Doxepin hydrochloride is a tricyclic antidepressant that also exhibits anxiolytic, analgesic, anti-ulcerative, and hypnotic activities. This compound displays inhibitory activity at a wide range of receptor subtypes, including 5-HT1/2 receptors, muscarinic acetylcholine receptors (M1-5 mAChRs), α1-adrenergic receptors, and histamine (H1/2) receptors; additionally, doxepin hydrochloride competitively antagonizes the serotonin transporter (SERT) and the norepinephrine transporter (NET). Doxepin hydrochloride is most often prescribed as an orally bioavailable treatment for depression, anxiety, insomnia, or when topically applied, dermatological itch. In addition to its modulation of neurotransmitter levels, doxepin hydrochloride also inhibits the H⁺/K⁺ ATPase through K⁺ antagonism and intravesicular neutralization; like other antidepressants, this compound also regulates HPA axis signaling, decreasing stress-induced corticosterone release, potentially through an endocannabinoid-mediated signaling pathway. Doxepin also acts as a functional inhibitor of acid sphingomyelinase (FIASMA).

References


