Introduction

• Isometheptene (IMH) is a racemic drug that has been used clinically in the US for more than 70 years primarily as a treatment for headache. Yet its mechanism of action remains unknown.

1. MigraTen Prescribing Information; Pharmelle; Gilbert AZ, 2004.

2. Sympathomimetic activity


5. PS29.55(53) 172.

6. Tonix discovers TNX-201 (R-isomer of IMH) in 2013.

7. Binds to I1-imidazoline receptor

8. α

9. β

10. PKC ζ

11. MAPK Cascade

12. Clonidine (R)-isometheptene


14. R-IMH mucate is being investigated in the US for tension-type headache as TNX-201 under US Investigational New Drug and is not approved for any indication.

15. Our finding that R-IMH binds to LR with high affinity suggests that the receptor is the primary site of action for R-IMH’s analgesic effects. This is supported by recent results in the LR knockout mouse in which there is a decreased pain threshold.

16. PS29.55(53) 172.

17. Complete loss of R-IMH’s hypotensive effects using consecutive doses of 0.03, 0.1, 0.3, 1, 3, and 10 mg/kg IV with 10-minute intervals of saline, (R)-IMH mucate, and (S)-IMH mucate in anesthetized male Wistar rats were studied using stereoscopic light microscopy.