IMIDAZOLE CONTAINING COMPOUNDS, DERIVATIVES THEREOF, AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATION

This application claims priority to U.S. Patent Application No. 63/498,049 filed April 25, 2023, U.S. Patent Application No. 63/515,229 filed July 24, 2023, U.S. Patent Application No. 63/550,274 filed February 6, 2024, U.S. Patent Application No. 63/550,228 filed February 6, 2024, and U.S. Patent Application No. 63/557,039 filed February 23, 2024, the disclosures of which are incorporated herein by reference in their entireties.

FIELD OF THE DISCLOSURE

The present disclosure describes novel alpha2 adrenergic receptor (α2AR) agonists and uses thereof. In particular, the present disclosure describes novel imidazole containing compounds and their derivatives. These compounds can be useful as α2AR agonists for the treatment or prevention of diseases thereof.

BACKGROUND OF THE DISCLOSURE

The alpha2 adrenergic receptor (α2AR) family, as part of the G-protein–coupled receptors, plays a critical role for many central nervous system (CNS) biological functions. α2ARs are key in modulating neurotransmitter release, thus influencing a spectrum of central physiological processes. Agonists targeting these receptors, such as clonidine and dexmedetomidine, have been successfully used to treat several conditions predominantly within the CNS. Related applications include treating hypertension, sedation in intensive care, and for problems like attention-deficit/hyperactivity disorder (ADHD) and agitation associated with schizophrenia or bipolar disorder.

Clonidine was first developed to manage hypertension. Later, clonidine was found to induce sedation by acting through the activation of central pre- and postsynaptic α2AR in the locus coeruleus (LC), a nucleus in the medial dorsal pons, thereby inducing sedative effects. The later development and approval of dexmedetomidine for sedation, particularly in initially intubated and mechanically ventilated adult patients in intensive care settings, was attributed to its superior α2AR selectivity and pharmacokinetic properties better suited for sedation.

Beyond its antihypertensive and sedation effects, clonidine has been approved for epidural use under the trade name Duraclon, marking a significant advancement in the