Gold, Dynamite, and Drug Discovery:
Rags and Riches with Chemistry

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This curriculum unit—Gold, Dynamite, and Drug Discovery: Rags and Riches with Chemistry—uses the historical success of chemistry as a mechanism to interest high school students in learning chemistry. Gold refers to the practice of alchemy. This early root of our chemical science sought to turn base metal into gold. Dynamite refers to the invention of Alfred Nobel, which made him one of the richest men in the world. Drug discovery as it is currently practiced integrates medicine and chemistry in a high-tech race to bring new drugs to market to achieve the dual goals of disease cure and commercial profit. This unit uses the history of chemistry as an introduction and foundation for learning high school chemistry.

INTRODUCTION

Many HISD High School students take chemistry in their junior or senior year to fulfill the graduation requirement of three science credits. A significant number are apathetic or suffering through the course, believing that two science credits are too much or that the science would be okay if they could have just gotten into that easier course that is either full or not being offered this year. Many feel trapped and have no motivation to expend an honest effort toward the course. All too many do not see the relevancy of chemistry to their personal lives and that of our world. These negative beliefs sabotage any true engagement, stifle the student, and frustrate both student and teacher.

This unit uses history to make the study of chemistry come alive. Students will learn how chemical discoveries have shaped their world view and that their future is tied to the knowledge of change currently taking place. Dramatizing chemistry with the stories we would have remembered had we been part of them will increase student engagement and thereby build student competence through increased student participation and performance.

This unit includes introductions and lessons to be interweaved by the instructor into the HISD CLEAR curriculum for the introductory two-semester Chemistry A and B course. The goal is to bring alive our existing topics through a historical drama that culminates in hands-on practice in drug discovery. The unit should be introduced early in the first semester and remain thematic through the entire course. During the second semester, the unit builds momentum as structural chemistry is explored through physical and computer models. Prior knowledge from biology about protein structure and catalysis will then be reinforced, and the drug discovery topic will be the focus of applying chemical knowledge to explore how to discover a new drug. The unit can also be taught in an IPC (Integrated Physics and Chemistry) course, and the drug discovery lesson can be taught in a biology course by emphasizing the conceptual aspects of pharmaceutical science.

Three lessons are included in this unit. The lesson titles and the topics they are taught in conjunction with are:

Gold—Atoms, Periodic Table, and Chemical Formulas,

Dynamite—Chemical Reactions, States of Matter, and Gases,

Drug Discovery—Chemical Bonds, Geometry, and Structure.

The Gold Lesson begins with the history of the atom and then the periodic table itself, all with reference to the early practice of alchemy. The Dynamite Lesson gains its underpinning from our historical understanding of chemical reactions and the dramatic effect of sudden changes in the state of matter as solid instantly becomes gas. The Drug Discovery Lesson starts with the study of the chemical bond and continues as a lesson in chemical geometry and structure that explores how to discover a new drug.

GOLD

Before chemistry became a science, alchemy developed over a period of centuries to become the roots of chemical science. Gold was the advertised goal and promise of alchemical pursuit. Gold was highly regarded because it was the most stable substance known. All other known metals were considered inferior because none had the stability of gold. These lesser metals were considered on their way to becoming gold because the Aristotelian thinking of purpose toward perfection demanded that all lesser metals become gold. Thus the alchemists pursued methods to hurry along the natural process of lesser metals becoming gold, a process termed transmutation.

The alchemists and their supporters believed that metals could be changed into gold. This was considered so entirely possible that the British Parliament passed a law against the transmutation of the lesser metals into either gold or silver. Naturally, the government was concerned with currency and controlling the value of coinage. The law was repealed in large part due to the influence of Sir Robert Boyle, the natural philosopher credited with the discovery of the law concerning gasses that bears his name. Boyle was a colleague of Sir Isaac Newton, and both Boyle and Newton were practitioners of alchemy. However, neither of these 17th century legends made gold from lesser metals, nor did they publish any procedure that allowed others to follow and carry forth with success.

The reason that no one could ever successfully change another metal into gold was unlocked through the discovery of the elements and the subsequent organization of the periodic table. Only a few substances were recognized in ancient times, and they were not thought of as being elemental and composed of atoms in the modern sense. In fact, the concept of an element was not proposed until 1661 when Boyle referred to the idea of an element as "laboriously useless" (Morris 58). This position that sounds so strange today was not a heresy in that time when extreme effort was required to produce a supposedly pure substance that through lack of unifying chemical principles was of little or no practical use. It is of no wonder then that alchemy persisted since no evidence existed to show that other metals could not be turned into gold.

Although the chemical definition of an element was only stated in the mid-17th century, the idea had been around since ancient times in another context. Two millennia earlier philosophers thought to answer the question of what we, and all we see in this world, are made of. Three names from the fifth century Greek world are synonymous with the elements they proposed as the answer. Thales of Miletus thought that the world is composed of water and that water is the fundamental element, all other things being derivatives of water. This was reasoned from observation of a seashell in part of a rock with the conclusion that the hillside containing the rock must have at one time been part of the sea. Thus, Thales is considered the first philosopher for his scientific thought process of observation and conclusion. Anaximenes, a student of Thales, argued that the fundamental element must be air. He reasoned that air turned to water as it became more compacted and then in turn became stone with further compacting such that everything we see is fundamentally composed of air. Heraclitus of Ephesus proposed fire as the fundamental element from which all substances are derived. Without clear evidence to support one element over another as the fundamental element, a multi-element theory became attractive. Empedocles, a contemporary of Pythagoras, is credited with the idea that four elements are the substance of all existence: water, air, fire, and earth. Empedocles proposed that everything in existence is made up of a combination of the four fundamental elements. The four-element theory lived on for two thousand years, considerably longer than Empedocles, who having convinced himself of his own immortality, jumped into the crater of Mount Etna (Strathern 9-19). Mount Etna was home to Vulcan—god of fire. Having been consumed by the volcano and transformed into the element of fire, one can at least agree that herein Empedocles did achieve his own immortality.

Another Greek philosopher took a different approach to understanding the composition of matter. Leucippus of Abdera is credited with the idea that matter is not infinitely divisible (Strathern 21). The *atomos*, Greek for uncuttable, of Leucippus, is the foundation of our atomic theory. Democritus, Leucippus' student, developed the atomic theory and is often given credit for the foundation of the first atomic theory. By this view, everything in the world is made up of different kinds and combinations of atoms. Even with this as insight, atoms were not directly connected to elements and vice versa at that time. The atomic and four-element theories were different explanations of the composition of the natural world. The modern explanation that would unify elements and atoms would wait two thousand years. It is incredible that an atomic theory could be so accurate in its infancy and that the same philosophical thought processes could deter the chemical understanding of the elements until the 17th century. This is largely due to Plato's persistence with Socrates' introspective bias of know thyself at the expense of asking questions about the natural world; thus, scientific thought was held stagnant until its eventual emergence as natural philosophy through Aristotle.

Elements were known to the ancient world. Carbon in the form of charcoal was known as soon as the age of fire. Of course, those observing and experiencing charcoal were not cognizant of it as an element. Early elements were known because they either existed in nature in pure form or were purified through chance. One can imagine that bits of iron metal must have formed in the remnants of a fire created for warmth and set by chance next to rocks of iron ore.

Emsley divides the elements according to their date of discovery in the ancient world (prehistory to 1000 BC), Middle Ages (1200 AD to ca. 1700 AD), and eighteenth through twentieth centuries (Emsley 529-532). An impressive timeline emerges for the discovery of the elements: 10 between 5000 and 1000 BC, none between 1000 BC and 1200 AD, five in the Middle Ages, 17 in the eighteenth century, 50 in the nineteenth century, 33 in the twentieth century, and three or more predicted in the twenty-first century. Thus, when Robert Boyle defined the chemical element in 1680 (Morris 58) only 15 elements were known. Atoms were then forever married to elements as that fundamental quantity that can no further be refined.

As chemistry emerged as a science in the nineteenth century, confusion grew over what was becoming a long list of elements. More and more became known about the elements, but without a systematic way of organizing this knowledge in a way that made properties fit and prediction possible. Dmitri Mendeleyev, a Russian chemist teaching in St. Petersburg, was destined to change this in 1869. In a fit of work lasting three days, Mendeleyev noticed a similarity between the elements and the card game of patience. Exhaustion brought sleep and a dream that unlocked the secret that he recorded on awakening as the Periodic Table of the Elements (Strathern 285-287). Mendeleyev's periodic table organized properties in horizontal rows with vertical columns of increasing atomic weights. Thus, it took two centuries after the chemical definition of the elements to devise a systematic understanding of their interrelationships.

The twentieth century brought an ever-increasing understanding of the atom and the subatomic particles that formed the organization of matter. The picture of the atom currently accepted is one of a cloud of negatively charged electrons surrounding a much smaller and denser nucleus that contains non-charged neutrons and positively charged protons. An atom's identity is determined by the number of protons in its nucleus, which is termed the atomic number. Henry Moseley was the first to arrange the elements according to nuclear charge. Arranged in this way by increasing atomic number, the modern periodic table takes its form with vertical columns that are termed groups or families. Seven horizontal rows form the periods by which the periodic law is enforced: a periodic repetition of physical and chemical properties occurs through each period as long as the elements are arranged in order of increasing atomic number. Thus elements in each vertical column have similar physical and chemical properties since these are repeated in each period according to periodic law for each group or family as one travels down the column. Each horizontal step inside a period results in an element with one more proton than the preceding. The atomic weights do not increase in regular steps since the numbers of neutrons vary. In essence, the periodicity is still Mendeleyev's.

DYNAMITE

Gunpowder was invented in China in an attempt to create a tonic that would make the consumer live forever (*Adventures in Science: KABOOM!*). Instead, the Chinese alchemists invented the world's first explosive. Gunpowder, also called black powder, is referred to as a low explosive. Everyone has observed the fuse of a firecracker burning in quick progression toward the firecracker. The sparks seem to disappear as the fuse vanishes and the burn continues inward. Then all of a sudden: bang! We see a fireball and hear the loud crack of the firecracker at detonation.

The name firecracker foretells what this bit of paper and powder will become. The prefix fire tells us that something is going to burn, and the suffix cracker tells us to expect a rather loud noise. This only happens through proper construction. If the paper is burned on its own, no noise is apparent. If the gunpowder is burned on its own, one will detect a hissing sound as the gunpowder quickly disappears into bright light—but no bang. Not even if the paper and powder are mixed will one hear a bang. The paper will simply burn much faster as the gunpowder serves as an accelerant. The bang is only present if the burn takes the form of an explosion. The explosion occurs only if the gunpowder is wrapped tightly enough in the paper for the burn to create enough pressure to break the paper, which is heard as the loud cracking sound.

This is the essence of a low explosive. Unrestricted, it is simply a very fast burn—a sparkler set to full-throttle high-speed combustion. On its own, it cannot blow up, explode, or go boom. It can only fizzle. However, when combusted in a confined space the expanding gasses instantly push against the containment and at the breaking point rush outward as a pressure wave that strikes as an invisible hammer followed by debris, smoke, and the sound of the ruptured source breaking into countless bits of rubbish.

The chemical reaction taking place in the abrupt transformation of gunpowder to fire and smoke is termed a combustion reaction. A typical combustion reaction starts with some form of carbon mixed with oxygen as reactants, and the reactants are heated to an initiation temperature that is sufficient to start the reaction. The reaction then proceeds with reactants being transformed into products until one or both of the reactants are used up, or until in some cases the reaction reaches a point of equilibrium and appears to stop. The combustion products of a carbon compound and oxygen are carbon dioxide and water with the liberation of heat. This reaction is familiar to anyone that has witnessed a campfire and can be represented symbolically as Log +

Air ? Ash + Smoke + Heat. The combustion reaction for a hydrocarbon can be represented generally as $C_xH_y + (x + y/4)\ O_2$? x CO_2 + (y/2) H_2O + heat, as for example the combustion of the hydrocarbon methane, first only showing what is termed the unbalanced skeleton equation: $CH_4 + O_2$? $CO_2 + H_2O$ + heat. The subscript numbers of reactants in the general (x, y, and 2) and methane (4 and 2) equations indicate the number of times the atom preceding it is represented. The reactants appear on the left of the arrow and the products on the right. The arrow is read as yields or goes to. Thus, the hydrocarbon example would be read as methane plus oxygen yields carbon dioxide, water, and heat. The balanced equation includes coefficients [1, (x + y/4), x, and (y/2) in the general case] that enforce the Law of Conservation of Mass by making the number and kind of atoms on the left of the arrow exactly equal to those on the right since matter may be neither created nor destroyed but only rearranged in the transformation from reactants to products. The balanced equation for the methane reaction becomes $CH_4 + 2\ O_2$? $CO_2 + 2\ H_2O$ + heat. Another useful detail is the state of the individual reactants and products, meaning the solid, liquid, or gaseous state, and abbreviated as (s) for solid, (l) for liquid, and (g) for gas. The hydrocarbon reaction becomes CH_4 (g) + 2 O_2 (g) ? CO_2 (g) + 2 H_2O (g) + heat and it is apparent that all reactants and products are in the gaseous state. This is an important detail since gases occupy much more volume than solids or liquids. Gasses occupy proportionally more volume with increasing temperature, such that a solid reactant on combustion to a gas will instantaneously exhibit a dramatic increase in volume. Such is the case with the firecracker after ignition in our example.

The balanced equation for the combustion of gunpowder is 4 KNO_3 (s) + 7 C (s) + S (s) ? 3 CO_2 (g) + 3 CO (g) + 2 N_2 (g) + K_2CO_3 (s) + K_2S (s). The skeleton equation given in words is potassium nitrate and carbon and sulfur go to carbon dioxide and carbon monoxide and nitrogen and potassium carbonate and potassium sulfide (Le Couteur & Burreson 89). The important detail is that all of the reactants are solids and three of the products are gasses. Unlike the log fire, the oxygen for combustion comes not from the air but from the solid compound potassium nitrate. In essence, a tremendous increase in volume takes place in the instant following ignition; and since the balanced equation is known, the volume increase can be calculated. The coefficients in the balanced equation represent not just the relative number of atoms, but also the relative number of moles. The mole is a quantity equal to 602,000,000,000,000,000,000,000 atoms, molecules, or any other representative particle. This very large number is referred to as Avogadro's Number, and it is usually represented more conveniently in scientific notation as 6.02 x 10^{23}. Thus, the coefficient 4 in front of potassium nitrate in the balanced equation for gunpowder can mean either 4 molecules or 4 moles of molecules. Since 4 moles of KNO_3 (s) would be 2,408, 000,000,000,000,000,000,000 molecules, it is more convenient to use the mole quantity, just as it is easier to bring home three-dozen eggs instead of 36. Using the relationship that one mole of any gas occupies a volume of 22.4 liters (abbreviated L) at standard temperature and pressure (abbreviated STP), one can begin to calculate a volume increase for the combustion of gunpowder. Another relationship is needed since the reactants may be taken at STP (273 Kelvin temperature and 1 ATM pressure); however, the products are much hotter. The needed relationship is provided by Jacques Alexandre Cesar Charles, who working in the latter half of the 18th century discovered the relationship existing between the volume of a gas confined at constant pressure and its temperature. Charles' Law is written $V_1/T_1 = V_2/T_2$ and for comparative purposes the temperature of the products (T_2) will be taken as 1365 K. This is a conservative estimate since ºC = K - 273, our T_2 is just 1,092 degrees hotter than that of ice water. Since the reactants are solid, V_1 must be calculated for the moles of product at STP and then the volume increase from the final temperature may be calculated. Thus, for the gunpowder equation, V_1 = 22.4 L/mole x moles (g) products. After substituting for the total of 8 moles of volume increase for the combustion of 4 moles of KNO_3 for gunpowder at STP, V_2 may be calculated from Charles' Law as $V_2 = (V_1 \times T_2)/T_1$. Substituting, our equation becomes V_2 = (179.2 L x 1,365

K)/273 K = 896 L. This is an absolutely stunning increase in volume. Imagine 4 moles of KNO_3 in the form of a handful of powder instantly increasing to fill the volume of 448 two-liter root beer bottles, or 2,524 soda cans, or 105 cases of soda pop, or 210 12-packs! These are huge volumes to appear in just an instant.

The equation used to calculate the volume increase for gunpowder may be generalized to compare this reaction to other materials. Letting n stand for the total number of moles of gaseous products produced and substituting generally for V_1, our equation becomes V_2 = (22.4 L/mole x n moles (g) products x 1,365 K)/273 K. It is now possible to calculate volume increases for other materials that undergo sudden transformations and compare their volumes to an equal amount of gunpowder.

In the mid-nineteenth century, Ascanio Sobrero of Turin discovered nitroglycerine by pouring glycerol—also known as glycerin—into a mixture of sulfuric and nitric acids (Le Couteur & Burreson 89). Nitroglycerine is undoubtedly the most widely recognized high explosive, known by virtually all moviegoers and even children through anecdotes, stories, and cartoon dramatizations. Nitroglycerine is known to detonate unexpectedly through shock, temperature increase, and for undeterminable reasons because of the sudden and permanent loss of all evidence and witnesses. Nitroglycerine explodes readily without the necessity of the confinement required by gunpowder, and this characteristic differentiates a high explosive from a low explosive.

The key to nitroglycerine's instability and hence reactivity is in the structure of the molecule. All of the products for the reaction are stored in the molecule itself, the balanced equation being 4 $C_3H_5N_3O_9$ (l) ? 6 N_2 (g) + 12 CO_2 (g) + 10 H_20 (g) + O_2 (g). Notice that all of the products are gaseous, a total of 29 moles are produced from four moles of liquid reactant. This is a dramatic difference compared to the gunpowder reaction with 4 moles of KNO_3 solid reactant producing only 8 moles of gaseous products. Accordingly, the volume increase for nitroglycerine is calculated from our equation as V_2 = (22.4 L/mole x n moles (g) products x 1,365 K)/273 K. Substituting 29 moles for n gives V_2 = (22.4 L/mole x 29 moles (g) products x 1,365 K)/273 K = 3,248 L. Amazing! Nitroglycerine produces more than three-and-a-half times more volume than gunpowder (3,248 L/896 L = 3.6). Nitroglycerine's products will fill 1,624 two-liter root beer bottles, or 9,150 soda cans, or 380 cases of soda pop, or 760 12-packs!

One of the world's great fortunes—that of Alfred Nobel—was secured by solving the problem of nitroglycerine instability. The instability of nitroglycerine became a worldwide problem with some countries banning production. Nobel lost his younger brother to a nitroglycerine explosion that destroyed one of their laboratories in Stockholm; subsequently, the city banned its production. Nobel was relentless in pursuing a solution and constructed a new factory outside of the Stockholm city limits to continue production (Le Couteur & Burreson 94-95). The solution to instability was eventually accomplished by mixing the unstable liquid with diatomaceous earth, an adsorbent material, to produce the material known as dynamite. In the form of dynamite, the explosive could be transported securely and detonated consistently. Dynamite is detonated using a small controlled explosion delivered by a blasting cap that is sensitive to an electrical pulse. A number of roads and construction projects simply could not have been attempted without the aid of dynamite; mining is also dependent on the routine use of controlled high explosives. It is an unfortunate paradox in our world that this tool is also used for evil.

DRUG DISCOVERY

Drugs or therapeutic agents that one takes to ameliorate disease have been used since ancient times by the Egyptians. Examples are senna and castor oil as laxatives (Jones 10) and preparations from both the poppy and henbane (Bettex 147) for the sleep inducing effect of the scopolamine contained by these plants. The earliest remedies, dating from 8,000 BC, were administered directly from the plant by the Shaman, whereas, by 2,000 BC extracts were prepared by the Egyptians in the earliest known pharmacy (Porter 2-3).

The time of Hippocrates was between about 460 and 377 BC. Hippocrates defied the then current belief that disease was punishment from the gods and proposed the theory of the four humors, giving a scientific basis to disease. Galen was a Greek physician that had studied medicine in Alexandria, Egypt. He moved to Rome after Greece fell and was a proponent of the four humors, stressing that understanding must come before treatment. His main work in 160 AD was surgery for wounds from battle (Porter 3).

During the middle ages, 500-1400 AD, medicinal extracts were outlawed as being part of witchcraft and the church dominated healing with its emphasis that sickness was in essence God's punishment. Thus, the true cure was repentance to gain God's forgiveness and the prescription for the sick was overwhelmingly prayer for forgiveness of sins. Doctors were either clergy or religious scholars. Surgery for broken bones and wounds was performed, with opium sometimes serving as an anesthetic and wine used as an antiseptic to cleanse a wound (Porter 5).

Arabian pharmacy thrived in stark contrast to the medicine of Europe in the middle ages. The Arab world had hospitals, physicians, pharmacies, and indeed universal healthcare by 931 AD. Avicenna published his masterwork in 1030 AD, and the *Laws of Medicine* was translated into Latin in the 12th century and was extensively used in Europe for centuries afterwards (Porter 5).

The Renaissance, 1400-1600 AD, marked a time of exploration by wealthy individuals, exploration into science and medicine and a rediscovery of the knowledge of ancient Rome and Greece. New materials were discovered from plants brought back by explorers, such as quinine, still used to treat malaria. The printing press created an information explosion (Porter 7), priming society for the Industrial Revolution that was to follow between 1750 and 1900.

Paracelsus lived during the Renaissance between 1493 and 1541. He was an alchemist that turned alchemy toward the goal of healing. Paracelsus is the most widely known proponent of iatrochemistry, medicinal chemistry, which had the goal of healing but lacked the scientific basis that differentiates chemistry from alchemy. Paracelsus was a wanderer and specifically correlated local knowledge gained from gypsies and old wives' tales with chemical compounds and their effects. He was flamboyant, dogmatic, and had an abrasive personality that was part of why he moved around so much. He amazed his followers and the hopeful like a traveling salesman, yet he was a spendthrift and prone to drink heavily so never held on to any money earned. He argued against the doctrine of the four humors, and in 1527 on St. John's Day he publicly burned a book in Basel espousing the theories of Galen and Avicenna (Bettex 29), declaring his superiority over a millennium and a half of accepted medical wisdom. Because he cured a local businessman of great influence, he became a lecturer at the University of Basel and the town medical officer. After his supporter died, he was forced to leave Basel over a dispute that ended with him libeling the magistrate in his court case, a crime punishable by prison or death. Paracelsus is known for taking alchemy to the verge of being chemistry and for popularizing medical cures through medicinal chemistry. However, his doctrine of signatures claimed that nature speaks its function in iatrochemistry through natural form; thus, a heart-shaped lilac leaf must be good for heart disease. Therefore, Paracelsus is regarded as only a highly flamboyant alchemist that popularized iatrochemistry as the method to cure disease and not the true father of medicinal chemistry (Strathern 70-98).

Paracelsus had argued that imbalance of the humors was not responsible for disease, but that disease was caused by factors outside the body. It took three more centuries for that insight to be proven, and proven it was by none other than Louis Pasteur (1822-1895) whose research led to the germ theory of disease that was proven by Robert Koch (1843-1910). Later, Joseph Lister

(1827-1912) developed a method using carbolic acid as an antiseptic agent to reduce infection during surgery. Then during the First World War Alexander Fleming (1881-1955) discovered penicillin, the world's first antibiotic. In 1935 Howard Florey and Ernst Chain undertook the first clinical trials for the antibiotic drug penicillin and for this won the 1945 Nobel Prize in medicine (Porter 11). Thus, it took from the time of Egyptian medicine in 2,000 BC to 1935 to prove that a known chemical compound could act as a cure for disease.

During the four millennia from Egyptian pharmacy to the unequivocal proof that a chemical compound could cure a disease, alchemical pursuits fell and chemical science flourished as chemistry matured. The twentieth century saw such great chemical advances as understanding the detailed structure of DNA, proteins, and enzymes. The main metabolic chemical pathways and cycles responsible for human physiology were mapped and correlated with states of wellness and disease. Biology, chemistry, and medicine became intertwined as disciplines as investigation in one area led to questions in another. This interdisciplinary focus with the goal of conquering disease continues into the twenty-first century. In the future the choice may present itself in medicine to stop the disease symptom or to erase the disease from the patient's DNA.

The need for disease management using medicine in the form of a chemical compound will be with us in the foreseeable future. Molecular biology based gene therapy is still an infant science and therefore genetic cures will not develop fast enough to replace drug therapy anytime soon. New drugs are always needed since, for example, antibiotic resistant strains of pathogens develop over time and these resistant strains must be combated with new compounds that are both safe and effective treatments.

Drug discovery today is practiced in a systematic fashion. A research team in a pharmaceutical company first picks a disease that needs a treatment. The cause and effect of the disease is studied and chemical compounds are selected as drug therapy candidates. The compounds may be ones that already exist and are available as natural products, or they may exist in the drug company's database of synthesized compounds. New molecules are often considered based on computer models. This is termed in-silico study. In-vitro study uses the actual compound as applied to cells growing in cell culture. In-vivo studies of the molecule in an animal are usually not conducted at this stage of discovery. The discovery stage of research may involve the screening of ten thousand new compounds for activity against the disease (Porter 14). Testing or screening compounds is also referred to as looking for hits, and the compound being tested may be referred to as a lead or new lead. Thus, a researcher might describe a promising result as getting a hit on a new lead. This is analogous to a batter getting a hit in a baseball game. No one bats a homerun every time. However, a base hit might be promising enough to apply for a patent to prevent competing companies from using the new compound. Since drug discovery is capital intensive, patent protection is necessary to provide enough incentive for companies to invest in the lengthy research, approval, and production of a new drug.

Taking a new drug to market involves the initial discovery, pre-clinical trials, phase 1 and phase 2 clinical trials, product license application and approval cycle, and full-scale manufacturing (Porter 14). This is a daunting and expensive task. The world's first AIDS drug, AZT, took 20 years and 800 million dollars to develop (GlaxoSmithKline). Research and funding are the keys to continuing the cycle of discovering new drugs and making them commercially available to combat disease. Funding comes primarily from the revenues obtained from drug sales. Thus, it is vital to choose a disease to work on that affects enough people to pay for the drug development. Then research may proceed with the discovery phase—finding candidate chemical compounds that exhibit activity against the chosen disease.

Chemical compounds exhibit drug activity because of their structure and function in the presence of a disease state. Perhaps Paracelsus was on the right track with his Doctrine of

Signatures; however, how a drug looks must be assessed at the atomistic scale to see if its structure has the chance of bringing therapeutic benefit. On this scale, the look of the molecule itself is not the answer but the key to what it unlocks. Drugs function through interacting with other three-dimensional surfaces. These surfaces may represent the active site of an enzyme or a binding site on a cell membrane. The details vary based on the disease and the strategy chosen to combat the disease. The common factor though is the need to find target molecules that interact favorably with the chosen binding site without affecting other healthy parts of the body. Molecular modeling and molecular simulation are primary tools in finding target molecules that are hits and eliminating those structures that show less promise as active drugs. This in-silico research speeds and automates the search for disease cure.

LESSONS

Lesson I—Gold

Students will gain in this lesson a historical perspective concerning the discovery of the elements and their organization into a table, and the subtle understanding of why gold is gold and no other element can be chemically changed to become gold. It is important for students to discover the pattern inherent in the periodic arrangement of the elements since the periodic table is all-too-often something they had to commit to memory without any emphasis on why the elements are so arranged.

Procedure

Students may work individually, paired, or in groups; however, each division of labor is required to present findings to the class. Students and groups are assigned particular elements and groups of elements to research the history of the element or group from their earliest known occurance (See appendix, Emsley 529-532). The lesson extends through two periods or one 90-minute block. The first half of the lesson is devoted to introduction, research, and analysis. The second half begins with presentations, includes discussion and questions, and produces summary conclusions with the class and finally in individual groups. It may be advisable to schedule library time depending on the printed and computer resources available in the classroom. Each student hands in a lab report as their deliverable from the lesson.

Safety

Except for demonstration elements that may be available to some instructors, this laboratory research exercise does not involve any hazardous materials. Standard chemical laboratory safety precautions should be taken for any elements that are demonstrated.

Materials

This lesson requires minimal materials: modern periodic table, historical reference to the discovery of the elements, paper or data sheet, pencil, ruler, blank periodic table template either constructed from modern table or software created, and highlighters are recommended. Demonstration elements may be employed such as a charcoal briquette, gold, copper, and diamond.

Analysis

Student analysis should be directed toward determining when the element was discovered and the details of the discovery. Sources used should be cited, including the assigned textbook if used. The analysis method should be open ended and encourage individual expression.

Questions

Focus each group or individual on answering why the element or assigned group was discovered when it was. Does a pattern exist in the group being researched? What are the characteristics of the elements being researched and how many of these were known at the time of discovery? What determines the identity of the different elements in the group? Why are they different and were these differences understood at the point of discovery? If it were possible to do surgery on an atomic scale, what would one have to do to an atom of lead to turn it into an atom of gold? How about an atom of copper?

Presentation

Each student or student group presents findings to the class. The goal is to have all of the presentations completed in the first half of the class period so that the second half of the period may be devoted to class discussion. The results of the discussion must include discovery of the periodic law. Mendeleyev's contribution must be emphasized as well as the difference in his original published table and that in use today. The instructor should use discretion on when the laboratory report is due based on the classroom sessions.

Lesson II—Dynamite

Students will gain in this lesson the knowledge of the interrelationships in chemistry of chemical reactions, the mole, and gas calculations. It is important for students to combine skills learned to answer a scientific question. All too often students take in information, master it for a test, and then don't use it again until it is time to study for another test. This lesson requires the skills of balancing an equation, predicting products, calculating molar volumes, and calculating gas law volume changes; these are all used to complete the exercise.

Procedure

Students may work individually, paired, or in groups. Everyone is assigned the same exercise. The lesson extends through two periods or one 90-minute block. The first half of the lesson is devoted to introductory material. The *Adventures in Science: KABOOM!* video (*Adventures in Science: KABOOM!*) is recommended as an introduction. The second half of the lesson consists of analysis activities that differentiate a low explosive from a high explosive, and explores the fundamental differences between these types of transformations and that of a nuclear explosion. Analysis and calculations may be made on instructor-supplied data sheets or notebook paper. Each student hands in an analysis report as their deliverable from the lesson.

Safety

First and foremost it must be stressed that the lesson is not intended to be instructions or encouragement for any student to go out on their own and make any kind of explosive. The lesson is a safe way of exploring the chemistry of explosions and does not involve any hazardous materials.

Materials

This lesson requires paper or data sheet, and pencil. A calculator, ruler, and highlighters are recommended.

Analysis

Student analysis should be directed toward discovering the fundamental difference between low and high explosives, and differentiating these from a nuclear explosion.

Questions

Focus each group or individual on completing the calculations and analysis activities. These should include balancing equations, predicting products, and calculating volume changes using known equations. The combustion of gunpowder should be balanced from the skeleton equation KNO_3 (s) + C (s) + S (s) ? CO_2 (g) + CO (g) + N_2 (g) + K_2CO_3 (s) + K_2S (s). The explosion of nitroglycerine provides a good opportunity to predict the products for the reaction 4 $C_3H_5N_3O_9$ (l) ? ? . Students should be able to state at this point the difference between a high and low explosive. With the balanced equations for gunpowder and nitroglycerine, the total number of moles of gasses produced on reaction should be calculated assuming STP and the volumes compared. Volumes should also be calculated by assuming a final temperature of the reaction products such as 1,365 K. Have the students differentiate these explosions from a nuclear explosion using the assumption that at STP the volume for the nuclear reaction will be the same as that calculated for nitroglycerine, 650 L. Students should calculate V_2 for the nuclear transformation using either the minimum temperature for the fusion of hydrogen of 5×10^6 K (Astronomy HyperText Book) for T_2, or the temperature created in a thermonuclear hydrogen bomb explosion of 3×10^8 K (Sublett 2.2.2) for T_2. Have students compare the volumes that result from 4 moles of gunpowder, 4 moles of nitroglycerine, and the nuclear transformation using the volume assumption and temperatures given. One expects the ratio of nitroglycerine to gunpowder volumes to be 3,248 L/896 L = 3.6, showing that nitroglycerine produces 3.6 times move volume of expanding gas than gunpowder. The volume ratio of the nuclear reaction to gunpowder is 1.2×10^7 L/9.0×10^2 L = 1.3×10^4, or 13,000 times more volume for the minimum allowable fusion reaction. The volume ratio for the hydrogen bomb blast would be 7.1×10^8 L/9.0×10^2 L = 7.9×10^5, or 790,000 times more volume. Students should write comments about the different chemical transformations and new understanding gained through the calculation exercise.

Presentation

Each student turns in an analysis report. Instructors should use discretion on the due date based on the amount of in-class practice and the level of group interaction in solving the problems, and on the depth of class discussion that is generated from the exercise.

Lesson III—Drug Discovery

Students gain in this lesson both the basics of molecular structure and the application of how three-dimensional structures are used in drug discovery. It is important for students to appreciate that the theories they study are not isolated bits of information for test recall, but interrelated in ways that bring giant benefit to mankind. Drug discovery uses pure and applied science from chemistry, biology, and medicine to further the noble goal of conquering disease.

Procedure

Students may work individually, paired, or in groups. Everyone is assigned the same exercise. The lesson extends through two periods or one 90-minute block. The first half of the lesson is devoted to the basics of molecular structure. The second half of the lesson allows individuals and teams to choose a molecule of interest and create a three-dimensional map of its distinguishing characteristics. Analysis and calculations may be made on instructor-supplied data sheets or notebook paper. Each student hands in an analysis report as their deliverable from the lesson.

Safety

This exercise does not involve any hazardous materials. Standard classroom safety precautions should be taken.

Materials

This lesson requires paper or data sheet, pencil, ruler, tape, and a molecular model kit or parts for construction atom centers and bonds. A calculator and highlighters are recommended, as well as the chemistry textbook or other structural chemistry references.

Analysis

In part one, students analyze the basic structures and differences in models they construct of carbon monoxide, carbon dioxide, water, hydrogen peroxide, sulfur dioxide, ammonia, nitric oxide, nitrous oxide, hydrogen cyanide, and hydrogen bromide. Students write the formula and a three-dimensional representation based on their model building. In part two, students and teams pick a molecule to build that has some biological relevance. Examples are cyclic adenosine monophosphate, 9-cis-retinoic acid, and vitamin A. Students build a three-dimensional map of the structural hallmarks, such as areas of electronegativity or unsaturation. Methods for constructing the map are student-directed and documented in the analysis report.

Questions

Students should answer the question of what are the basic shapes of the molecules that were constructed in part one. Students should identify unshared pairs of electrons and multiple bonds in their structures. In part two, students should state their rationale for choosing their molecule and state how and why it is biologically relevant. What are the overall dimensions of the molecule? What are the distances between the hallmarks chosen for analysis? If the molecule were envisioned as a hand, what would be the characteristics of the glove that provided a perfect fit?

Presentation

Each student turns in an analysis report. Instructors should use discretion on the due date; however, it is recommended that the reports be handed in separately. Part one should be efficiently completed in a period. Based on the level of group interaction in building the biological molecule and analyzing the problem of creating a three-dimensional map, additional discretionary time should be allowed for students to complete part two.

CONCLUSION

The history of chemistry has been sampled briefly and used as both launch pad and fuel to gain student involvement in learning chemistry. The lessons included are supported substantially herein and by the appendix and supplemental resources. As a society we return back to our beginning: Ten millennia ago the Shaman produced needed cures when possible and today our best scientists struggle to produce the needed cures when possible. Our understanding of scientific theory and the nature of matter has certainly changed, yet the gold we seek today is the luster in the faces of those that have benefited from science’s relentless march forward. Our greatest hope is that some students will be inspired enough to pursue meaning in their lives from accepting the challenge and responsibility of pushing our scientific knowledge forward to the benefit of our world.