Chemistry: The Human Science

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A tiny molecule harvested from a soil bacterium on Easter Island that evolved billions of years ago for no obvious purposes should have nothing to do with human beings. Yet it turns out miraculously to have potent immunosuppressive properties that allow doctors to successfully perform a liver transplant in a young girl.

Chemistry for a New Era

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Figure 1: A plaque on Easter Island commemorating the discovery of a bacterium producing rapamycin, a potent immunosuppressant. Since its discovery, rapamycin has allowed the successful transplantation of organs into millions of patients (Image credit: Wikipedia)

In India, an excited young bride celebrates her upcoming wedding by coloring her hands bright yellow with turmeric, a spice that has been used for centuries as a key culinary ingredient. In France, a similar hallowed tradition demands a copious flow of red wine at weddings. In China, a bride and groom offer ginseng tea to their parents as part of a ritual.

Oblivious of all these events, thousands of miles away in the United States, scientists are struck by the remarkable effect that the active ingredients in turmeric, red wine and ginseng tea seem to have on a variety of disorders, from cancer to Alzheimer's disease. Perhaps, they ardently hope, there's a cure in there somewhere.

Chemistry is the human science. What the general public refers to as "chemicals" have a profound effect on our way of life. They can forge a bridge between the metabolism of a billion year-old sponge and the fervent hopes of a mother for her daughter's life, between the joy of traditional weddings and food and that of seeing a loved one being cured of a terrible malady. Physics may concern itself with the beginnings of deep time and biology turns its eye on the origin of humanity itself. The wonders of physics and biology are undoubtedly spectacular, but chemistry is the science that most directly engages with our senses, the discipline that confronts us face-on every single day of our lives and demands that we react.

Chemicals delight, enrage, tease, beguile, provoke, subdue, reward, bully, soothe, punish, kill and save as directly and dramatically as human beings. Just like humans they have

personalities that manifest themselves under the right circumstances. Like long-lost friends they can materialize in our lives in the form of a life-saving drug, a dab of color on a dull day or the material in a particularly comfortable new mattress. And like sworn enemies they can incapacitate us on battlefields, deform our children and provoke us to endless debate and politicking about the effects of their vanishingly small traces in the environment. Chemistry is the middle kingdom, the land which engages us with its familiarity at all levels, from the trite to the life altering. Like the landscape of Middle Earth, it is full of fascinating and baffling curiosities, triumphs and tragedies, foolishness and wisdom.

As we celebrate the International Year of Chemistry this year, it is worth pondering the nature of this "central science" [1]. What makes chemistry unique is that its defining constituents- molecules- can have a startlingly direct relationship on an individual basis with world events and the rise and fall of nations. No other science can claim such well-defined and powerful connections between a handful of its building blocks and key aspects of history, economics culture. Consider just two facts. Even today, the strength of the economy of a country can be judged by the magnitude of its production of a single chemical- sulfuric acid [2].

Or consider that it was cellulose- in the form of cotton- that was at the root of slavery and the American Civil War. During the early days of imperialism, it was avarice for a select few materials like indigo dyes and silk that led expansion and trade in the East [3]. And wars have been fought over substances like saltpeter in South America [4] and opium in China [5] whose properties and allure were defined by one or two dominant molecules; sodium nitrate in the case of saltpeter and morphine in the case of opium. It is not an exaggeration to say that individual molecules have held remarkable sway over entire economies, cultures and political relationships. Throughout history, chemistry through its forging of precious and unique arrangements of atoms has influenced the fortunes of humans in visceral and vivid ways.

Figure 2: A battle scene from the Opium Wars from the mid-nineteenth century. Opium which is extracted from the seeds of the poppy plant owes its properties to one dominant molecule- morphine. (Image)

It is precisely because chemistry is the human science that people have a decidedly ambivalent and often confused relationship with it. You won't hear many heated debates on television about the fine tuning of the cosmological constant or the evolution of the opposable thumb, but the media is rife with vociferous controversies about the side effects of drugs against heart disease, the apparent proliferation of bisphenol A in the environment [6] or the rise of 'designer' narcotics that provide 'legal highs' [7]. Every one of these controversies centers directly on a molecule or a family of molecules, and each one affects millions of people personally every day.

This direct connection to all our problems and promises is what makes chemistry stand out and elevates it from its reductionist roots in physics. Molecules are more than the sum of their constituent atoms, and they connect with our senses in ways that are much more tangible and diverse than abstract notions of energy, forces and fields.

When I smell freshly cut grass, I am directly smelling a simple molecule called cis-3-hexenol; when I first smelt this compound and then smelt cut grass, it etched an unforgettable connection in my mind. Gravity may be all encompassing, but you can't gift a small piece of gravity to someone on his or her birthday in a box, which they can then spray on their

clothing. Quarks may be the ubiquitous building blocks of matter, but a quark does not allow you to readily distinguish between two compounds with exactly the same chemical formula, one of which can cure your diabetes while the other kills you by paralyzing your nerves.

Such diversity cannot be captured by physics alone. And for all the profound implications of the second law of thermodynamics for life, liberty and the pursuit of happiness, it's hard to have a personal relationship with entropy. It's equally hard to fathom the ages of geological time that drive evolution or to directly see the folding and unfolding of DNA on an everyday basis. But to experience the very soul of chemistry, the actual molecules without which the science would not exist, one only has to reach out into his or her medicine closet, kitchen, insecticide drawer and laundry room. In each one of these places you will find a microcosm of molecules which directly impact the look, smell, touch, and sound of everything that you see.

It is this very personal impact of molecular structures on our senses and sensibilities that has created the perceived and real fear of everything "chemical". This fear often causes confusion, leading us to brand anything "natural" (supposedly including snake venom) as good and anything "artificial" (supposedly including a synthetic drug for heart disease) as bad. It has caused the lexicon of chemistry to collide with popular culture in ways that leave chemists perplexed; the word "organic" for instance, especially as connected to the organic food movement, has completely transcended its original meaning in the chemist's dictionary. For a chemist, many organic compounds like dioxin and botulism toxin are extremely toxic, while inorganic compounds like sodium chloride or lithium are harmless or even beneficial.

The fear of chemicals is often unjustified but its roots reach out into the very nature of chemical substances and indeed into human nature itself. There is a deep-seated reason why the tale of Jekyll and Hyde has transcended cultures and ages. It is because we understand that there is a Jekyll and Hyde in each one of us, waiting for the right moment to step out of the shadows. This ambiguity in human behavior translates faithfully to chemical behavior; like Jekyll and Hyde, almost every arrangement of atoms inherently presents two faces to us and this has led us to sustain a love-hate relationship with chemicals.

But it is up to us to decide which face we want to see. Do we want to see the murderous face of nitrogen mustard gases which were used in World War 1 during the first large-scale waging of chemical warfare? Or do we want to see the noble face of nitrogen mustard analogs which peace-loving men and women harnessed a few decades later into the first anticancer drugs [8]?

Some of the most beneficial compounds in anticancer therapy owe their origin to some of the most gruesome agents used in war. The adage "what does not kill you makes you stronger" applies more to chemistry that we can imagine. Phosphate fertilizers pose another example of a chemical Jekyll and Hyde; these compounds which have saved literally billions from starvation are also responsible for algal blooms in streams and rivers which can kill off entire ecosystems by choking their nutrient and oxygen supply.

Sometimes it takes a simple change in the orientation of certain atoms to transform a cure into a monster. Thalidomide infamously caused birth defects when it was administered to pregnant women as a pill for morning sickness. In this case the culprit was not a different molecule but simply the mirror image counterpart of the compound (created by metabolism inside the body) that caused such grievous harm.

Alice herself could not have imagined the nightmare waiting for her on the other side of the looking glass. But ironically, thalidomide has recently seen resurgence on a limited scale as a therapy for multiple myeloma, a deadly disease. Like some human beings, molecules can be forgiven and resurrected for useful purposes after being cast aside as pariahs. We all deserve a second chance.

Figure 3: The tale of Jekyll and Hyde- dramatized here in a movie poster- serves as an accurate metaphor for molecules, many of which can demonstrate strikingly different properties depending on subtle changes in shape, concentration or arrangement of atoms. (Image)

We may not have witnessed this proliferation of beneficial and harmful qualities from such a multitude of molecules had it not been for the one property of chemistry that makes it a unique science. Chemistry is the sole human activity which can truly create that which never existed before in stunningly diverse quality and quantity [1].

In the last one hundred years or so, chemists and especially organic chemists have transformed the science of creating molecules to the level of a finely honed art. Making molecules of arbitrary complexity on demand is an ability that reinforces humans' position as the dominant species on our planet as much as any other. It exemplifies the highest forms of creativity of the kind signified by Shakespeare, Beethoven, Michelangelo and Newton. It is not an exaggeration to say that from a conceptual standpoint, chemical synthesis has been a world-shattering paradigm underpinning all of modern civilization, equal in importance to the invention of the calculus and the discovery of electricity.

Synthetic chemical substances so fully permeate our environment that it is all too easy to forget that someone had to discover them. Everything from the chair that we sit in to the clothes that we wear to the food that we eat to the drugs that we are prescribed to the buildings that we inhabit to the modes of transportation that get us to work consist in large part of synthetic molecules that did not exist before in nature. The ability of chemists to design and make these molecules is almost fearsome in its efficiency and versatility. Part of the fear of chemicals stems from the sheer novelty of new chemical substances and their all-pervasive presence in our lives. Sometimes we tend to fear the most, that which is most familiar.

Figure 4: This sequence of steps illustrates the complex series of reactions- involving dozens of reagents and intermediate compounds- typically required for synthesizing a useful molecule. In this case the molecule is merrilactone A, a compound isolated from the Chinese star anise spice which may have have therapeutic value against neurodegenerative diseases. (Image credit: Wikipedia)

One thing is for sure; whether we love or despise these chemicals, we cannot imagine a life without them. Much is made sometimes of the evils of the chemical and pharmaceutical industries, but there cannot be a soul who would deny the untold number of lives saved by antibiotics and antiviral drugs largely developed by the pharmaceutical industry. Oil companies may be everyone's favorite villains, but it is prudent to consider the tremendous net impact which the refining of crude oil by chemical means has had on transportation and power generation in the twentieth century. "Plastic is fantastic", not only in the popular song but in all aspects of real life, from surgical sutures to the powdery material used in diapers.

The organic food movement eschews the use of artificial fertilizers, yet we can never forget a simple fact; nitrogen fertilizers were made possible by the Haber-Bosch process, a method literally of turning air into bread, which by some estimates kept a fifth of the world's population alive [4]. Whatever our feelings are about the humans who have created these molecules, the life-saving properties of the molecules themselves stand proudly in splendid isolation. More than any other science chemistry has directly fed us, clothed us and kept us from dying. It has overwhelmingly contributed to the high standard of living which we aspire to and take for granted.

A world without chemistry would be a dystopia in which humans would lack the means to protect themselves from the elements, be unable to travel long distances for want of efficient fuels, be powerless against microorganisms and would die from simple pinpricks and would starve to death from inadequate food production. Put simply, a world without chemistry would most certainly be a world which most of us- including even the most dedicated environmentalist and alternative medicine enthusiast- would not want to live in.

As we advance into the twenty-first century, this most human of all sciences will continue to amaze and thwart us with its complexity, utility and ambiguity. Chemistry will continue to be at the center of our efforts to solve the energy crisis, develop personalized drugs and transform agriculture. There will no doubt be tension between humans and the molecules they create. Under such circumstances public education will go a long way in dispelling unrealistic fears about molecules and their impact on human health and the environment, and this is one goal which the International Year of Chemistry is vigorously trying to promote. While these practical problems are being solved, chemists will continue to quietly enjoy what they have enjoyed doing for hundreds of years. They will gaze at colorful crystals, unravel the structures of alkaloids from frog skin, simulate the complex motion of enzymes on computers and study the cellular reactions that fuel life.

Ultimately the truth about this human science goes deeper. We need to realize that the power of molecules to shock and awe resides in their creators. The physicist Richard Feynman once quoted an old Japanese proverb: "To every man is given the key to heaven. The same key opens the gates of hell". Interestingly, the dominant model for the mechanism by which a small molecule like a drug fits into the active site of a disease-promoting enzyme and modulates its activity is that of a "lock and key". Many drugs act by being the ideal key in a particular lock, but they can also fit into other unwanted locks and cause toxic side effects; the same key that cures a disease may open the gates of hell by causing overwhelming side effects. Chemists who design drugs keep on trying to make the key fit only one lock.

The metaphor extends to all of chemistry. Every chemical substance is a key to the gates of heaven and hell. Ultimately we are the ones who decide what gate it will open. We hope to choose wisely.

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