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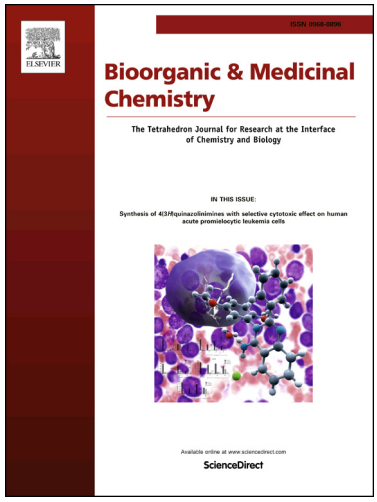

Identification of a novel fluoropyrrole derivative as a potassium-competitive acid blocker with long duration of action

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PII: S0968-0896(17)30497-2
DOI: http://dx.doi.org/10.1016/j.bmc.2017.04.014
Reference: BMC 13684

To appear in: *Bioorganic & Medicinal Chemistry*

Received Date: 11 March 2017
Revised Date: 9 April 2017
Accepted Date: 11 April 2017

Please cite this article as: Nishida, H., Arikawa, Y., Hirase, K., Imaeda, T., Inatomi, N., Hori, Y., Matsukawa, J., Fujioka, Y., Hamada, T., Iida, M., Nishitani, M., Imanishi, A., Fukui, H., Itoh, F., Kajino, M., Identification of a novel fluoropyrrole derivative as a potassium-competitive acid blocker with long duration of action, *Bioorganic & Medicinal Chemistry* (2017), doi: http://dx.doi.org/10.1016/j.bmc.2017.04.014

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Identification of a novel fluoropyrrole derivative as a potassium-competitive acid blocker with long duration of action

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Keywords: H^+,K^+-ATPase; potassium-competitive acid blocker; fluoropyrrole; low lipophilicity; long duration of action

Abbreviations: absorption, distribution, metabolism, excretion, and toxicity (ADME-Tox), hepatic cytochrome P450 2C19 (CYP2C19), hepatic cytochrome P450 3A4 (CYP3A4), differential scanning calorimetry (DSC), Diisobutylaluminium hydride (DIBAL-H), 1,2-dimethoxyethane (DME), *N*,*N*-dimethylformamide (DMF), drug metabolism and pharmacokinetics (DMPK), half-maximal inhibitory concentration (IC_{50}), high-performance liquid chromatography (HPLC), high-resolution mass spectrometry (HRMS), human ether-a-go-go-related gene (hERG), intravenous injection (iv), ligand-lipophilicity efficiency (LLE), liquid chromatography with tandem mass spectrometry (LC/MS/MS), lithium diisopropylamide (LDA), melting point (mp), methoxy (MeO), molecular sieves 4 angstrom (MS4Å), *N*-chlorosuccinimide (NCS), *N*-methylmorpholine *N*-oxide (NMO), parallel artificial membrane permeability assay (PAMPA), per os (po), potassium-competitive acid blocker (P-CAB), proton pump inhibitor (PPI), pyridyl (Py), relative light units (RLU), room temperature (rt), structure-activity relationship (SAR), tetrahydrofuran (THF), thermogravimetry-differential thermal analysis (TG-DTA), thin-layer chromatography (TLC), p-toluenesulfonyl chloride (TsCl), tetrapropylammonium perruthenate (TPAP)

Abstract

With the aim to find a novel long-lasting potassium-competitive acid blocker (P-CAB) that would perfectly overcome the limitations of proton pump inhibitors (PPIs), we tried various approaches based on pyrrole derivative **1b** as a lead compound. As part of a comprehensive approach to

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