Drug Interactions in the Liver and the Resulting Implications for Aquatic Organisms

by Phil H Carver, 2017 CTI Fellow
James Martin Middle School

This curriculum unit is recommended for:
8th Grade Integrated Science

Keywords: Metabolite, Metabolism, Enzymes, Drug, Nano, Biotransformation, Excretion, Absorption, Distribution, Liver, Water Pollution, Law of Conservation of Mass, Chemistry, Chemical Equations Balancing Equations, Hepatic System, Liver Function.

Teaching Standards: See Appendix 1 for teaching standards addressed in this unit.

Synopsis: This curriculum unit includes research and information for the middle school and high school teacher regarding prescription drugs' chemical processes in the human body, drug development, drug residue in our water supply, and wastewater treatment while treating drug residue. I teach an integrated 8th grade science class which covers almost all of the science disciplines. This teaching unit is a five-day unit, which can be dispersed throughout the year, or can be used for a testing review at the end of the year. There are 5 activities described in detail, along with teaching strategies and methods. All my activities include inquiry based learning. Vocabulary words are also included along with an annotated bibliography and instructions on how to integrate the teaching standards, with the rationale and research included. I teach a diverse population of students in a high-needs school and I believe this unit will help assist teachers and students to make connections with topics such as chemistry, water quality, and how drug compounds are broken down, added to, and rearranged by body systems, such as the hepatic system.

I plan to teach this unit during the coming year to 115 students in 8th Grade Integrated Science using North Carolina Standards.

Introduction

While browsing the internet and searching for engaging 8th grade science activities and lessons related to the standards I teach, I discovered some emerging research regarding the subject of prescription drug residue in the world's drinking water. As I researched, I discovered this pollution comes from the elimination of prescription drug waste from the body and the dumping of expired drugs down the toilet. Drugs released into our water supply can cause problems for aquatic life, whether they travel through the kidneys or liver, or just get dumped down the toilet.

Drug residue also travels into the drinking from other places, such as farm runoff and the actual manufacture of the drug itself. In this Curriculum Unit (CU), I will primarily be discussing the biotransformation of prescription drugs and medicines in the human body and the implications waste water treatment and for aquatic life.

This new research involves dealing with human and animal waste, drinking water, and sewage treatment and the effects (both unknown and proven) on micro and macro organisms in our environment. Some preliminary research has revealed potential consequences in the future for the environment. So, the topics involving the chemical makeup of drugs, the design and research of drugs, and how drugs are disposed of and treated at wastewater plants, will be explored. Processes in which the liver tears apart drug molecules, how it metabolizes the drug, and eliminates them through the digestive system will be explored in this CU. The subject of drug residue and the environmental affects has been explored in blogs, particularly in University research blogs.

Unit Goals

My goal in this CU is not to condemn or judge drug manufactures or water treatment plants, but to educate the teacher of how drug residue relates to 8th grade science topics such as chemical reactions, the formation of new compounds in the liver, the human microbiome, and water conservation. I intend to integrate this research into the 8th grade North Carolina Science Standards.

Demographics of students at James Martin Middle School

I teach at an inner city middle school with a diverse population of 60% African American and 40% Hispanic students. The student body is transient with some living in hotels and extended stay motels. Standardized test scores are low and my school is a designated a high impact school. This means that financial and curriculum support is in place. Any activities I can design that can keep the students away from their cell phones and relates to everyday life is important in capturing the attention of these high needs students.

North Carolina 8th Grade Essential Standards

The topic of drug residue in drinking water contains data and information can relate to North Carolina 8th Grade science standards. Below is a short list of topics:

- Evidences of Chemical reactions
- Elements, Compounds and molecules
- Food energy and Digestion
- Biotechnology in North Carolina
- Infectious Diseases.

This CU can easily be integrated into the North Carolina Middle Grades Curricula. Antibiotics, vaccines, infectious disease drugs are discussed in the 8th grade, as are other drugs that are released into our water supply. I believe this CU is the perfect opportunity to educate the average middle school teacher and relate this issue to the 8th grade curriculum. The reader of this unit will need some background information related to the standards and academic level of their students to teach this unit. A key component of this CU will include; determination of the evidences of chemical reactions that occur in the liver as it processes and chemically changes the drug molecules. Other key components will include an overview of the process of drug development, FDA procedures, and an elementary breakdown of elements used and reasoning behind the selection of certain elements.

Biotransformation in the liver is another term that will be researched in this unit. Primarily, I am writing generally about drug interactions in the human body with details about drug development, molecular design, elements, compounds, molecules, metabolism chemical reactions, and drug interactions. Potential liver damage by the drugs themselves will be covered as well as facts such as the number of elements in a typical drug molecule and the reasons behind the choice of the elements and design of molecules will also to be discussed in a manner that can be useful to the typical middle school teacher. Also, basic vocabulary words such as enzymes, activators, inhibitors, catalysts, and metabolism will be addressed.

Also, the teacher will be informed about processes such as basic liver and kidney functions, liver and kidney functions in eliminating drugs from the body, emerging research with regards to drugs and water pollution. I hope to educate teachers about the possible side-effects that may occur within micro and macro organisms in the environment. I have attempted to present the activities and research in a format that can be useful and easy to implement for Middle Grades.

Teaching Strategies

This CU provides fun classroom experiments and demonstrations, and should be used to motivate students to write good sentences, paragraphs, and essays. The teacher should integrate collaboration, problem solving, research, writing, using writing prompts, and sharing information in any lesson plan. Using 21st Century Learning skills such as communication, collaboration, and media technology skills are necessary in order for students to be able to analyze and complete inquiry based projects. The ability to analyze and write about the observation is paramount in achieving a higher level of understanding in science. Graphic organizers should be used to help students organize the work in their minds in order to understand it. Chromebooks are invaluable in writing and analyzing work as well as utilizing different writing apps that can

be used to quickly grade papers. Any demonstration or hands-on inquiry must be directly related to the standard and should increase standardized test scores in science. I have included I can statements easy to understand for the student. An assessment, such as an exit ticket, or quick quiz should be provided immediately after any demonstration or hands-on activity to provide data about which Essential Questions and standards were or were not mastered.

Content research

The topic of drug interactions in the body and the resulting environmental concerns is a fascinating subject that a middle school teacher can connect to oceans, water properties, water conservation and stewardship, and especially chemistry. Drugs have molecules/compounds engineered by drug companies. These drugs, when in our bodies transform through chemical reactions in the liver. Our liver tears apart drug compounds, adds to existing compounds, and forms new substances. This chemistry can be directly related to The Law of Conservation of Mass (which I have included an activity further down in this unit). Other drugs are expelled without changing, through kidney function.

I discovered that according to the EPA, these molecules are at levels which are no of concern at this time, because of dilution. Basically, today's viewpoint about drug molecules that move into the water supply, after elimination from the body, are diluted to a point where they shouldn't be a problem[1]. Dilution is the solution to the pollution. Primarily, I researched how the water supply is being tainted with prescription drugs, and in this CU research is geared primarily towards drug residue being released into the water supply from personal use and elimination from humans through the body's systems. The failures and success of some common wastewater treatment methods in dealing with drug residue was also researched.

The FDA and Drug Development

We have all seen the drug commercials on TV. They show happy, normal people living healthy lives, and then discusses all those nasty side effects that MIGHT occur in some people. Simply put, the FDA strives to make sure drugs are as safe and effective as possible to the public. Of course, there is a delicate balance between possible side effects and safety and efficacy of a drug. According to the FDA, Americans have the safest and most advanced system of pharma in the world, however Europe is a close second[1]. The process that helps to decide if a drug is safe and if its benefits outweigh its side effects is rigorous. The testing and data collection is labor-intensive and takes many months or years to even get to clinical trials (which are real life tests on people). And, it may cost drug companies millions or even billions of dollars to bring the drug to market.

I researched Merck Pharmaceuticals Corporation, which is one of the largest pharmaceutical corporations in world, with annual sales of $39.8 billion dollars worldwide in 2016. On Merck's website, they list concepts such as code of conduct, corporate responsibilities, ethics, integrity transparency, and respect for people. Merck has issued policy statements on the topic of drug residue in the water supply. On the Merck, website, they discuss the presence of unwanted or expired medicines in households and the trace amounts of pharmaceuticals in the environment.

They also state that these expired and transformed compounds are a concern to regulators, policy makers, community groups and the public.[2]

How Drug Companies Design, Produce and Market Drugs

The drug discovery and development process is a lengthy and expensive process.[2] First, researchers discover new drugs, through research, about a disease. Marketing studies highlight potential diseases for treatment or cure. This allows researchers to design a drug to stop or reverse the effects of the disease. Existing molecular designs that are already patented may be used. Thousands of compounds may be considered for development. Early testing that narrows down potential compounds is an important part of the first stages of a drug's development. Further study occurs and then moves the process into the development stage.

In the development stage, researchers identify a compound for development, then conduct experiments to gather information. This information consists of how it is absorbed, how it is distributed by organs and systems in the body, how it is metabolized by the liver, and how is excreted by the kidneys and digestive system. Researchers study and design dosage amounts, how the medicine is given (such as by mouth or possibly injection), side effects, and toxicity. Also, gender, race, and ethnicity affects how a drug is metabolized and is studied closely. And how a drug interacts with other drugs and treatments is researched and tested. Competitor's drugs are compared to the drug in the development process and marketing studies are conducted.

How a Drug Travels Through the Human Body

There are many ways prescription drugs can enter your body. The most common methods include orally, intravenous, a shot, absorption through skin, and rectally. Also, it can dissolve on the tongue and be absorbed. But, how does the drug arrive at the source of the pain or sickness or disease? To help explain the journey of a drug through the body, here is a summary of the four basic stages of a medicine's life in the body.

- Absorption: Getting a drug from its site of action to the blood
- Distribution: Drug transport via blood to/from site of action
- metabolism: Chemical breakdown of drug (normally in liver)
- Excretion: filtration of drug by kidneys or elimination through feces

A drug faces its biggest obstacles during the absorption stage. Medicines taken by mouth are transported in a special blood vessel leading from the digestive tract to the liver, where large amounts may be destroyed by metabolic enzymes. Some routes bypass the liver, entering the bloodstream directly or by the skin or lungs.

Once a drug is absorbed, the next stage is distribution. The bloodstream carries medicines throughout the body. During this second step, side effects can occur when a drug has an effect on an organ other than the intended one. For a pain drug, the intended organ might be a sore muscle in the back; however, irritation of the stomach could be a side effect. Many factors alter distribution, such as proteins and fat molecules in the blood that can cause drug molecules to become inactive by latching onto them.

In the third stage, metabolism, in which there is chemical changes going on in the liver. After a drug has been circulated through the body and has done what was expected of it such as stop pain or perhaps kill bacteria, the drug is broken down, or metabolized. The breaking down, or sticking together, and or tearing apart of the molecules happens in the liver. The liver's enzymes chemically change the molecules and makes new substances.

The breaking down of a drug molecule involves two steps that take place mostly in the liver. The liver is a place of continuous drug biotransformation and is carefully controlled. Everything that enters the bloodstream, no matter if it is swallowed, injected, inhaled, absorbed through the skin, or created by the body itself, is transported to the liver, which is the largest internal organ. There, substances are chemically changed becoming twisted, cut apart, put back together, and bio-transformed.

The biotransformation that occurs in the liver are performed by the body's proteins, the enzymes. They act as catalysts. Every one of your cells has many different enzymes, selected from hundreds of thousands. Each enzyme has a particular job. Some break and tear molecules, apart, while other molecules join into long chains. With drugs, the first step is usually to make the substance easier to get rid of in urine.

The final stage of the drug's journey through the body is called excretion. The transformed drug exits the body either through the urine or feces. Most of the products of enzymes' breakdown of the drug molecules, which are called metabolites, are less chemically active than the original molecules. Therefore, scientists refer to the liver as a "detoxifying" organ. Occasionally, however, drug metabolites can have chemical activities of their own, and can be as powerful as the original drug. When prescribing drugs, doctors must take into account these added complications. Once liver enzymes are finished working on the drug, the used up and inactive drug undergoes the final stage and leaves the body in the toilet.

The Liver and Metabolism

There are two processes that take place in the liver. The 1st pass effect occurs when the liver encounters a drug before it enters the circulatory system. The first pass effect only applies to oral drugs. The drug may pass through the stomach and be absorbed into intestine, then into the portal circulation connected to the liver. The first pass effect is a phase of drug metabolism, by which the concentration of a drug is greatly reduced before it reaches the circulatory system. Drugs can be metabolized by oxidation, reduction, condensation, isomerization, conjugation, and hydrolysis, When the process happens, the objective is to make the drug easier to excrete. Metabolism happens in two phases.

- When the drug exits the body it will be either changed or unchanged.
- If it travels through the kidneys, it is basically the same drug as entered the body.
- If the drug travels through the liver it is either chemically altered (biotransformation), torn apart or added to.

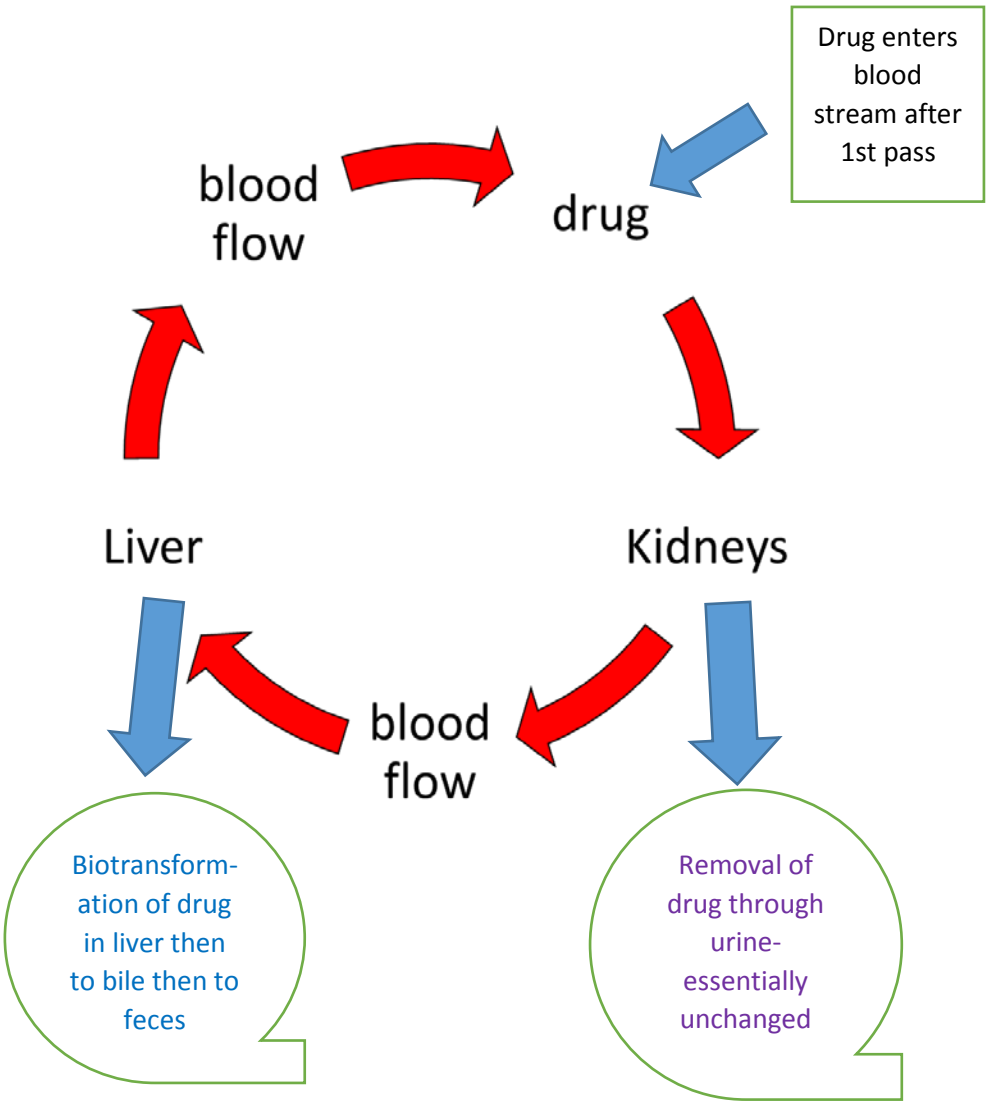
The drug will exit the body either in a changed or unchanged form or a metabolite. Whether or not a drug forms a metabolite depends on whether the liver enzymes act upon the drug. Almost all drugs pass through the liver, but not all are metabolized. Chemical changes (reactions) take place and new molecules (compounds/substances are produced). Thus, there are the two ways in which the drug enters the water supply, and most drugs are excreted by the kidneys in urine.

How the Liver and Kidneys Treat Drugs Differently

A few facts:

- The liver breaks down drugs to metabolites.
- The kidneys remove drugs and metabolites from the blood.
- Both cause drug concentrations in the blood to drop.
- There are other elimination routes; lungs, sweat, and tears.
- The liver is just doing its job (removing potential toxins), but unfortunately, the liver doesn't know how to determine a potential toxin from a beneficial drug.
- Phase one reactions tend to break off pieces of a drug molecule.
- Phase two tends to add to the molecules.

The two processes often work together. For example, when a phase one breaks off a piece, it leaves behind a place, to add a piece by phase two. The pieces added in phase two help the new molecule (a metabolite) become filtered by the kidneys.



Implications of Drug Residue for Aquatic Organisms

Studies have shown that extremely low levels of drug residue in drinking water may not affect humans in the short term, however the levels that won't affect large organisms will affect microorganisms and small aquatic organisms because of their smaller size and weight. One study found types of drug residue in treated tap water, such as atenolol (a beta-blocker), carbamazepine (an anticonvulsant), gemfibrozil (an antilipidemic), meprobamate (an antianxiety medication), and phenytoin (an anticonvulsant). The concentrations of these compounds were very low, less than 10 nano grams per liter, (parts per trillion). For example, one part per trillion is equivalent to about one second in 64 years.[3] According to the EPA,

> "Contaminants of emerging concern (CECs), including pharmaceuticals and personal care products (PPCPs), are increasingly being detected at low levels in surface water, and there is concern that these compounds may have an impact on aquatic life. It is important for EPA to be able to evaluate the potential impact of CECs and PPCPs on aquatic life and have an approach for determining protective levels for aquatic organisms".[4]

Currently, the EPA doesn't regulate any drug in the U.S. drinking water. Within our drinking water, prescription drug residue interacts with microorganisms such as bacteria, fish, other drug

compounds, and other basic environmental elements, as well as water. Also, drugs make their way into our water from farms, sewage treatment plants, and landfills. Chemical and biological interactions can result in a host of transformed stuff—new chemicals with new properties. As we know, when a chemical reaction occurs, totally new substance are made, totally different from the original. Thinking back earlier, we discussed how the liver transforms drugs into totally new molecules into new substances with new properties. The liver chemically changes the drug molecules and they end up in our drinking water. They interact with existing organisms and also with drugs that are essentially unchanged as they traveled through the kidneys. Some metabolites can sometimes be more toxic than their parent compounds. However, just because humans might not be affected too much, there's some evidence that drugs in the water might affect aquatic life, mainly fish. Some studies have shown that estrogen could have a feminizing effect on male fish and can change female-to-male numbers. Sources of estrogen include birth control pills. Some intersex fish with both male and female sex organs have been found in sections of the Potomac River. And in other research, antidepressants have been found in the brain tissue of fish downstream from wastewater treatment plants.[5]

Generic Waste Water Treatment Systems Operation and Alternatives

Pollutants such as drug and medical residue go through the traditional wastewater purifying process and go back to the environment. Concern over their increasing numbers in waste and drinking water is growing worldwide. The wastewater cleaning process used today in nearly all cities and counties only removes the substances that easily biodegrade or which stick to the sludge in the process. This process, which less expensive than membrane treatment methods, however allow most of the non-biodegradable substances to pass through. Research has shown that improving present wastewater treatment methods such as adding specific microbes to wastewater and upgrading membrane filtering processes can remove over 95 percent of drug residue from wastewater[6].

Wastewater treatment varies widely across the world. Many different types of water treatments are available and the most inexpensive methods to operate are the most common. Wastewater treatment systems generally have three stages of operation. The wastewater treatment plants have a primary treatment stage to reduce the Biological Oxygen Demand (BOD is the amount of oxygen needed by microorganisms to decompose the organic material in a sample of water) and amount of solids that will settle to the bottom of a settling tank in the wastewater.

The second treatment uses the biological removal of BOD, solids, and other pollutants. Pathogens and other toxic pollutants are removed in the final stage, through the use of mostly chlorine. Today, most waste water treatment plants are not equipped to remove drug residue. Estimates show that about 10% is eliminated at the treatment plants while 20% ends up in the sludge and as much as 70% ends up in the water supply.[7] There are available technologies that effectively reduce the level of drug residue in our water. Ozone is an oxidant and attacks electron structures in molecules and is efficient in breaking down drugs in sewage systems. Microbes can break down drug residue in the water supply making them useful in water treatment plants. Adding enzymes and using wetlands and photosynthesis can be used to treat drug residue in the water.[8]

Nano Medicines and Wastewater

One type of drug remains stable in the water—nanomedicines. These new drugs are used to treat diseases such as cancer, because of the side effects of chemotherapy. With nanomedicines, scientists create a tiny ball that's filled with medication, like a balloon. The ball actually goes to the part of the body that needs the drug and releases its drug load, so only the cancer cells get the drug, not every cell in the body. However, these new nanodrugs have a potential to harmful for the water supply.[9] Most drugs tend to be slightly hydrophobic, which means they don't move through water very well. But, nanomedicines go where they need to such as cancer cells. Studies have shown that if the nanomedicine is absorbed into a plant, the medicine can be eaten by herbivores and move up the food chain. Other scientists have found that nanoparticles, such as gold, can move up the food chain from plants to caterpillars, raising some concerns about these types of drugs.

One example of a nanomedicine is Paclitaxel. It is listed by the World Health Organization's List of Essential Medicines, as it is one of the most effective and safe medicines. In 2005, it was approved in the United States by the FDA for the treatment of breast, pancreatic, and non-small cell lung cancers. Thus, new medicines using nanotechnology provide an ongoing challenge to sewage treatment facilities.

Activities

Researching Drugs Used in Students' Homes

One awesome activity that could be easily conducted in a middle school classroom could be researching and creating a list of drugs in the students' homes and side effects, purpose, and if are they expired. Questions to ask family members could include;

- What do you do with expired drugs?
- What do these drugs do in the body?
- How do they change in the liver?
- Predict and research affects would they have on the environment and aquatic organisms.

Balancing Equations and Hydrogen Peroxide and Enzymes in the Liver

Hydrogen peroxide (H_2O_2), which is a by-product of metabolic reactions is used in the below experiment. In high concentrations, it is toxic and it's accumulation in a cell would be harmful. Most tissue contains the enzyme catalase, which catalyzes the breakdown of hydrogen peroxide to water and oxygen. Catalase is a common enzyme found in most living organisms that live in the presence of oxygen, such as bacteria, plants, and animals. It speeds up (catalyzes) the breakdown or decomposition of hydrogen peroxide to water and oxygen. In activity below, it helps break down hydrogen peroxide which is a toxic chemical, into 2 substances-water and oxygen. The hydrogen peroxide solution which is commonly sold in stores, is only 2% hydrogen peroxide. An interesting fact about H_2O_2 is that light causes a chemical reaction to occur, which is why the chemical is sold in dark containers.

$$\mathbf{2H_2O_2 \rightarrow 2H_2O + O_2}$$

Also, this equation of the decomposition of hydrogen peroxide by enzymes in the liver can be used to easily determine if this reaction satisfies the Law of Conservation of Mass. An 8th grade student can use a t-chart to determine if the equations is balanced or not. Sometimes this is just called counting atoms on each side. We can use a t-chart to makes easy and simple. Using basic math rules such as exponent rules, multiplication, and addition, a student can easily check to see if the equation is balanced.

Using the above equation, we can use a t chart and multiply the coefficient X subscript and use the distributive property to calculate the number of atoms on each side. I f we determine that the equation is balanced we can they say this equation satisfies "The Law of Conservation of Mass".

$$2H_2O_2 \rightarrow 2H_2O + O_2$$

REACTANT	PRODUCT
H 4	H 4
O 4	O 4

Raw Liver and Hydrogen Peroxide Activity

You can easily simulate chemical reactions that occur with drugs in the liver. This simulation using real raw liver and hydrogen peroxide is perfect for a middle school lab activity. This replicates the reactions and processes of enzymes rearranging compounds within real liver. Using liver and hydrogen peroxide, you can conduct a fun enzyme experiment and show a how a gas in produced within a closed container (the balloon). Liver contains an enzyme (catalyst) which breaks down hydrogen peroxide. You can inflate a balloon with the gas produced and also test it for oxygen. This will demonstrate evidences of a chemical reaction and demonstrate a chemical change.

What you need:

- Liver (about 200g)
- Hydrogen peroxide (about 75ml / 1/3 cup of 9% / 30 vol)
- Balloon
- Small plastic water bottle
- Funnel
- Peg or clip
- Knife

If you want to test for oxygen gas (O2) you'll also need**:**

- Thin piece of wood or matchstick
- Lighter or matches

1. Cut the liver into pieces small enough to insert into the bottle
2. Pour the hydrogen peroxide into the balloon using the funnel
3. Put the neck of the balloon over the bottle so that the hydrogen peroxide goes onto the liver
4. Hold the balloon in place as it inflates with gas, then using a large binder clip to keep it closed
5. To test the gas for oxygen, light the match then blow out the flame. Immediately put the glowing matchstick into the bottle

As soon as the hydrogen peroxide touches the liver, foam appears and the bottle gets warm. After a few seconds the balloon begins to inflate. When you lower the glowing matchstick into the bottle, the flame rekindles. There should be enough oxygen to do this over and over again. the hydrogen peroxide is broken down into water and oxygen in the presence of a catalyst. (A catalyst speeds up chemical reactions without being changed itself.) The reaction is exothermic – it produces heat.

$$2H_2O_2 \text{ —-> } 2H_2O + O_2$$

Just as the liver in our experiment breaks down a poisonous chemical into harmless substances, an animal's liver breaks down toxins and bio transforms them into compounds that are harmless to the human body. Remember that heat and cold affect how enzymes work.

Identifying Compounds, Atoms, and Elements Activity

Students can identify the number of elements and compounds in common pharmaceuticals formulas commonly known to 8th grade students. Elements from the periodic table and found in common drug compounds such as Carbon, Nitrogen, Oxygen, and Hydrogen, Molecules atomic weight in a drug is usually less than 500 and usually consist of 4-5 elements per molecule. They can identify and list all elements from the drug using the periodic table. Atomic number, number of atoms, number of subatomic particles such as protons neutrons and electrons could be listed. Some examples might include:

- Tylenol / Acetaminophen. $C_8H_9NO_2$
- Advil / Ibuprofen. $C_{13}H_{18}O_2$
- Bayer / Aspirin (salicylic acid). $C_9H_8O_4$
- Zoloft / Sertraline. $C_{17}H_{17}Cl_2N$

Questions in the activity may include:

- How many atoms in each drug?
- How many elements in each?
- What are the names of the elements?
- What do the subscripts mean?
- Are these drugs compounds?

“I can” statements for students

- I can identify compounds
- I can count the atoms
- I can identify the elements in the formula and use the Periodic Table to determine the characteristics of each.

Using Predictive Websites to Simulate Liver and Drug Interaction.

An interesting activity to help 8th graders understand whether or not a chemical equation satisfies The Law of Conservation of Mass would be to use software provided below to identify a chemical reaction within the liver with rearranging drug molecules and provides some readings about drug interactions in the liver.

There are websites available that are helpful in simulating liver actions in metabolizing drugs. These websites also have information about a drug's physical properties and can be useful during a research project in a middle grades classroom. Some of these websites listed can determine toxicity, absorption, metabolism, and lists proteins, and predicting potency. For the purposes of this I will primarily be discussing ways to predict new molecular substances that occur in the liver during metabolism. These online tools can predict biological activity, and these predictions can be helpful in finding drug molecules that have been metabolized and might make it through the waste treatment plant and reside in the water supply and may be potentially beneficial or harmful to other organisms.

Below is step by step instructions of how to find the molecular structure of a drug, then convert it to a line text, along with other tools, and to finally predict what the which molecules the liver will convert the drug into so that a student can the substance and conduct research if it has been determined to be harmful to organisms in the water supply.

The first tool to start with is the *simplified molecular input line entry system* (SMILES). All the tools and sites listed here require the use of SMILES. This system takes a complex structure of a molecule and converts it to a line of text. For example, the SMILES text line for aspirin is C(C)Oc1ccccc1C(=O) O. SMILES makes it easy to convert a complex molecular structure into an easy to read text line using information from sites such as Wikipedia.

Next, Wikipedia lists the SMILES of every drug in its index. Just look under the heading, chemical and physical data and you will see a capitalized SMILES logo that you can click on.

Then, all you have to do is plug in the SMILES code string from Wikipedia into the search bar in another website called Molinspiration. It's a site that predicts whether a molecule will have biological activity, and it lets you draw a structure or input a SMILES text and compares its structure to known drugs in six different classes of molecules. Here you can find out information such as drug likeness, bioactivity score, and view graphs.

Another user friendly site is admetSAR. admetSAR is a site that predicts absorption of the drug), metabolism, and toxicity. Like Molinspiration, admetSAR either takes a drug as a structure (drawn) or as a SMILES. In theory, you could submit molecules to Molinspiration to see if the drug will be potent and then to admetSAR to see if it is behaved in the body, gets absorbs, gets metabolized, and is not toxic, etc.

MetaPrint2D is a site that predicts how a drug will be metabolized; remember most of this occurs in the liver. This site can predict both types of metabolism (Phase I and Phase II). *Most drugs found in waste water are detected as their metabolites.* This is important to know because in this CU we are primarily looking for substances that are harmful to aquatic life. When you obtain the desired results the student can research the metabolite and determine if it has been discovered in drinking water.

Appendix 1

- 8th Grade Science as Inquiry
- Traditional laboratory experiences provide opportunities to demonstrate how science is constant, historic, probabilistic, and replicable.
- Although there are no fixed steps that all scientists follow, scientific investigations usually involve collections of relevant evidence, the use of logical reasoning, the application of imagination to devise hypotheses, and explanations to make sense of collected evidence.
- Student engagement in scientific investigation provides background for understanding the nature of scientific inquiry.
- In addition, the science process skills necessary for inquiry are acquired through active experience.
- The process skills support development of reasoning and problem-solving ability and are the core of scientific methodologies.[10]

Matter: Properties and Change

8.P.1 Understand the properties of matter and changes that occur when matter interacts in an open and closed container.

8.P.1.1 Classify matter as elements, compounds, or mixtures based on how the atoms are packed together in arrangements.

8.P.1.2 Explain how the physical properties of elements and their reactivity have been used to produce the current model of the Periodic Table of elements.

8.P.1.3 Compare physical changes such as size, shape and state to chemical changes that are the result of a chemical reaction to include changes in temperature, color, formation of a gas or precipitate.

8.P.1.4 Explain how the idea of atoms and a balanced chemical equation support the law of conservation of mass. Energy: Conservation and Transfer Essential Standard Clarifying Objectives

Earth Systems, Structures and Processes

8.E.1 Understand the hydrosphere and the impact of humans on local systems and the effects of the hydrosphere on humans.

8.E.1.1 Explain the structure of the hydrosphere including:
• Water distribution on earth
• Local river basins and water availability

8.E.1.2 Summarize evidence that Earth’s oceans are a reservoir of nutrients, minerals, dissolved gases, and life forms:

- Estuaries
- Marine ecosystems
- Upwelling
- Behavior of gases in the marine environment
- Value and sustainability of marine resources
- Deep ocean technology and understandings gained

8.E.1.3 Predict the safety and pot ability of water supplies in North Carolina based on physical and biological factors, including:

- Temperature
- Dissolved oxygen
- pH
- Nitrates and phosphates
- Turbidity
- Bio-indicators

8.E.1.4 Conclude that the good health of humans requires:

- Monitoring of the hydrosphere
- Water quality standards
- Methods of water treatment
- Maintaining safe water quality
- Stewardship

Structures and Functions of Living Organisms

8.L.1 Understand the hazards caused by agents of diseases that affect living organisms.
8.L.1.1 Summarize the basic characteristics of viruses, bacteria, fungi and parasites relating to the spread, treatment and prevention of disease.
8.L.1.2 Explain the difference between epidemic and pandemic as it relates to the spread, treatment and prevention of disease.
8.L.2 Understand how biotechnology is used to affect living organisms.
8.L.2.1 Summarize aspects of biotechnology including:

- Specific genetic information available
- Careers
- Economic benefits to North Carolina
- Ethical issues
- Implications for agriculture ecosystem

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Vocabulary Words and Terms

Metabolite
Metabolism
Enzymes
Drug
Nano
Biotransformation
Excretion
Absorption
Distribution

Endnotes

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