Enteral Petrochemistry (Pharmaceuticals)

Critical Media Lab Basel
Institute of Experimental Design and Media Cultures
FNSNF Swiss National Science Foundation
SHIFT REGISTER
Published by Shift Register – www.shiftregister.info
For the workshop The Eye Altering (cur. Garance Malivel)
Within the event We Are Not the Number We Think We Are
February 2–3, 2018, Cité Internationale des Arts, Paris
Edited by Jamie Allen, Martin Howse, Jonathan Kemp
Designed by Merle Ibach

SSEUE
Solar Sourcing & Economies of Ultimate Expenditure

The green parts of the plants of land and sea endlessly implement the appropriation of an important part of the luminous energy of the sun. In this way light—sunlight— produces us, animates us and engenders our excess. This excess, this animation, is the effect of this light (we are essentially only an effect of the sun). In practice, from the point of view of wealth, the radiation of the sun distinguishes itself with its unilateral character: it loses itself without taking account, without compensation. The solar economy is founded on this principle. Usually, if one envisions our economy on the ground, one isolates it. But this is only a consequence of that which engenders and dominates it.

— Georges Bataille, The Economy Equal to the Universe: Brief Notes Preliminary to the Preparation of an Essay on "General Economy" Forthcoming Under the Title 'The Accursed Share'

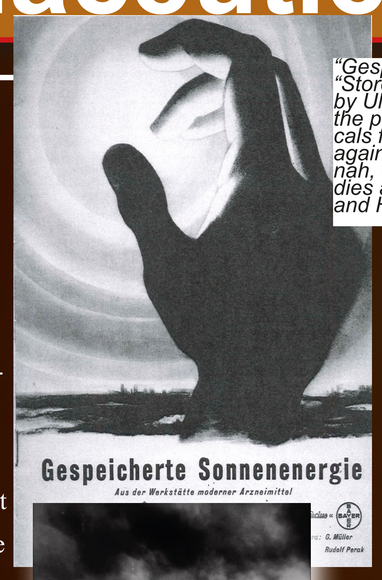
"What was I seeking when you arrived dyed by the sunrise
With the sea's age in your eyes
And with the sun's health in your body"

— Odysseas Elytis, Age of Glaucous Memory

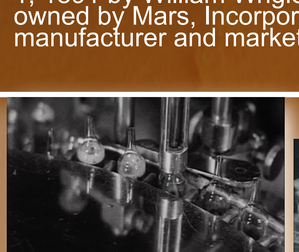
Histories and trajectories of solar geology can be told that link to synthetic opiates and birth control pills to universal labours; between the oil well and the pharmacy are the twined realities, imaginaries and projections of chemical engineering hopes and practices: on the one hand, "catalytic cracking" breaks down, aka "converts", petroleum in the refinery to isolate high-boiling, high-molecular weight hydrocarbon fractions of crude oils into more valuable gasoline, olefinic gases, and precursors like acetyls, alcohols, acetates, and others. On the other hand lies the dream of "total synthesis", the complete chemical synthesis of a complex molecule, often a natural product, from simple, commercially available, most often petrochemical, precursors. Synthetic drug production chemistry analyses and calculates petroleum hydrocarbons, opening and reconfiguring their structures. Often, a compound "synthesised by nature" and solar energies is felt to be all too rare, expensive or unruly, and the orientations and efforts of petrocultures becomes to replace these rogue creativities with understood and productive processes and delivery mechanisms. There is a conservationist argument to the use of petrochemical precursors for the synthesis of rarer hydrocarbons, in that the harvesting of difficult to find or un-farmed ecologies is lessened by the presence of.

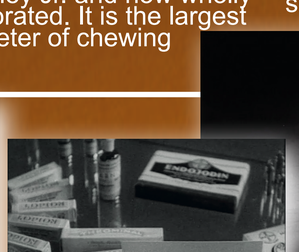
Petroleum is used in health care, as everywhere else, primarily as a transport fuel, but also significantly as feedstock for pharmaceuticals, plastics, and medical supplies. Few substitutes for these hydrocarbons, besides oil, are available. This dependence theoretically makes health care reliant on "Stored Sun Energy", and vulnerable to petroleum supply shifts, and it is a reliance that is particularly heavy in the United States, which consumes petroleum disproportionately on a per capita basis compared with other nations. There is increasing consensus that petroleum production has already declined or will soon begin to decline and that constrained supplies will adversely affect all sectors include health care. Health care's exposure to declines in petroleum production is a fact hiding in plain sight — the issue has received little attention from economists or policymakers, and little has been done to further assess and manage the potential risk. There are historical associations between petroleum supply shocks and health care prices. The In anticipation of future supply contractions lasting longer than previous shifts and potentially disrupting health care delivery, we propose an adaptive management approach and outline its application to the example of emergency medical services.

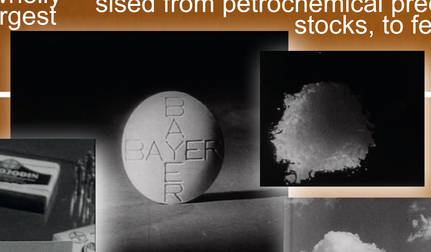
(American Journal of Public Health. 2011;101:1568–1579)



"Gespeicherte Sonnenenergie" / "Stored Sun Energy" a 1934 film by Ulrich Kayser for Bayer tracing the production of pharmaceuticals from sun to pill and back again (Thanks to Christian Bonah, Department for Social Studies and Humanities in Medicine and Health)







It is sunlight in modified form which turns all the windmills and waterwheels and the machinery which they drive. It is the energy derived from coal and petroleum (fossil sunlight) which propels our steam and gas engines, our locomotives and automobiles. ... Food is simply sunlight in cold storage.

— John Harvey Kellogg. New Dietetics: What to Eat and How (1921), 29

ENTERAL PETROCHEMISTRY
Precursors, Distillations, Reactants, Pharmaceuticals, Medicines, Preparations, Nutrition & Digestion

"Strange, strange are the dynamics of oil and the ways of oilmen."
— Thomas Pynchon, Gravity's Rainbow (1973)

"Enteral Petrochemistry" describes those ways that petroleum serves as a precursor to the synthesis stages of internally administered pharmaceutical products. There is widespread understanding that the (American, long) Twentieth Century has (d)evolved into a petroculture, inescapably revolving, reacting and resulting from the petrochemical abundance of planet Earth: "In brief, while the 20th century was the century of oil, the 21st already is unfolding as the century of whatever follows oil, or the century of fighting over what's left of oil—or both." (Gerald F. Seib, "Oil Dependency Overshadows US Policy," *Wall Street Journal, 22 August 2005)*

Likewise and at the same time, internal cultures — microbiomes, gastric tissues, respiratory tracts and circulatory systems — are regularly, oftentimes knowingly and purposefully coated, soaked and contacted by the pure and applied, reactive and inert products of petrochemistry. This inner petro-fication results in and allows us to to preserve, manage, medicate and preservation, manage, tolerate and ignore endemic and intermittent disease, discomfort, disability and deregulations of the body. We are, all, oil women and oil men.

Tlazolteotl is an Aztec goddess of purification, steam baths, midwives, filth, and a patroness of adulterers. Her dual her/dual nature was as the goddess of dirt, but also of purification as she ate a person's sins to absolve them before death. Both the „Goddess of Dirt" (Tlazolteotl) and „Eater of Ordure" (Tlahelcuani), she was frequently portrayed with bitumen on her face and around her mouth to indicate divine excrement (holy shit).

EIISC
Edible Inedible Indelible Snack Cakes

The Twinkie is an American snack cake, a "Golden Sponge Cake with Creamy Filling" made and distributed by Hostess Brands, Inc. which trades on National Association of Securities Dealers Automated Quotations (NASDAQ) securities exchange as "TWNK". Twinkie production was suspended on November 21, 2012, and resumed after an absence of at least ten months from American store shelves, becoming available again nationwide on July 15, 2013

There are 39 ingredients in a Twinkie, and all but one are processed. The list, which includes cellulose gum, calcium sulfate and polysorbate 60 are useful chemical additives for sheetrock building materials, shampoo, laundry detergent and jet fuel. Each of these processed ingredients — all vitamins, artificial flavors, colorings, and sorbic acid are made from natural gas and petroleum. To stay fresh on a grocery-store shelf, Twinkies can't contain anything that might spoil, like milk, cream, or butter. Each such perishable ingredient, systematically removed and reengineered as cellulose gum, lecithin, and sodium stearoyl lactylate give the cakes a maximum shelf life of approximately 45 days (1.5 months).

"Well, let's say this Twinkie represents the normal amount of psychokinetic energy in the New York area. According to this morning's sample it would be a Twinkie…thirty-five feet long weighing approximately six-hundred pounds."
—Egon Spengler, Ghostbusters (1984)

COHBOL
Chewing On the Humming Bird On the Left

The Gulf Coast of Mexico is an area of major oil drilling today and a region where Huitzilopochtli, the Aztec God of Sun and War once held dominion. Huitzilopochtli's name is a combination of two Aztec words: huitzilin, meaning "hummingbird", and opochtli, which means "left" — literally, "Hummingbird on the Left".

Chicle is a chewing gum substance made in part from bitumen, or chapapote, a black, natural petroleum tar that washes up onto the beaches of the Mexican interior, the Caspian sea, and the coasts of Norway and China. In addition to chewing chicle, ancient peoples used it for many practical purposes such as adhesives or sealants. Aztec women mixed bitumen together with axin, a yellowish oily substance that they obtained by cooking a small fly-like insect. Bitumen apparently had a refreshing taste. Spanish chronicler Fray Bernardino de Sahagun made note of the chewing of bitumen in his multi-volume treatise on Aztec culture known as The Florentine Codex (a twelve volume project he worked on from 1545 up until his death in 1590). Bernardino de Sahagún wrote that when it is chewed, bitumen "tires one's head; it gives one a headache." (from "The Florentine Codex : General History of the Things of New Spain" by Bernardino de Sahagún,). In Aztec society, the way in which you chewed this gum and where helped orient social, sexual and marital status. Aztec norms strongly disapproved of gum chewing among men, particularly in public.

Chapopote also had numerous domestic, religious, industrial and craft related applications, and Aztec priests used asphaltum for face and body painting. Sahagún write of its harvesting from the Gulf:

Bitumen [is] black, very black, black; [it is] that which flakes, crumbles, breaks up. It comes from the ocean, from the sea; it is produced within the ocean. When it comes forth, [it is] according to the time count. The waves cast it forth. It comes forth, it drops out according to the phase of the moon. When it comes forth [it is] like mat, wide, thich. Those of the seashore, those of the coast lands gather it there. They gather it, they pick it up from the sand."

– The Florentine Codex

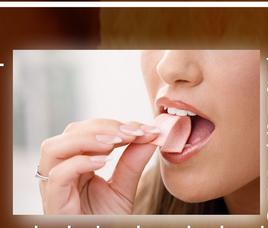
The nearby Chumash people, California's prehistoric peoples collected and chewed tar balls which seeped from the ground in places in that region (like the La Brea tar pits in Los Angeles). They also used tar to to waterproof woven baskets to make drinking vessels. More recent research reported in New Scientist in 2011 indicates that "Asphalt May Have Poisoned Ancient Americans". Bitumen is a source of polycyclic aromatic hydrocarbons (PAHs), which are pollutants that have been linked to a number of health problems.

"The chicle chewer" from The Florentine Codex, Book X. Axtecs created chewing gum by mixing bitumen (aromatic tar) with axin (a greasy oil made from crushed insects).

Of the over 100 polycyclic aromatic hydrocarbons (PAHs) found in oil, coal and tar, many are harmful to humans and life, causing infertility and stunting the growth of fetuses by damaging or altering DNA. (Note that psoriasis, often treated with coal tar, is characterized by an abnormally excessive and rapid growth of the epidermal layer of the skin due to excesses of DNA released from dying cells, which acts as an inflammatory stimulus in psoriasis). PAHs may also have been crucial for the first forms of life, as they contain most of the carbon found in space, and under the right conditions can be transformed into some of the complex molecules necessary for life.

Modern chewing gum is made from synthetic substitutes for natural rubbers, for the most part, butadiene-based synthetic rubbers. The material used as a base for chewing gum is High-Purity Iso-Butylene (HPIB). Isobutylene is an olefin petrochemical that is manufactured from feedstocks in the petroleum refinery, and is a four-carbon branched alkene (olefin) — one of the four isomers of butylene.

Other chemicals approved for use as a base in chewing gum include styrene-butadiene rubber (SBR), isobutylene-isoprene copolymer, paraffin wax, petroleum wax, polyethylene, poly-vinyl alcohol and synthetic terpene resin. Rubbers become softened when they absorb oils, and gum bases are similarly made softer when waxes are added; the waxes act as a kind of 'lubricant' between the strands of the hydrocarbon polymers in the rubber. Other petrochemically derived ingredients in chewing gum include emulsifiers such as glyveryl-monostearate, which are also softening agents and enable other components (including flavouring and sugars) to form a homogeneous mixture.



Humectants, a general term for substances that are used to keep things moist (the opposite of a desiccant) are also added to the mix; these can include chemical substances like triacetin, the triester of glycerol (that is, glycol with three 'ester' groups) first prepared in 1854 by the French chemist Marcellin Berthelot who was born born in Rue du Mouton. Humectants are chemicals with an affinity to form hydrogen bonds with molecules of water, and are used in many products — food, cosmetics, medicines and pesticides — to decrease evaporation and increase shelf life.

There are Internet forums rife with stories and anxious questioning about people chewing tar on the job or as children, mostly in poor areas in the U.S. and the Soviet Union in the late 19th and early 20th centuries, but also right up until today. "Wrigley's" is an American chewing gum company that was founded on April 1, 1891 by William Wrigley Jr. and now wholly owned by Mars, Incorporated. It is the largest manufacturer and marketer of chewing gum in the world. In the year 2000, this maker of Juicy Fruit, Big Red and Doublemint gums signaled the expansion of its offerings in being granted a U.S. patent to develop a gum that contains a dose of the generic chemical in Viagra (patent No. 6531114). The active ingredient of Viagra is sildenafil citrate, itself a drug synthesised from petrochemical sources and patented by the chemical company Pfizer Corp. Chewing gum is used and promoted as a delivery agent for numerous pharmaceutical, medicinal and therapeutic products and treatments. Examples include the addition of fluoride for strengthening tooth enamel and Nicorette, the brand name for gums and a number of other products that effect nicotine replacement therapy (NRT), against addiction to that chemical. Nicotine is itself now synthesised from petrochemical precursors and feedstocks, to feed the growing

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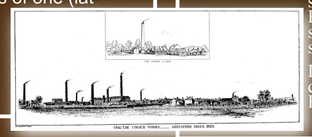
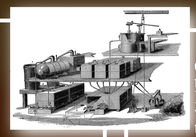
FEEDSARR
Coloration Cookbooks and Contrasting

Anne Ewbanks writes in a January 23, 2018 post at Atlas Obscura of a time "When Food Dye Was Made From Coal Tar" from the factories of one (later, Sir) Henry Perkins. "It was considered almost magical…" Petroleum now





In 1856, an 18-year-old British chemist made a mistake in one of his experiments. That mistake marked the beginning of synthetic food dye. William Henry Perkin wasn't trying to make Red #40 in his lab that day. As a research assistant for a famed chemist, he was trying to whip up synthetic quinine, a treatment for malaria. Perkin was interested in the properties of coal tar, an abundant byproduct of coke fuel, which comes from heating coal. But instead, he ended up with a dark powder. Washing out his flask with alcohol, Perkin was struck by the residue's bright purple color. He tried using it to dye silk, and it was a success. Perkin had found the world's first synthetic dye.

Dozens of illnesses caused by brightly colored Halloween candy in 1950 led the FDA to strike coal tar colors Orange #1, Orange #2, and Red #32 from the list. Any potential renewal of their status was squelched when testing of all three colors made lab animals seriously ill. Twenty years later, another scare involved Red #2. Some tests showed that female rats develop tumors. The backlash was so intense that some companies stopped selling red-dyed food for the next decade. The red M&M disappeared until 1987.

The 1906 Pure Food and Drugs Act empowered American regulators to decide which colors could be used for food, and they only approved seven colors. A writer for The New York Times described with awe the difference: As manufacturers adjusted to the new rules, the "masquerade" was temporarily stripped away. Some formerly red, jarred cherries, for example, were naturally yellow. The coal tar dye used to brighten them had been banned.

Perkin also visited New York in 1906. Fifty years after his mauve discovery, hundreds of chemists celebrated the "magician of coal tar" at a dinner at Delmonico's, the country's most famous restaurant. The Americans all wore mauve bow ties in his honor.

— Ewbanks

FEEDSARR
Front End Engineering Design Actants, and Reagents

There are established naming conventions and product matrixes that travel from the petrochemical cracking and refining factory to the floor of pharmaceutical manufacturing plants. As with any raw material based on extraction, testing for quality and purity are paramount, and various 'grades' are set for uses. Higher grade materials are used and produced variably for customers in pharmaceutical and food industries, and monitored by quality control offices at the shipping and receiving end. The specific petrochemical reagents used in the arsenal of offerings by big pharmaceutical development, delivery, marketing and manufacturing companies would be impossible to list exaustively for all drugs on the market. A partial listing of pharmaceutically relevant precursors derived from oil and gas refineries is included here (all from Burdick & Leffler, "Petrochemicals in Nontechnical Language" (2010)

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The C16 AND C18 ALCOHOLS are used extensively in the cosmetics and pharmaceutical industries as emollient additives (the heaviest of the higher alcohols are actually waxlike), intermediates for perfume and avor components, and as a basis for creams, ointments, and suppositories.

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Until 1959, all the PHTHALIC ANHYDRIDE was made from coal tar NAPHTHALENE... which was easily oxidized directly to phthalic acid. But with phthalic anhydride being only a small share of coal oil, and with the demand for phthalic anhydride escalating rapidly, coal tar became an inadequate source. The frantic search for an alternative route led to the development of the recovery process for ORTHOXYLENE from re nery aromatics streams… and the conversion of ORTHOXYLENE to phthalic acid and anhydride. With the continued growth in the need for plasticizers and the inelasticity of naphthalene supply, orthoxylene now accounts for 90% of the phthalic anhydride supply in the United States.

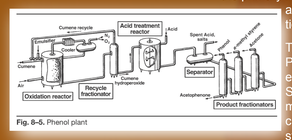

Fig. 8–5. Phenol plant

PHTHALIC ANHYDRIDE is used largely to make plasticizer for polyvinyl chloride. It is also a feed for alkyd resins and for unsaturated polyesters that are widely used in construction, marine, and synthetic marble applications. Other minor applications are dyes, esters, drying oil modi ers, and pharmaceutical intermediates.

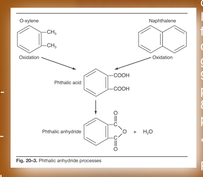

Fig. 20–3. Phthalic anhydride processes

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PHENOL has been used for decades in the medical eld as an antiseptic under its alias, carbolic acid, and at one time as a preservative of human organs under the name creosote (from the Greek kreos, " esh," and sogein, "to preserve"). The name creosote eventually became associated with the wood preservative, but phenol remains the principal ingredient in this product.

The early sources of phenol were the destructive distillation of coal and the manufacture of methyl alcohol from wood. In both cases, phenol was a by-product. Recovered volumes were limited by whatever was made accidentally in the process. Initial commercial routes to on-purpose phenol involved the reaction of benzene with sulfuric acid (1920), chlorine (1928), or hydrochloric acid (1939). All these were followed by a subsequent hydrolysis step (reaction with water to get the –OH group) to get phenol. These processes required high temperatures and pressures to make the reactions go. They are multistep processes requiring special metallurgy to handle the corrosive mixtures involved. None of these processes is in commercial use today.

In 1952, a technological breakthrough was found: the cumene oxidation route. It was much cheaper, and it quickly proliferated. It is now the primary route, accounting for almost all of U.S. production.

The powder form of PHENOL is usually traded either as a United States Pure (USP) (98% minimum) grade or a chemically pure (CP) or synthetic grade (95% minimum), using nomenclature from the pharmaceutical industry. The first indicates a grade suitable for human consumption or for manufacture of a consumable. In the liquid form, the commercial grades are 90%–92% purity and 82%–84% purity.

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PHOSGENE was one of the rst poisonous gases used in the ghastly chemical warfare during World War I. It was later replaced by (and should not be confused with) the more vicious mustard gas (dichlorodiethyl sul de).

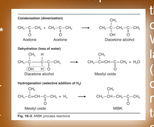

Fig. 19–5. MIBK process reactions

Phosgene is also notorious for being one of the deadly gases created from the disastrous leak at a Bhopal, India, chemical plant in 1984, which resulted in more than 10,000 deaths. Clearly this is nasty stuff that calls for those extraordinary safety procedures.

The rapid industrial growth of PHOSGENE is related to the manufacture of isocyanates for producing polyurethanes and bisphenol A for polycarbonates. After these two applications, about 10% of the phosgene finds its way into chemical intermediates for pharmaceuticals, pesticides, and agricultural chemicals.

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METHYL ISOBUTYL KETONE (MIBK) is more complicated than the one-step conversion process for acetone and MEK. Manufacture of MIBK takes the three-step process shown in gure 19–3, starting with acetone.

Some unique applications for MIBK include metallurgical extrac- tion (particularly plutonium from uranium), coating solvent for resins, a reaction solvent in pharmaceuticals, and as an adhesive. It is also used in the manufacture of methyl isobutyl carbinol.

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The fermentation of sugar in the presence of yeast to produce ETHYL ALCOHOL in the form of wine goes back beyond written history. The sugar came from grapes. Later, starch from grain, potatoes, or "corn squeezins" was used also. The yeast came from living matter in the form of mold or fungus. Yeast contains the enzyme zymase. It is this enzyme that catalyzes the fermentation of sugar. Mix sugar (in grape juice) with yeast, and they will react slowly over weeks, months, or maybe years to form ETHYL ALCOHOL and carbon dioxide, as well as minor amounts of some aldehydes. Depending on preferences, some of the nonalcoholic contents can be separated by distillation.

Alcoholic beverages in the United States are made exclusively by the fermentation process, not the petrochemical process. It has nothing to do with the chemistry. It is due to a law enacted to protect the grain growers, not the consumers.

Until World War I, fermentation accounted for all the ETHYL ALCOHOL produced in the United States. In 1919, a petrochemical route based on ethylene, sulfuric acid, and water was developed commercially and called indirect hydration. By 1935, only 10% of the ETHYL ALCOHOL was produced this way, primarily because of the expense of the ethylene at that early stage of the industry. With the rapid improvements in ethylene technology, the share quickly grew to 90% by the 1960s. At that time, an alternate route, direct hydration, was developed, eliminating the use of sulfuric acid and one step in the process. Direct hydration replaced the indirect hydration process by the 1970s. Advantages were higher yields, less pollution, and lower plant maintenance due to less corrosion—all leading to better economics.

Currently, almost all synthetic ETHYL ALCOHOL is produced via the direct catalytic hydration of ethylene. That volume is totally overwhelmed by the fermentation-produced alcohol for the motor fuels market.

The balance of the industrial ETHYL ALCOHOL is in demand as a solvent in personal care products (aftershave lotion, mouthwash), inks, cosmetics, detergents, household cleaners, pharmaceuticals, industrial coatings, and as a processing solvent.

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BASF introduced high-pressure technology way back in 1960 to make ACETIC ACID out of METHANOL and carbon monoxide instead of ethylene. Monsanto subsequently improved the process by catalysis, using an iodide-promoted rhodium catalyst. This permits operations at much lower pressures and temperatures. The methanol and carbon monoxide, of course, come from a synthesis gas plant.

More than 65% of the ACETIC ACID produced in the United States goes into vinyl acetate. Nearly all the vinyl acetate ends up as polyvinyl acetate, used to make plastics, latex paints, and adhesives. About 12% of acetic acid is converted to acetic anhydride that is mostly used to make cellulose acetate, the white stuff in cigarette liters. It is also used in the manufacture of plastic sheeting and film and in formulating lacquers.

ACETIC ACID also finds use as a chemical intermediate in the production of acetate esters for paint solvents and as a reaction solvent for the manufacture of terephthalic acid. Also, acetic acid is the source of the acetyl group in the manufacture of ACETYL SALICYLIC ACID (ASPIRIN)

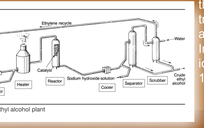
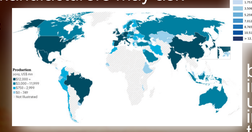


Fig. 16–2. Ethyl alcohol plant

PPP
Planetary Petrochemical Pharmaceutics

Pharmaceuticals, generally speaking are now vital to modern, bodily health. This chemical category represents a relatively small but increasing proportion of total petroleum usage. More than half of most adult Western citizens take prescription medications at some point in their lives. Approximately 2.3 billion medication orders or prescriptions were written in 2006 in the U.S. alone. Analgesics, antidepressants, antihyperlipidemics, antidiabetic agents, antiemetics, and antihistamines are the leading medications prescribed. Approximately 3% of petroleum production is used for pharmaceutical manufacture, but just under 99% of pharmaceutical feedstocks and reagents are derived from petrochemicals (Joyce Easter, PhD, Virginia Wesleyan College, December 2010).

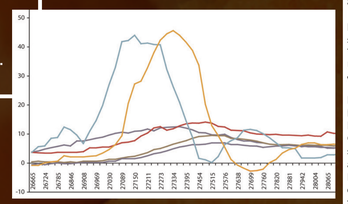
Pharma- and petro-chemistry two highly interlinked industries, yet they are so in a highly asymmetrically interdependent way. If "big pharma" matters little to big oil, big oil matters a great deal to big pharma. (One is reminded of Canadian Prime Minister Pierre Trudeau's comment that living next to America "is in some ways like sleeping with an elephant. No matter how friendly and even-tempered is the beast, if I can call it that, one is affected by every twitch and grunt.").

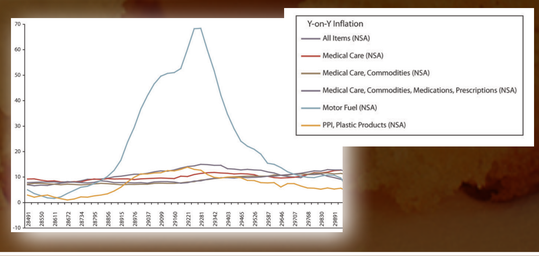


Drug manufacturers may ask where the starting materials for drugs purchased, but traceability can be difficult. they chase from, Asking "where do you get your butyl lithium from?" is somewhat akin to asking the name of the farmer who raised the specific chicken for a chicken sandwich bought at a McDonalds. The lines of flight, mixing and transport are many and complex, and those commissioning a drug to be manufactured to specification will be dealing with pharmaceutical engineering firms in India, and China. The suppliers of these Chinese and Indian industries come from other smaller industries which make the petrol cracking and small chemical conversions of these cracking products. Problems of supply and temporal latency in material pipelines such as "using up the world's supply of magnesium bromide" for a short time, to conduct a single synthetic step, can arise in what is a surprisingly disparate and wild industrial landscape.

A number of synthetic steps which are changed in scaling up from laboratory to manufacturing scales have to do with (chemically relatively simple, but costly) manufacturing limitations. Not every company, region or industrial plant can do, for example, cryo-reactions which require large, one thousand litre liquid nitrogen cooled vessels. Not every company, region or industrial plant has a large enough palladium catalyst contraptions to do relatively dangerous hydrogenation reactions that require large vessels of highly explosive hydrogen gas under high pressure. Less a matter of money, than time, plants and manufacturers are less likely to buy into processes that can take many months to commission, startup and test. Validation batches are high-loss, lengthy steps for new production manufacturers to bring online.

Glenmark Pharmaceuticals is a pharmaceutical company headquartered in Mumbai, India that was founded in 1977 by Gracias Saldanha as a generic drug and active pharmaceutical ingredient manufacturer; he named the company after his two sons. Glenmark's first manufacturing facility in Nashik, India, which commenced operations in 1983. The facility is equipped to manufacture products across various dosage forms: Oral solids, Liquid orals, External creams and Powders, and was ISO 14001 (environmental responsibilities and management) approved in 2004 and has regulatory approvals with ANVISA Brazil, MOH Ukraine, INVIMA Columbia, NDA Uganda, MOH Nigeria, TFDA Tanzania, MOH Ethiopia, MCC South Africa, MOH Congo, MOH Oman, WHO – GMP. Products made at Nashik are exported to Glenmark's emerging markets including Asia, India, Africa, Russia, the Commonwealth of Independent States and Russia, and Latin America.





The trajectories of year-on-year inflation several non-seasonally adjusted price variables including motor fuel, health care, health care services, health care commodities, prescription medications, plastics, and the consumer price index for the years 1973—1977 and 1978—1982 show declining associations between oil and health care prices. (Hess, J., Bednarz, D., Bae, J., & Pierce, J. (2011). Petroleum and health care: evaluating and managing health care's vulnerability to petroleum supply shifts. American journal of public health, 101(9), 1568-1579.) There often appears to be an association between decreased petroleum supply (indicated by a rise in inflation in motor fuel prices, which covary closely with petroleum supply), a rise in the price of plastics, and, lagged by several months, the prices of healthcare commodities such as pharmaceuticals and health care as a whole.

AOPS
Aspirin Offloading, Production and Storage

Aspirin is an anti-inflammatory and one of the first drugs to come into common usage. It remains the mostly widely used drug in the world. Approximately 35,000 metric tonnes of the pharmaceutical are produced and consumed annually, or approximately 100 billion standard aspirin tablets each year. Aspirin is acetylsalicylic acid (ASA) which, typically for medicinal chemistry, comes originally from a natural source, although today is difficult to find as a commercial nonsynthetic. It was redeveloped in the laboratory and developed into pill form to be sold at mass market. Natural aspirin can be derived from the herbs meadowsweet and willow bark, but as a chemical and process was patented by Bayer in Britain (filed 22 December 1898) and the United States (US Patent 644,077 issued 27 February 1900). The word Aspirin was Bayer's brand name, a drug who's popularity grew over the first half of the twentieth century but declined after the development of acetaminophen and paracetamol in 1956, and then ibuprofen in 1962. Bayer's profits were eaten into after its brand name and rights to the trademark were lost or sold in many countries, and generic products by other manufacturers proliferated.

When SALICYLIC ACID (100.0 parts) is heated with acetic anhydride (150.0 parts) for 3 hours under reflux, the salicylic acid is quantitatively acetylated. After distilling off the acetic acid one obtains the above in the form of needles, which, when crystallized from benzene, melt at 136 degrees (value in the literature is 118 degrees). In contrast [with] the literature reports, my acetyl product no longer gives a reaction with ferric chloride, which readily distinguished it from salicylic acid. By its physical properties, e.g. its sour taste without being corrosive, the acetylsalicylic acid differs favourably from salicylic acid, and is now being tested in this respect for its usefulness.

— From the laboratory journal of Felix Hoffman, 10 August 1897 (from Diarmuid Jeffreys' 2010 book "Aspirin.")

On the 10th of August, 1897, Felix Hoffmann synthesized acetylsalicylic acid while working at Bayer under Arthur Eichengrün. By acetylating salicylic acid with acetic acid, he succeeded in creating acetylsalicylic acid in a chemically pure and stable form. The pharmacologist responsible for verifying these results was skeptical at first, yet once several large-scale studies to investigate the substance's efficacy and tolerability had been completed, it was found to be a pain-relieving, fever-lowering and anti-inflammatory substance. The company then worked to develop a cost-effective production process that would facilitate the promising active ingredient to be supplied as a pharmaceutical product. In 1899 it was marketed for the first time under the trade name Aspirin, initially as a powder supplied in

ACKNOWLEDGEMENTS

Special thanks to Dr. E. Villemin of the Organometallic chemistry and Polymerization catalysis group, Institut de Recherche de Chimie Paris (Prof. C. Thomas) and Laboratory for Inorganic Chemical Biology (Dr. G. Gasser), Chimie ParisTech, PSL Research University. Thanks as well to

Professor Sylvie Michel of the Equipe Pharmacognosie, Chimie des substances Naturelles at Université Paris Descartes, Faculté de Pharmacie and for the wonderful visit to the museum there. Also, much appreciation for instructive exchanges with Christian Bonah, MD. PhD and Professor for History of Science as well as Nils Kessel, Maître de conférences à l'Université de Strasbourg, both of DHVS Département d'histoire des sciences de la vie et de la santé in Strasbourg. Gratitude and love to Nicolas Malivel, and family, and Darren Begley, and family.

As expected, the increase in health care inflation is small compared with the rise in the price of plastics. These patterns are most evident in the first oil price shock in the 1970s, diminishing over time. There is increasing volatility in oil price inflation that makes it difficult to discern a clear pattern in later shocks.

There is little likelihood that reverse causation is driving these observations because health care delivery consumes a relatively small proportion of total petroleum output and does not set demand for petroleum-based products. Oil supply shifts are presumed to not be related to health care delivery, so there is little likelihood that this association is significantly confounded by an unexamined factor.

The most likely reasons for the observed association are that health care delivery is petroleum dependent and that its cost is sensitive to shifts in petroleum supply. The apparent decline in the magnitude of effect over the two periods, 1973—1977 and 1978—1982, is important to note, however. This is likely because of the decreasing contribution of both transport and supply costs to overall health care costs. Health care is a service industry, and labor costs are increasingly dominant in its price structure. Overall, the analysis suggests an association between petroleum supply and health care prices that is inconstant over time because the costs of other health care components have risen disproportionately.

Oil price inflation has a modest impact on health care price inflation, with some time lags. Petrochemical feedstock costs are likely a relatively small share of total pharmaceutical costs, however, which are dominated by marketing, research, and development (largely labour and distribution costs). Also, the impact on medical commodity prices started later than did the impact on other medical care prices, likely due to manufacturing times, lengthy testing and delivery lags and transport and shelf life factors. The health care system exhibits high exposure, moderate susceptibility, and high resilience to short-term supply shocks; long-term shocks likely pose a more difficult challenge. (Hess, J., et. al 2011)