



FROM MOLECULES TO MEDICINE: THE SCIENCE BEHIND NSAIDS

How scientists use evidence to understand hydrophobic interactions between NSAIDs and COX enzymes

SCIENTIFIC EXAMPLE

Non-steroidal anti-inflammatory drugs, like ibuprofen, reduce pain and inflammation by inhibiting cyclooxygenase (COX) enzymes which are involved in the production of prostaglandins. Prostaglandins are hormone-like chemicals that are released when tissue is hurt or inflamed and causes swelling, triggers fevers and make nerve endings more sensitive to pain. **But how do we know how ibuprofen blocks these enzymes?**

Scientists are able to use techniques to determine the 3D position of drugs bound to their target and in the case of ibuprofen, they found a crystal structure of ibuprofen bound to COX-2 inside the enzyme's mainly hydrophobic binding channel. The ibuprofen molecule binds in a few ways, but hydrophobic interactions are the key to positioning and stabilizing itself in the binding site.

NATURE OF SCIENCE CONNECTION

This is a great example of scientific explanations being built through observation, experimentation, reasoning and interpretation.

Scientists can't observe hydrophobic interactions forming and breaking in living cells so instead they gather other evidence to develop an explanation of what's happening at the molecular level. In the case of ibuprofen, structural data reveals the location of the bound drug within the COX binding channel. This data can be compared to experimental measurements of binding and inhibition. Further tests can be done by modifying the structure of ibuprofen and seeing how it affects binding. For example, if they were to attach a hydrophilic group to the part that usually binds to the channel and the channel rejects it, that is strong evidence the binding site must be hydrophobic.

WHY THIS MATTERS

Understanding how scientists connect molecular structures to experimental observations helps us recognize that scientific- and more specifically biochemical- knowledge is developed through evidence and reasoning. New information and discoveries aren't always immediately visible or directly testable, meaning that observation, experimentation, reasoning and interpretation are all crucial to the scientific process.

USE IN LEARNING

This graphic could be useful:

- As an in-class discussion prompt to demonstrate how scientific explanations rely on observation, experimentation, reasoning and interpretation using a real word example
- To introduce a lesson about enzyme inhibition or hydrophobic interactions

REFERENCES

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- Gunaydin, C., & Bilge, S. S. (2018). Effects of Nonsteroidal Anti-Inflammatory Drugs at the Molecular Level. The Eurasian journal of medicine, 50(2), 116–121. <https://doi.org/10.5152/eurasianjmed.2018.0010>