergic receptors in mice.

Methods
BRL-44408 ($\alpha_{2A}$-adrenergic receptor antagonist), imiloxan ($\alpha_{2B}$-adrenergic receptor antagonist) and JP-1302 ($\alpha_{2C}$-adrenergic receptor antagonist) were used to determine the involvement of $\alpha_{2A}$-, $\alpha_{2B}$-, or $\alpha_{2C}$-adrenergic receptors, respectively. Antinociceptive responses were determined by the tail-flick and hot-plate latency methods in male Swiss-Webster mice treated with centhaquin citrate alone and in combination with BRL-44408, imiloxan, or JP-1302. Parameters were measured for 360 min and expressed as Mean±S.E.M. N=8 per group.

Results
Centhaquin citrate produced significant antinociceptive responses in mice (P<0.05) which were blocked by BRL-44408 (tail-flick test: 49.75% decrease, P<0.05; hot-plate test: 49.12% decrease, P<0.05) and imiloxan (tail-flick test: 46.98% decrease, P<0.05; hot-plate test: 46.42% decrease, P<0.05). Centhaquin citrate antinociception was not affected by JP-1302 in both tail-flick and hot-plate latency tests over the 6-hour observation period.

Conclusion
This is the first report demonstrating centhaquin citrate antinociception and its blockade by BRL-44408 and imiloxan. We conclude that $\alpha_{2A}$ and $\alpha_{2B}$ but not $\alpha_{2C}$ adrenergic receptors are involved in centhaquin antinociception in mice.