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Design, synthesis and pharmacological evaluation of some substituted dihydropyrimidines with L-/T-type calcium channel blocking activities

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Abstract:

New dihydropyrimidines bearing various lipophilic pharmacophores and functionalities at position 3 were designed and synthesized. The basic framework of the new compounds was designed to maintain the main structural requirements for calcium channel blocking activity of the known dihydropyridines and dihydropyrimidines calcium channel blockers. The newly synthesized compounds were evaluated as antagonists for Ca V 1.2 and Ca V 3.2 using the whole-cell patch clamp technique. Seven compounds (4b, 4c, 6c, 9, 13c, 13e and 17b) showed promising dual calcium channel blocking activity and three compounds (13b, 14b and 17a) were selective against Cav3.2. Their drug-likeness has been assessed using Molinspiration and Molsoft softwares. Their physicochemical properties and pharmacokinetic profiles recommend that they can be considered as drug-like candidates. © 2018

Reference:
https://08105w5k6-1104-y-https-www-scopus-com.mplbci.ekb.eg/record/display.uri?origin=recordpage&eid=2-s2.0-85056199120&citeCnt=0&noHighlight=false&sort=plf-f&src=s&nlo=&nlr=&nls=&sid=2816e924e0a00af2f5253ac3b4ed7c39&sot=aff&sdt=cl&cluster=scopubyr%2c%222019%22%2ct%2bscosubjabbr%2c%22PHAR%22%2ct&sl=49&s=AF-ID%28%22Pharos+University+in+Alexandria%22+60011287%29&relpos=17#