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<http://www.acs.org/chemmatters>

**Pain Relievers:
How Do They
Take Away Pain?**

*February/March 2018*

**Teacher’s Guide**



**Teacher's Guide for**

***Pain Relievers:
How Do They Take Away Pain?***

**February/March 2018**

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# Connections to Chemistry Concepts

|  |  |
| --- | --- |
| **Chemistry Concept** | **Connection to Chemistry Curriculum** |
| **Catalysts** | NSAIDs reduce pain by reacting with enzymes (biological catalysts) that would normally produce the prostaglandins that cause the pain. Identifying enzymes as catalysts may be useful for students. |
| **Inhibitors** | Students may be familiar with catalysts which accelerate reactions, but they may be less familiar with the important role of inhibitors. Understanding the role of NSAIDs as chemical inhibitors may provide an important chemical lesson. |
| **Activation energy** | Cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) are examples of enzymes that accelerate the biochemical reaction of converting arachidonic acid into prostaglandins in the body. They do this by providing an alternate reaction path, with a lower activation energy, for the conversion reaction. |
| **Carboxylic acids** | Common carboxylic acids such as acetic or lactic acids are used as examples in teaching about organic acids. By comparing the carboxylic acid functional group on these with that of arachidonic acid, students could see the similarities and understand organic acids. |
| **Skeletal formulas** | Students can view the skeletal formulas used in the article to reinforce functional groups, single and double bonds, organic chemistry, and catalysts. The simplicity and ease of visualizing skeletal formulas, compared to either molecular or structural formulas, are emphasized. |
| **Reaction mechanisms** | By using the sequence of reactions required to convert arachidonic acid into prostaglandins, students can visualize how reaction mechanisms are dependent on precursors. Inhibiting any step prevents the reaction moving forward. |

# Teaching Strategies and Tools

## Standards

Links to **Common Core Standards for Reading**:

* + ELA-Literacy.RST.9-10.1:Cite specific textual evidence to support analysis of science and technical texts, attending to the precise details of explanations or descriptions.
	+ ELA-Literacy.RST.9-10.5: Analyze the structure of the relationships among concepts in a text, including relationships among key terms (e.g., force, friction, reaction force, energy).
	+ ELA-Literacy.RST.11-12.1:Cite specific textual evidence to support analysis of science and technical texts, attending to important distinctions the author makes and to any gaps or inconsistencies in the account.
	+ ELA-Literacy.RST.11-12.4: Determine the meaning of symbols, key terms, and other domain-specific words and phrases as they are used in a specific scientific or technical context relevant to grades 11-12 texts and topics.

Links to **Common Core Standards for Writing**:

* + ELA-Literacy.WHST.9-10.2F: Provide a concluding statement or section that follows from and supports the information or explanation presented (e.g., articulating implications or the significance of the topic).
	+ ELA-Literacy.WHST.11-12.1E: Provide a concluding statement or section that follows from or supports the argument presented.

In addition to the writing standards above, consider asking students to debate issues addressed in some of the articles. Standards addressed:

* **ELA-Literacy.WHST.9-10.1B.** Develop claim(s) and counterclaims fairly, supplying data and evidence for each while pointing out the strengths and limitations of both claim(s) and **counterclaims** in a discipline-appropriate form and in a manner that anticipates the audience’s knowledge level and concerns.
* **ELA-Literacy.WHST.11-12.1.A.** Introduce precise, knowledgeable claim(s), establish the significance of the claim(s), distinguish the claim(s) from alternate or opposing claims, and create an organization that logically sequences the claim(s), counterclaims, reasons, and evidence.

## Vocabulary

**Vocabulary** and **concepts** that are reinforced in this issue:

Physical properties

States of Matter

Structural Formulas

pH

Oxidation & Reduction

Enzymes

Intermolecular forces

* To help students engage with the text, ask students which article **engaged** them most and why, or what **questions** they still have about the articles.
* You might also ask them how information in the articles might affect their consumer choices. Also, ask them if they have questions about some of the issues discussed in the articles.

# Reading Supports for Students

The pages that follow include reading supports in the form of an Anticipation Guide, a Graphic Organizer, and Student Reading Comprehension Questions. These resources are provided to help students as they prepare to read and in locating and analyzing information from the article.

The borders on these pages distinguish them from the rest of the pages in this Teacher’s Guide—they have been formatted for ease of photocopying for student use.

* **Anticipation Guide (p. 8):**  The Anticipation Guide helps to engage students by activating prior knowledge and stimulating student interest before reading. If class time permits, discuss students’ responses to each statement before reading each article. As they read, students should look for evidence supporting or refuting their initial responses.

*NEW! Instead of using the aforementioned anticipation guide, consider these ideas to engage your students in reading.*

* Ask students to describe how they think painkillers work, then compare their ideas to the information in the article.
* Ask students what questions about painkillers they would like to have answered in the article.
* **Graphic Organizer (p. 9):**  The Graphic Organizer is provided to help students locate and analyze information from the article. Student understanding will be enhanced when they explore and evaluate the information themselves, with input from the teacher, if students are struggling. Encourage students to use their own words and avoid copying entire sentences from the article. The use of bullets helps them do this.

If you use the aforementioned organizers to evaluate student performance, you may want to develop a grading rubric such as the one below.

|  |  |  |
| --- | --- | --- |
| **Score** | **Description** | **Evidence** |
| 4 | Excellent | Complete; details provided; demonstrates deep understanding. |
| 3 | Good | Complete; few details provided; demonstrates some understanding. |
| 2 | Fair | Incomplete; few details provided; some misconceptions evident. |
| 1 | Poor | Very incomplete; no details provided; many misconceptions evident. |
| 0 | Not acceptable | So incomplete that no judgment can be made about student understanding |

* **Student Reading Comprehension Questions (p. 10-11):** The Student Reading Comprehension Questions are designed: to encourage students to read the article (and graphics) for comprehension and attention to detail; to provide the teacher with a mechanism for assessing how well students understand the article and/or whether they have read the assignment; and, possibly, to help direct follow-up, in-class discussion, or additional, deeper assignments.

Some of the articles in this issue provide opportunities, references, and suggestions for students to do further research on their own about topics that interest them.

To help students engage with the text, ask students which article **engaged** them most and why, or what **questions** they still have about the articles. The “Web Sites for Additional Information” section of the Teacher’s Guide provides sources for additional information that might help you answer these questions.

“Pain Relievers: How Do They Take Away Pain?” *ChemMatters*, February/March 2018

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

## Anticipation Guide

“A Close-up Look at the Quality of Indoor Air” (*ChemMatters*, April/May 2016 Issue)

**Directions: *Before reading the article*,** in the first column, write “A” or “D,” indicating your agreement or disagreement with each statement. As you read, compare your opinions with information from the article. In the space under each statement, cite information from the article that supports or refutes your original ideas.

|  |  |  |
| --- | --- | --- |
| **Me** | **Text** | **Statement** |
|  |  | 1. When you injure yourself, pain is caused by chemicals released by your body.
 |
|  |  | 1. NSAIDs (non-steroidal anti-inflammatory drugs) stop production of chemicals that cause pain.
 |
|  |  | 1. Enzymes increase the activation energy of chemical reactions.
 |
|  |  | 1. Enzymes are needed for most chemical reactions in our bodies.
 |
|  |  | 1. All three common over-the-counter NSAIDs have the same chemical structure.
 |
|  |  | 1. The side effects of NSAIDs include bleeding.
 |
|  |  | 1. Aspirin is recommended for children and teens.
 |
|  |  | 1. The pain-relieving effect of all NSAIDs is the same.
 |
|  |  | 1. Unlike NSAIDs, acetaminophen contains nitrogen.
 |
|  |  | 1. Acetaminophen can help reduce swelling.
 |

## Graphic Organizer

Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

“Pain Relievers: How Do They Take Away Pain?” *ChemMatters*, February/March 2018

**Directions**: As you read the article, complete the graphic organizer below to describe the chemicals involved in producing and relieving pain.

.

|  |  |  |
| --- | --- | --- |
| **Chemicals** | **Examples** | ***What do they do?*** |
| **Prostaglandins**  |  |  |
| **Enzymes** |  |  |
| **Competitive inhibitors (painkillers)** | 1. |  |
| 2. |  |
| 3. |  |

**Summary:** On the back of this paper, write a short (15-18 words) one-sentence summary of the article.

## Student Reading Comprehension Questions

“Pain Relievers: How Do They Take Away Pain?” *ChemMatters*, February/March 2018

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Name

**Directions**: Use the article to answer the questions below.

* 1. What does the acronym NSAID stand for?
	2. List three common NSAID medicines.
	3. What are prostaglandins?
	4. List five different roles that prostaglandins have in the body.
	5. What molecule is the source of all prostaglandins in the body?
	6. How do NSAIDs relieve pain in the body?

**Student Reading Comprehension Questions, cont.**

“Pain Relievers: How Do They Take Away Pain?” *ChemMatters*, February/March 2018

* 1. Explain how NSAIDs act as competitive inhibitors.
	2. Analyze the chemical structures of the pain relievers in Figure 2, and describe how the ring structure is different in one of them.
	3. Why should teens and children avoid taking aspirin?
	4. (a) What are enzymes, (b) how do they work, and (c) why are they important in our body?
	5. Complete the table below comparing/contrasting these pain relievers.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Property** | **Naproxen** | **Aspirin** | **Ibuprofen** | **Aceta-minophen**  |
| Is this an NSAID? (yes/no) |  |  |  |  |
| List side effects (from article) |  |  |  |  |
| Longer lasting? (yes/no) |  |  |  |  |
| Treats swelling and clotting? (yes/no) |  |  |  |  |
| Treats pain and fever? (yes/no) |  |  |  |  |
| Inhibits prostaglandin formation? (yes/no) |  |  |  |  |
|  |  |  |  |  |

## Answers to Student Reading Comprehension Questions

1. **What does the acronym NSAID stand for?**

*The acronym NSAID stands for* ***n****on-****s****teroidal* ***a****nti-****i****nflammatory* ***d****rug.*

1. **List three common NSAID medicines.**

*Three common NSAID medicines are naproxen, ibuprofen, and aspirin.*

1. **What are prostaglandins?**

*Prostaglandins are chemicals, released by injured cells, which trigger pain.*

1. **List five different roles that prostaglandins have in the body.**

*Five different roles that prostaglandins have in the body include*

* 1. *pain,*
	2. *swelling,*
	3. *fever,*
	4. *regulating blood pressure, and*
	5. *blood clotting.*
1. **What molecule is the source of all prostaglandins in the body?**

*All prostaglandins in the body come from the molecule arachidonic acid.*

1. **How do NSAIDs relieve pain in the body?**

*NSAIDs relieve pain in the body when they stop the production of prostaglandins by inhibiting the arachidonic acid pathway.*

1. **Explain how NSAIDs act as competitive inhibitors.**

*NSAIDs act as competitive inhibitors by competing with the arachidonic acid for cyclooxygenase and binding with the cyclooxygenase so the arachidonic acid cannot form prostaglandins.*

1. **Analyze the chemical structures of pain relievers in Figure 2, and describe how the ring structure is different in one of them.**

*The ring structure of the pain reliever naproxen is different than the others because it contains two rings, while the other three contain only one ring.*

1. **Why should teens and children avoid taking aspirin?**

*Teens and children should avoid taking aspirin because its use is linked to Reye's syndrome, which could cause life-threatening liver and brain swelling.*

1. **(a) What are enzymes, (b) how do they work, and (c) why are they important in our body?**
2. *Enzymes are biological catalysts,*
3. *they work by speeding up chemical reactions; they do this by providing a new path that lowers activation energy required, and*
4. *they are important in our body because without them, most chemical reactions in the human body would be very slow, if they’d happen at all.*
5. **Complete the table below comparing/contrasting these pain relievers.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ***Property*** | ***Naproxen*** | ***Aspirin*** | ***Ibuprofen*** | ***Aceta-minophen***  |
| ***Is this an NSAID? (yes/no)*** | ***yes*** | ***yes*** | ***yes*** | ***no*** |
| ***List side effects(from article)*** | ***digestive irritation and bleeding***  | ***digestive ulcers and bleeding*** | ***digestive irritation and bleeding*** | ***none listed in article*** |
| ***Longer lasting? (yes/no)*** | ***yes*** | ***no*** | ***no*** | ***no*** |
| ***Treats swelling and clotting? (yes/no)*** | ***yes*** | ***yes*** | ***yes*** | ***no*** |
| ***Treats pain and fever? (yes/no)*** | ***yes*** | ***yes*** | ***yes*** | ***yes*** |
| ***Inhibits prostaglandin formation? (yes/no)*** | ***yes*** | ***yes*** | ***yes*** | ***yes*** |

# Possible Student Misconceptions

1. **“Sometimes people must learn to live with pain.”** *Occasionally this may be true for some chronic cases; however, for the majority of people, there are many options for managing either acute or chronic pain. Of course, there are numerous pain medications such as the NSAIDs, but there are other medications (some, much stronger) as well. The choice of pain medication to use depends on the type and location of the pain, the severity of the pain, and the side effects of the medication. In addition to traditional medicine, other options for relieving pain include relaxation techniques, physical therapy, surgery, acupuncture, massage, and injections. While total elimination of pain may not always be possible, pain reduction or pain management is possible.*
2. **“Comparable injury produces similar pain in different people.”** *Pain is unique to each individual; it is multidimensional and based on physical and psychosocial factors. When people touch a hot object, they feel pain. However, the intensity of the pain and the perception of that pain varies with each individual. Factors such as the thickness of the skin, previous injuries to that part of the body, previous burns to that area, mental status, perception of the possible danger, previous prolonged pain, etc. cause highly individual pain responses.*
3. **“Pain does not physically damage the body, so it can be ignored.”** *Pain takes both an emotional and a physical toll on our bodies. Physically, pain can increase respiratory rate, blood pressure, heart rate, and muscle tension. Emotionally, pain (especially chronic pain) can produce feelings of frustration, resentment, and stress—all of which can affect attitudes, relationships, and activities. The physical effects of pain on the body can lead to fatigue, sleeplessness, and changes in appetite, which can all be damaging in the long term. Any pain that persists or intensifies should not be ignored.*

# Anticipating Student Questions

1. **“Is the saying 'No pain, no gain' true?”** *Many bodybuilders and athletes believe this myth, but there is no evidence to support it. Trying to build strength or muscles by exerting them to the point of pain is not wise. Also, the thought of working or pushing through pain is not accurate, either. Pain is an indication of damage to the body, and wise people heed that warning.*
2. **“Why does pain exist?”** *While pain is no fun, it has an important role in our lives. Pain is a defense mechanism that has evolved to alert us to injury. Our response to this pain allows us to protect our bodies from further damage. Because pain is an autonomic response (pain reflex), it allows us to react efficiently and quickly, avoiding additional injury. Pain is usually the quickest and most effective way of getting our attention and forcing us to modify our behavior accordingly.*
3. **“Can the use of pain medications lead to addictions?”** *There are many types of pain medications, and all medications carry some risk of use. Addictions can be either physical or psychological. The NSAIDs discussed in the article are not physically addictive, although they may cause other medical concerns if used for a prolonged time. However, pain medications like opioids are addictive. Physical addictions occur when the cells in the body need the substance to function, and withdrawal produces tremors, nausea, diarrhea, chills, and body aches. Psychological addictions are associated with the perceived need to use the substance. Sometimes people think they need a substance in order to fall asleep, but they can eventually fall asleep without the drug. It is possible that some people may develop a psychological dependency on any painkiller medication.*

# Activities

**Labs and demos**

**Lab synthesizing aspirin:** Students in a well-equipped high school laboratory can synthesize aspirin using the college general chemistry lab procedure, “Synthesis of Aspirin.” The procedure provides student information to synthesize, recrystallize, and test the purity of aspirin, which requires multiple classroom periods to complete; however, there are no instructor notes provided. (<http://www.chem21labs.com/labfiles/uky_gl04_lab.pdf>; link to supporting information: <https://genchemlab.wordpress.com/5-aspirin/>)

**Virtual lab on enzymes:** “Enzyme Lab–Virtual” provides students the opportunity to study the effects of substrate concentration and pH on the rate of an enzyme-catalyzed reaction. The site includes a student sheet for collecting data and analysis questions. (<https://www.biologycorner.com/worksheets/enzyme-lab-virtual.html>)

**Simulations**

**Simulation of enzyme activity and inhibitors:** The KScience Web site provides an animation of enzyme action and a student-controlled simulation, investigating the effects of the concentrations of enzymes, substrate, inhibitors, temperature, container size, and pH. (<http://www.kscience.co.uk/animations/anim_2.htm>) An independent student data sheet for the KScience simulation is located at <http://www.sennhs.org/ourpages/auto/2014/12/18/42764837/Enzyme%20Simulation%20Lab%20HON.pdf>.

**Simulation of enzymes and concentrations:** This simple simulation allows students to manipulate only the type of enzyme (anabolic or catabolic) and substrate concentration (high or low), but it may be useful to help students with the concept of enzymatic action. (<https://scratch.mit.edu/projects/32615728/>)

**Media**

 **Video drawing skeletal structures:** “Drawing Skeletal Structures or Bond-Line Notations of Organic Molecules” (Organic Chemistry Basics) (14:53) clearly explains the process of drawing and interpreting skeletal structures for students who may be unfamiliar with these structures in the Hendricks-Sturrup article. (<https://www.youtube.com/watch?v=RP6AS7XVIC8>)

**Infographic of common painkillers:** The Compound Interest Web site contains the infographic "A Brief Guide to Common Painkillers", illustrating NSAID and opioid painkillers. In addition to the infographic, the site also includes brief information on these drugs. (<http://www.compoundchem.com/2014/09/25/painkillers/>)

**Lessons and lesson plans**

**Khan Academy lessons on enzymes:** *Introduction to Enzymes* is a lesson sequence that includes the video, "Introduction to Kinetics" (15:26), a reading activity, "Activation Energy," the video, "Enzymes" (8:12), another reading activity, "Enzymes and the Active Site," and a one-question assessment, "Practice: Enzymes and Activation Energy." (<https://www.khanacademy.org/science/biology/energy-and-enzymes/introduction-to-enzymes/v/introduction-to-kinetics>)

**Lab lessons on pain and pain reduction:** “No Pain, No Gain” is a complete teacher and student lesson for conducting a three-day activity on pain perception and reduction. The lesson from the National Association of Biology Teachers includes some useful line drawings and is an excellent lesson plan. (<https://www.nabt.org/files/galleries/09NLCAchp7.pdf> Note: The reference to the (optional) *NIH Image* computer program in the lesson is no longer available.)

**Projects and extension activities**

**Presentations on NSAIDs:** Divide students into four groups (aspirin, acetaminophen, ibuprofen, and naproxen) to research and prepare a visual (PowerPoint, poster, video, brochure, etc.) presentation on their NSAID drug. The presentations should include history, benefits, risks, uses, alternatives, and pharmacology/chemistry of their pain reliever.

**Research on Vioxx®:** Student can research why the effective COX-2 NSAID pain reliever Vioxx**®** was removed from sale in the U.S. in 2004. Students can compare the chemical structure, mode of action, side effects, and effectiveness of Vioxx**®** to the other common NSAIDs still in use.

**Lab experiments with aspirin:** "Experiments with Aspirin" is an AP or second-year high school lab activity that involves the synthesis and characterization of aspirin, the kinetics of the hydrolysis of aspirin, and the synthesis of copper(II) aspirinate and copper(II) salicylate. The article provides a generic description of the procedure, and the extensive supplemental material is accessed via an online link in the article. (<http://pubs.acs.org/doi/pdf/10.1021/ed077p354>)

# References

**The references below can be found on the *ChemMatters* 30-year DVD, which includes all articles
published from the magazine’s inception in October 1983 through April 2013; all available Teacher’s Guides, beginning February 1990; and 12 *ChemMatters* videos. The DVD is available from the American Chemical Society for $42 (or $135 for a site/school license) at this site:** [**http://ww.acs.org/chemmatters**](http://www.acs.org/chemmatters)**. Click on the “Teacher’s Guide” tab to the left, directly under the “*ChemMatters Online"* logo and, on the new page, click on “Get the past 30 Years of *ChemMatters* on DVD!” (the icon on the right of the screen)**

**Selected articles and the complete set of
Teacher’s Guides for all issues from the past three
years are available free online at the same Web site, above. Click on the “Issues” tab just below the logo, *“ChemMatters Online”*.**

***30* Years of *ChemMatters !***

Available Now!

 This 1993 article on aspirin contains a nice diagram with chemical structures on salicylates. It also provides an activity testing different types of aspirin compounds in a simulated stomach with acidic, basic, and neutral solutions. (Marcella, G. Aspirin. *ChemMatters*, 1993, *11* (1), pp 4–7)

 A 2004 article discusses pain, aspirin, NSAIDs, prostaglandins, and the mechanism of pain relief. This article also includes a brief history of aspirin and the other NSAIDs. (Kimbrough, D. The Aspirin Effect: Pain Relief and More. *ChemMatters*, 2004, *22* (1), pp 7–9)

 The February 2004 Teacher's Guide for “The Aspirin Effect: Pain Relief and More" (above) provides background information on the discoveries of aspirin, acetaminophen, ibuprofen, naproxen prostaglandins, and cyclooxygenase.

 This article about digestion has general information and two useful figures on how enzymes work by lowering activation energy. (Tinnesand, M. The Dog Ate My Homework. *ChemMatters*, 2006, *24* (2), pp 4–6)

 This brief *Did You Know?* article, "Organic Chemistry/Proteins: New Type of Painkiller from Sea Snails," describes a new family of painkillers made from polypeptides. (Karabin, S. Organic Chemistry/Proteins: New Type of Painkiller from Sea Snails. *ChemMatters*, 2011, *29* (4), p 4)

 This *ChemMatters* article includes an activity to test how quickly different pain relievers dissolve in an acidic solution simulating the stomach. The activity tests the brand-name NSAID pain relievers Motrin, Aleve, Tylenol plus aspirin. (Washam, C. Brand-Name vs. Generic Drugs. *ChemMatters*, 2013, *31* (1), pp 8–10)

 Painkillers made from snake venom and a little more about sea snail painkillers is found in "Venoms: From Lethal to Life Saving." The painkiller made from snake venom may be as effective as morphine. (Haines, G. Venoms: From Lethal to Life Saving. *ChemMatters*, 2015, *33* (2), pp 13–15)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

 This article describes an experiment to determine the ibuprofen concentration of an over-the-counter liquid-filled gelatin capsule. The procedure is for a first-year college chemistry course and would require access to a UV-Vis spectrometer. (Wheate, N, et. al. Determining the Ibuprofen Concentration in Liquid-Filled Gelatin Capsules to Practice Collecting and Interpreting Experimental Data, and Evaluating the Methods and Accuracy of Quality Testing. *J. Chem. Educ.*, 2017, *94* (8), pp 1107–1110; <http://pubs.acs.org/doi/10.1021/acs.jchemed.6b00955>. Note that this link takes you to a brief abstract only, the full article is only available to American Chemical Society members or subscribers to the journal.)

 The anti-inflammatory activity of freshly pressed extra-virgin olive oil is similar to that of ibuprofen. Details of the compound, oleocanthal, and its discovery are in this article. (Ritter, S. Olive Oil Compound Acts Like Ibuprofen. *Chem. Eng. News.*, 2005, *83* (36), p 15; <http://pubs.acs.org/doi/pdf/10.1021/cen-v083n036.p015a>. Note that this link takes you to a brief abstract only, the full article is only available to American Chemical Society members or subscribers to the journal.)

 Readers with access to a UV-Vis spectrometer can follow the procedure in this article to study the time release of acetaminophen from gel capsules. The article is suitable for first-year college and high school laboratories. (Smith, K., Cedillo, D. Determining the Mass and Time Release of Acetaminophen from Gel Capsules. *J. Chem. Educ.*, 2014, *91* (3), pp 437–439; <http://pubs.acs.org/doi/10.1021/ed400324k>. Note that this link takes you to a brief abstract only, the full article is only available to American Chemical Society members or subscribers to the journal.)

 This article from 1989, gives a thorough explanation of activation energy, and it clarifies some possible misconceptions associated with reaction mechanisms of catalyzed and uncatalyzed reactions. (Haim, A. Catalysis: New Reaction Pathways, Not Just a Lowering of the Activation Energy. *J. Chem. Educ.*, 1989, *66* (11), pp 935–937; <http://pubs.acs.org/doi/pdf/10.1021/ed066p935>. Note that this link takes you to a brief abstract only, the full article is only available to American Chemical Society members or subscribers to the journal.)

 *Chemical and Engineering News* published a cover story, "How Chemists Are Responding to the Opioid Epidemic," which contains sections on "Abuse-Deterrent Opioids: Worth the Cost and Effort?", "Powerful Detection Technology for Powerful New Street Drugs", and "Looking beyond Opioids for Safer Pain Relief". The graphics, information, and chemistry in these pieces provide insight into the troublesome problem of misuse of opioid pain relief drugs. (Nguyen, T; Hiolski, E; Halford, B. How Chemists Are Responding to the Opioid Epidemic. *Chem. Eng. News*, 2017, *95* (45), p 32–42; <https://cen.acs.org/articles/95/i45/chemists-responding-opioid-epidemic.html>; note that this link takes you to a brief abstract only, the full article is only available to American Chemical Society members or subscribers to the journal.)

# Web Sites for Additional Information

**Pain**

 The *WebMD* Web site provides detailed information on pain types and causes. The article includes sections on "Acute and Chronic Pain," "Other Ways Pain Is Classified," "Pain Caused by Tissue Damage," and "Pain Caused by Nerve Damage." ([https://www.webmd.com/pain-management/guide/pain-types-and-classifications#1](https://www.webmd.com/pain-management/guide/pain-types-and-classifications%231))

 "How Do Pain Relievers Work?" (4:13) on the *TED-Ed* Web site is a powerful video explaining pain, nociceptors, prostaglandins, competitive inhibitors, and more. It is a great companion piece to the Hendricks-Sturrup article. (<https://ed.ted.com/lessons/how-do-pain-relievers-work>)

**Arachidonic acid**

 Body Nutrition publishes "Arachidonic Acid Benefits and Side Effects." The article examines arachidonic acid when it is used as a supplement by athletes to build muscle mass. However, caution must be used when consuming any supplement. (<https://bodynutrition.org/arachidonic-acid/>)

 The role of arachidonic acid in forming the regulatory molecules called eicosanoids and their importance in homeostasis and inflammation is described and illustrated in "Paracrines Derived from Polyunsaturated Fatty Acids." (<https://courses.washington.edu/conj/membrane/arachidonic.htm>)

**Prostaglandins**

 "Prostaglandins and Inflammation" provides a scholarly discussion of the mechanisms of prostaglandin formation and their roles in inflammation. In addition, prostaglandins are relevant in atherosclerosis and the article includes information on this topic. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3081099/>)

The Society for Endocrinology hosts the Web page “You and Your Hormones,” which contains information on prostaglandins. The article is short and relatively easy to read. (<http://www.yourhormones.info/hormones/prostaglandins/>)

**Cyclooxygenase**

 A slide presentation converted to a pdf document, "Cyclooxygenase and NSAIDs," highlights information on the relationship among cyclooxygenase enzymes, prostaglandins, and NSAIDs. The colorful presentation enhances the Hendricks-Sturrup article. (<http://www.albany.edu/faculty/cs812/bio366/Cyclooxygenase_ppt.pdf>)

 Cyclooxygenase was a “Molecule of the Month” on the *Protein Data Bank* Web site. The article explains cyclooxygenase, prostaglandins, and how aspirin works with these materials. (<http://pdb101.rcsb.org/motm/17>)

**Nociceptors**

 For a visual and textual explanation of pain and the role of nociceptors, see the University of Texas McGovern Medical School article, "Chapter 6: Principles of Pain." The article shows and discusses the types of nociceptors and factors that activate them, along with other information about pain. (<http://nba.uth.tmc.edu/neuroscience/s2/chapter06.html>)

 "Nociceptors and the Perception of Pain" is a 153-page comprehensive explanation of the nociceptors. The eight chapters in the publication include "Introduction," "Chemical Mediators," "Neuropathic Pain," and "Pain in the Brain." (<https://cell.uchc.edu/pdf/fein/nociceptors_fein_2012.pdf>)

**NSAIDs**

 The *Medical News Today* Web site provides the article, "NSAIDs: Examples, Side Effects, and Uses," which supplements the information in the Hendricks-Sturrup article. The article includes information on how NSAIDs work, precautions, side effects, and some fast facts on them. (<https://www.medicalnewstoday.com/articles/179211.php>)

 For a thorough understanding of NSAIDs, readers can access "An Evidence-Based Update on Nonsteroidal Anti-Inflammatory Drugs". Although the article was published in 2007, it contains deeper content and extensive references. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1855338/>)

**Safety of NSAIDs**

 The Harvard Medical School provides additional information on the safety of taking NSAIDs in "Pain Relief: Taking NSAIDs Safely." The article contains information on NSAID cautions, tips for using them safely, and alternatives to NSAIDs. (<https://www.health.harvard.edu/pain/pain-relief-taking-nsaids-safely>)

 Also from the Harvard Medical School is the article "10 Things You Should Know about Common Pain Relievers." Information on understanding the differences between NSAIDs and acetaminophen, over-the-counter pain relievers, and prescription NSAIDs are provided on the site. (<https://www.health.harvard.edu/pain/12-things-you-should-know-about-pain-relievers>)

**NSAID method of action**

 The mechanism of action of NSAIDs is explained in "Pharmacology of NSAIDs". Visuals and a general explanation of the competitive inhibition by NSAIDs help readers understand the action of these drugs. (<https://pharmafactz.com/pharmacology-of-nsaids/>)

 "Non-Steroidal Anti-inflammatory Drugs (NSAIDs)" is a 2002 article with a clinical explanation of NSAIDs and their mechanism of action. Additional information includes details on salicylates, profens, anthranilates, COX-2 inhibitors, and much more. (<http://www.auburn.edu/~deruija/nsaids_2002.pdf>)

**Information on Individual NSAIDs**

* **Aspirin**

 The NIH Web site, MedlinePlus, has a consumer-friendly article for aspirin that contains information on why it is prescribed, how it is used, special precautions, side effects, and other information. To prevent overdoses of aspirin, a list of brand names of combined medicines containing aspirin is provided. (<https://medlineplus.gov/druginfo/meds/a682878.html>)

 In addition to its use as a pain reliever, aspirin is widely used to reduce the risk of heart attack and stroke. The U.S. FDA supplies the article, "Aspirin for Reducing Your Risk of Heart Attack and Stroke: Know the Facts," to educate consumers on the risks and benefits of using aspirin. (<https://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/UnderstandingOver-the-CounterMedicines/SafeDailyUseofAspirin/ucm291433.htm>)

* **History of aspirin**

 *Chemical and Engineering News* featured an article on aspirin in 2005 as part of “The Top Pharmaceuticals That Changed the World.” The article provides information on its then-current uses, classification as an NSAID, ancient origin in willow and myrtle trees, and its formulation by Felix Hoffman at Bayer into the modern form as we know it. (<https://pubs.acs.org/cen/coverstory/83/8325/8325aspirin.html>)

 The Chemical Heritage Foundation published a history of aspirin titled, "Aspirin: Turn-of-the-Century Miracle Drug" in its summer, 2009 issue of *Distillations* magazine. The article highlights the 2,000-year history of salicylic acid and aspirin, and the chemical secrets of aspirin that were not uncovered until the 1970s. (<https://www.chemheritage.org/distillations/magazine/aspirin-turn-of-the-century-miracle-drug>)

* **Reye's Syndrome and aspirin**

 The National Reye's Syndrome Foundation's Web site has links to a vast number of resources and links to further information on this disease. Links include "What Is Reye's Syndrome?", "After Reye's Syndrome," "The Aspirin Link," "Reye's and Teens," "Aspirin Lists," "Article Library," "Medical Library," "Video Library," and more. (<http://www.reyessyndrome.org/index.html>)

* **Acetaminophen**

 The U.S. National Institutes for Health's (NIH) Web site, *MedlinePlus*, provides consumer-friendly information on acetaminophen, including health warnings, how it should be used, precautions, side effects, and much more. Because acetaminophen overdoses can easily occur due to the drug being combined with other medicines, a list of brand names of these combination products is provided. (<https://medlineplus.gov/druginfo/meds/a681004.html>)

 The U.S. Food and Drug Administration (FDA) Web site has a page, “Acetaminophen Information,” with links to numerous articles for the safe use of this medication. (<https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm165107.htm>)

* **Ibuprofen**

 Similar to acetaminophen and aspirin, the MedlinePlus Web page has an article on ibuprofen for consumers. Again, warnings, usage, special precautions, side effects, and other information are supplied. The list of combined medicines containing ibuprofen is shorter but included. (<https://medlineplus.gov/druginfo/meds/a682159.html>)

 “An Overview of Clinical Pharmacology of Ibuprofen" provides an in-depth explanation of ibuprofen. Since ibuprofen's introduction in 1969, it has been a popular analgesic, and this article looks at the pharmacology, applications, and adverse reactions. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3191627/>)

* **Naproxen**

 MedlinePlus continues with a page devoted to naproxen containing information similar to the other NSAIDs on warnings, why it's prescribed, usage, special precautions, side effects, and a short list of brand name combination drugs. (<https://medlineplus.gov/druginfo/meds/a681029.html>)

 The Drugs.com Web site has its page devoted to naproxen with the tabs for information including "Overview," "Side Effects," "Dosage," "Professional," "Tips," and "Interactions." The "Professional" tab includes information on pharmacology, chemical structure and properties, excretion, and more. (<https://www.drugs.com/pro/naproxen.html>)

**Choosing an NSAID pain reliever**

 *Business Insider* published a chart to help people determine which NSAID painkiller to take for a specific ailment or pain. The easy-to-use chart provides a "thumbs up" painkiller for problems including fever, headache, menstrual cramps, sore muscles, earaches, and toothaches. (<http://www.businessinsider.com/tylenol-vs-advil-vs-aleve-2015-5>)

 "OTC: Taking the Pain Out of Choosing a Pain Reliever" from the UC San Diego Health Wed site offers six questions with discussions for selecting an effective OTC (over-the-counter) pain reliever. (<https://health.ucsd.edu/news/features/Pages/2016-12-21-otc-pain-relief-meds.aspx>)

**Opioid and narcotic pain relievers**

 The U.S. FDA's Web site, "Opioid Medications," contains links to many articles related to opioid or narcotic medications used as painkillers. Links include: "Information on Opioid Medications," "Treating Pain," "Consumer Information," "FDA's Role in Preventing Opioid Abuse," and more. (<https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm337066.htm>)

 The Drugs.com Web site provides the article "Narcotic Analgesics" and a list of brand-name and generic-name narcotic analgesics. Click on the name of each of these drugs to link to additional information on that narcotic (opioid) drug. (<https://www.drugs.com/drug-class/narcotic-analgesics.html>)

**Pain relief alternatives**

 "Natural Anti-inflammatory Agents for Pain Relief" includes a review of the literature about the pathways of inflammatory pain in the body, the potential side effects of NSAIDs, and commonly-used and clinically-studied natural alternatives to these drugs. Alternatives include the omega-3 essential fatty acids (in fish oil), white willow bark, turmeric, green tea, chili pepper, and others. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3011108/>)

 The Harvard Medical School's Web site discusses "8 Non-invasive Pain Relief Techniques that Really Work." These techniques include the use of cold or heat, exercise, physical therapy, mind-body techniques, massage, and others. (<https://www.health.harvard.edu/pain/8-non-invasive-pain-relief-techniques-that-really-work>)

**Activation energy**

 A thorough explanation of activation energy, the Arrhenius Law, effects of enzymes, and Gibbs energy are found on the LibreTexts Chemistry site. Diagrams, formulas, problems, and solutions are on the site as well. (<https://chem.libretexts.org/Core/Physical_and_Theoretical_Chemistry/Kinetics/Modeling_Reaction_Kinetics/Temperature_Dependence_of_Reaction_Rates/The_Arrhenius_Law/The_Arrhenius_Law%3A_Activation_Energies>)

 The Study.com Web site's lesson, "Function of Enzymes: Substrate, Active Site, & Activation Energy," provides a lesson that is presented in a video, lesson text, and a quiz. Information in this lesson complements the discussion of enzymes and activation energy in the Hendricks-Sturrup article. (<http://study.com/academy/lesson/function-of-enzymes-substrate-active-site-activation-energy.html>; note that a free trial registration is required to access the content.)

**Enzymes**

 The Royal Society of Chemistry has an excellent Web site, *Enzymes*, with the subsections: "Function and Structure," "How Enzymes Work," "Factors Affecting Catalytic Activity of Enzymes," "Immobilized Enzymes," and "Test Your Knowledge." The explanations and illustrations are simple and clear. (<http://www.rsc.org/Education/Teachers/Resources/cfb/enzymes.htm>)

 "The Virtual Laboratory: Enzyme Assay" is a more complex activity than “Enzyme Lab–Virtual” in the Labs and Demos section above. The Enzyme Assay lab allows students to manipulate the effects of pH, time, enzyme quantity, temperature, and substrate concentration for five different enzymes with the results graphed and the ability to export the virtual data to Excel for further manipulation. (<http://www.ucl.ac.uk/~ucbcdab/enzass/enzymass.htm>)

**Inhibitors**

 The LibreText Chemistry Web page presents "Drugs as Enzyme Inhibitors," which complements the Hendricks-Sturrup article very well. Penicillin is used as an example of an inhibitor interfering with the action of an enzyme similar to the action of NSAIDs. ([https://chem.libretexts.org/Textbook\_Maps/Organic\_Chemistry\_Textbook\_Maps/Map%3A\_Organic\_Chemistry\_(Bruice)/31%3A\_The\_Organic\_Chemistry\_of\_Drugs%3A\_Discovery\_and\_Design/31.07%3A\_Drugs\_as\_Enzyme\_Inhibitors](https://chem.libretexts.org/Textbook_Maps/Organic_Chemistry_Textbook_Maps/Map%3A_Organic_Chemistry_%28Bruice%29/31%3A_The_Organic_Chemistry_of_Drugs%3A_Discovery_and_Design/31.07%3A_Drugs_as_Enzyme_Inhibitors); note: readers may need to register for free to access some information.)

 The Khan Academy supplies a great lesson, "Enzyme Regulation." The content explains cofactors and coenzymes; reversible, irreversible, competitive, and noncompetitive inhibitors; allosteric enzymes; and feedback inhibition, with diagrams and text. (<https://www.khanacademy.org/science/biology/energy-and-enzymes/enzyme-regulation/a/enzyme-regulation>)

**Skeletal formulas**

 "Drawing Organic Molecules" provides readers with reviews on molecular formulas, structural formulas, and skeletal formulas. Text and diagrams help readers understand the purpose for each and a discussion of how to decide which formula to use. (<http://www.chemguide.co.uk/basicorg/conventions/draw.html>)

 Newcastle University in the United Kingdom shares a colorful and simple guide to skeletal formulas. "Basic Guide to Skeletal Formulae" is a quick way to review or learn about these types of organic formulas. (<http://www.ncl.ac.uk/media/wwwnclacuk/schoolofchemistry/files/C1-basicguidetoskeletalformula_000.pdf>)

# About the Guide

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Articles from past issues of *ChemMatters* and related Teacher’s Guides can be accessed from a DVD that is available from the American Chemical Society for $42. The DVD contains the entire 30-year publication of *ChemMatters* issues, from February 1983 to April 2013, along with all the related Teacher’s Guides since they were first created with the February 1990 issue of *ChemMatters*.

The DVD also includes Article, Title, and Keyword Indexes that cover all issues from February 1983 to April 2013. A search function (similar to a Google search of keywords) is also available on the DVD.

The *ChemMatters* DVD can be purchased by calling 1-800-227-5558. Purchase information can also be found online at <http://tinyurl.com/o37s9x2>.