Targeting ion channel trafficking mechanisms for novel analgesics



"Perhaps the Drug Enforcement Agency, with its billion-dollar budget, could devote a portion of its resources to fund research whose sole purpose is to develop nonaddictive analgesics. It may be as cost effective as trying to protect pharmacies from bandits gallivanting down the Oxu Express."

Arin Bhattachariee'

In February of this year, the New York Times reported on the increasing number of brazen robberies occurring at pharmacies throughout the USA. One thief in Rockland (ME, USA) brandished a machete and leapt over the pharmacy counter to grab oxycodone. He gulped down some of it even before he fled. In Florida, thousands of doses of oxycodone pills are dispensed in pain clinics, resulting in some calling the highway that leads into Florida, 1-75, the 'Oxy Express'. In 2008, Ohio pharmacists dispensed 4.8 million prescriptions for hydrocodone medications, one for every 2.5 people in the state port. Although we have been treating pain effectively for millennia, the need for efficacious, safe but especially nonaddictive analgesics remains strong. We require analgesics that can specifically act on peripheral pain-sensing neurons and not centrally to avert addiction. In this article, I argue that the future of pain research must include the development of compounds that directly target the ion channel trafficking machinery of nociceptors.

Analgesics act by reducing the firing properties of neurons within the pain pathway. For treatment of mild pain, nonsteroidal antiflammatory drugs (NSAIDs)

are recommended. These agents reduce algogenic substances, such as prostaglandins, which directly affect the firing properties of nociceptive neurons. NSAID use is widespread; however, gastrointestinal and renal toxicities associated with these agents are prevalent, with an estimated 10-20% of NSAID patients experiencing dyspepsia [1]. The development of cyclooxygenase-2 selective inhibitors, which minimize gastrointestinal effects, seemed promising, but their severe cardiovascular toxicities have dramatically restricted their use. Vioxx®, the most famous of the cyclooxygenase-2 inhibitor drug class, had to be removed from the market owing to its toxic effects. For moderate-to-severe pain, moderate opioid agonists, such as hydrocodone, strong opioid agonists, such as oxycodone, or even morphine are used. These agents act on opioid receptors in the CNS, especially on descending pathways originating from the periaqueductal gray matter, to block pain transmission in the dorsal hom of the spinal cord. They can also act presynaptically by inhibiting neurotransmitter release from the central terminations of nociceptors in the spinal cord. Opioids do so via u-receptors, ultimately affecting potassium and calcium conductances. As

"If we can elucidate the molecular underbinnings of nociceptor huperexcitabilitu. It will lead to better and safer analgesics. Unfortunately, within the USA, the NIH devotes only a fraction of a percentage of its total budget to pain research and ... it is unclear where the impetus will come for the development of novel channel targeted drugs."





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Ari Kusuma Wardana

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ultrashort acting opioids with high therapeutic indices which many researchers dreamt about but never before materialized The side effect liabilities of these new opioids are minute as compared to morphine and meperidine Regional Opioid Analgesia could not have been more authentically written than by Drs De Castro Zenz and Meynadier who have conducted daily clinical investigations on all known opioids for regional analgesia as well as for neurolept analgesia Therein lies the great value of this monograph it is the most authentic work on this topic **Index of Conference Proceedings Received** British Library. Lending Division, 1985-07 **Psychopharmacology Abstracts** ,1976 Federal Register ,1977-07 **Information Circular** ,1962 Complete Catalogue of Scientific and Scholarly Books and Periodicals in Languages Other Than Hungarian Published Since 1950 Akadémiai Kiadó,1978 Bibliography of Bureau of Mines Investigations of Coal and Its Products, 1910-60 United States. Bureau of Mines. Division of Bituminous Coal, 1962 **Index of Conference Proceedings** British Library. Document Supply Centre, 2003 Hearings United States. Congress. House. Committee on Armed Services. Hearings, Reports and Prints of the House Committee on Armed Services United States. Congress. Medical and Health Care Books and Serials in Print ,1997 House. Committee on Armed Services, 1971 National Union Catalog ,1978 Includes entries for maps and atlases **Chemical Control** Michael Crowley, 2016-01-26 This thoroughly researched study highlights the international community s failure to regulate contemporary state research development marketing and or deployment of riot control agents and incapacitating chemical agent weapons Hearings on H.R. 9503 (H.R. 12846) to Amend Title 10, United States Code, to Authorize a Treatment and Rehabilitation Program for Drug Dependent Members of the Armed Forces, and for Other Purposes United States. Congress. House. Committee on

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Table of Contents Symposium On Analgesics Vol 1

- 1. Understanding the eBook Symposium On Analgesics Vol 1
 - The Rise of Digital Reading Symposium On Analgesics Vol 1
 - Advantages of eBooks Over Traditional Books
- 2. Identifying Symposium On Analgesics Vol 1
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
- 3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Symposium On Analgesics Vol 1
 - User-Friendly Interface
- 4. Exploring eBook Recommendations from Symposium On Analgesics Vol 1
 - Personalized Recommendations
 - Symposium On Analgesics Vol 1 User Reviews and Ratings
 - Symposium On Analgesics Vol 1 and Bestseller Lists
- 5. Accessing Symposium On Analgesics Vol 1 Free and Paid eBooks
 - Symposium On Analgesics Vol 1 Public Domain eBooks
 - Symposium On Analgesics Vol 1 eBook Subscription Services
 - Symposium On Analgesics Vol 1 Budget-Friendly Options
- 6. Navigating Symposium On Analgesics Vol 1 eBook Formats

- o ePub, PDF, MOBI, and More
- Symposium On Analgesics Vol 1 Compatibility with Devices
- Symposium On Analgesics Vol 1 Enhanced eBook Features
- 7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Symposium On Analgesics Vol 1
 - Highlighting and Note-Taking Symposium On Analgesics Vol 1
 - Interactive Elements Symposium On Analgesics Vol 1
- 8. Staying Engaged with Symposium On Analgesics Vol 1
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - $\circ\,$ Following Authors and Publishers Symposium On Analgesics Vol 1
- 9. Balancing eBooks and Physical Books Symposium On Analgesics Vol 1
 - Benefits of a Digital Library
 - o Creating a Diverse Reading Collection Symposium On Analgesics Vol 1
- 10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
- 11. Cultivating a Reading Routine Symposium On Analgesics Vol 1
 - Setting Reading Goals Symposium On Analgesics Vol 1
 - Carving Out Dedicated Reading Time
- 12. Sourcing Reliable Information of Symposium On Analgesics Vol 1
 - Fact-Checking eBook Content of Symposium On Analgesics Vol 1
 - Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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