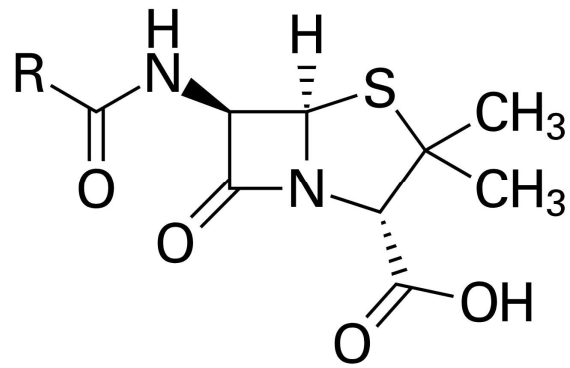


“晶体魔术师”



In same 1945, A. Fleming, H. Florey, and E. Chain split the Noble Prize.



Penicillin was at that time the largest molecule to have succumbed to X-ray methods. Hodgkin's proposed structure- β -lactam ring, was not so easily accepted by the scientific community.

To date, she's the only female British scientist to receive a Nobel Prize.

“晶体化学皇后”



She was elected to the Royal Society
in 1947



"I was captured for
life by chemistry
and by crystals."

Dorothy Hodgkin



Among the 71 British Nobel Prize
winners for science,

**Meet the
only woman.**

We all need science.
Science needs women.
You can help.



www.dorothyhodgkinproject.org



Dorothy Crowfoot Hodgkin

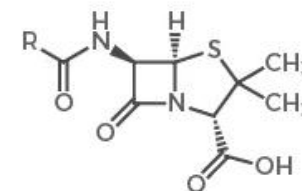
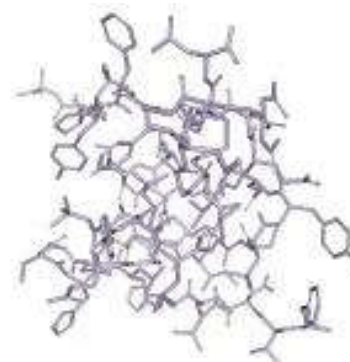
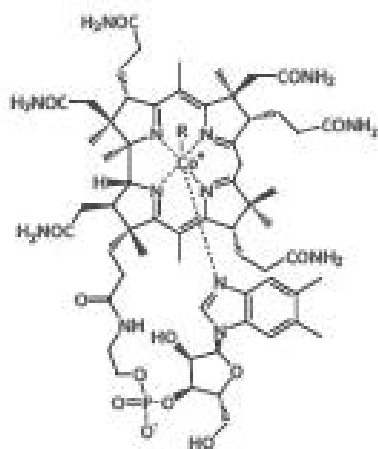
Dorothy Hodgkin, one of the outstanding scientists of the 20th century, solved the structures of

—Penicillin, 1945

—Vitamin B12, 1954

—Nobel Priz, 1964

—Insulin, 1969



These achievements had an immense impact on chemistry, biochemistry and medical science, establishing the power of X-ray crystallography, and changing the practice of synthetic chemistry.

“Combining two careers and three children proved “reasonably easy”...

**A devoted couple with 3 children
9 grandchildren,
3 great-grandchildren**

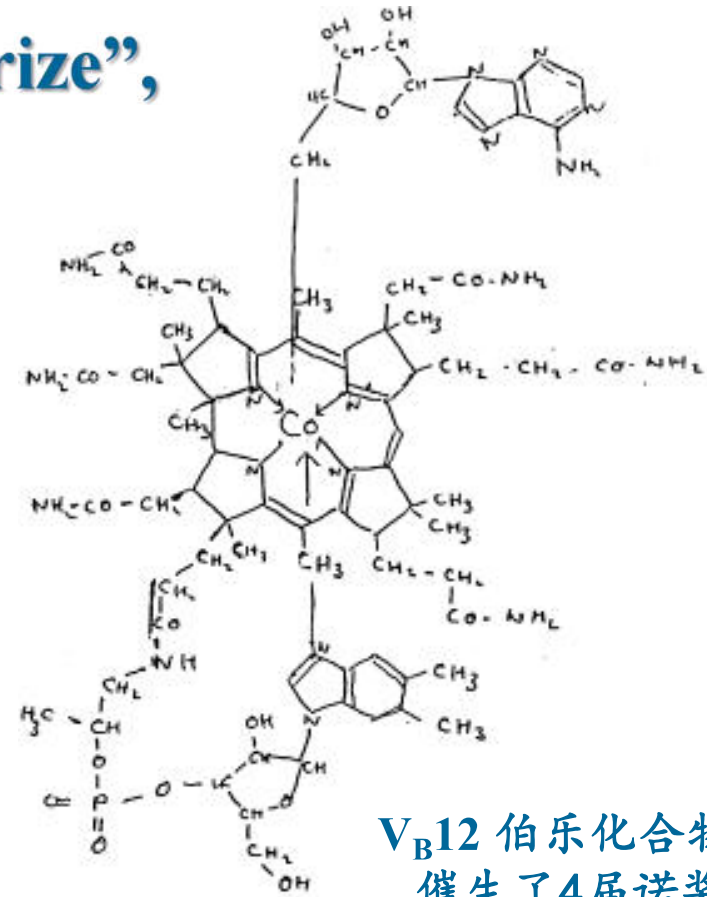
- **Thomas also taught at Oxford**
- **Her arthritis improved w/each pregnancy**
- **She made time for her kids**
- **She could switch easily from deep calculations to kid talk!**



“Oxford Housewife Wins Nobel Prize”, “Nobel Prize for British Wife”...



Hodgkin与中国科学家和学生撒切尔夫人



V_B12 伯乐化合物
催生了4届诺奖



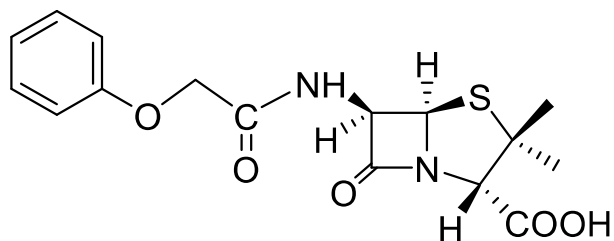
Dorothy Crowfoot Hodgkin
Sept. 23rd 1965

B₁₂ - coenzyme.

with apologies for my
shaking hand

First disclosed at a symposium in
1961; then in a publication in 1962

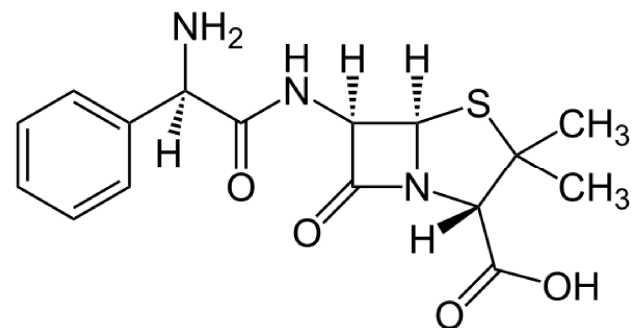
Synthesizing Penicillin



Penicillin V



John Clark Sheehan
(1915 –1992)



Ampicillin, a commonly used semi-synthetic penicillin that is taken orally rather than by injection, was discovered in 1958 and came into commercial use in 1961.

After nine years of hard work at the Massachusetts Institute of Technology (M.I.T.), he became the first to discover a practical method for synthesizing penicillin V in 1957.

Synthesizing Penicillin



Dr Wilson Baker hard at work



**Sir Robert Robinson and
Tetrahedron创始人
生物碱之父
Nominated on 51 occasions
for the Nobel Prize**

Sir Ernst Boris Chain与华北制药厂

Chain is the father of the modern antibiotic industry



Ernst Chain
A great man of science



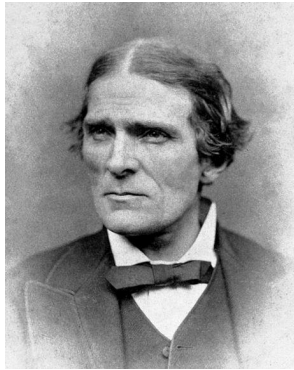
华北制药



Chain was also responsible for helping several countries to start up a modern penicillin industry following World War II.

[Applied Microbiology and Biotechnology](#),
2013, 97 (15) : 6613-6622.

Contribution to the Discovery of Penicillin



John Burdon-Sanderson (1828-1905)
1871:*Penicillium* inhibited growth of bacteria



Sir William Roberts
(1830 –1899)



Ernest Duchesne
(1874 –1912)

In 1896, the French medical student Ernest Duchesne discovered the antibiotic properties of *Penicillium*, but failed to report a connection between the fungus and a substance that had antibacterial properties, and *Penicillium* was forgotten in the scientific community until Fleming's rediscovery.

Duchesne was posthumously honoured in 1949, 5 years after Alexander Fleming had received the Nobel Prize.

Ernest Duchesne

Forgotten Father of Penicillium



Ernest Duchesne
(1874-1912)



Duchesne was posthumously honoured in 1949, 5 years after Alexander Fleming had received the Nobel Prize.

A history of antibiotics contains a suggestion on why it was forgotten:

While Fleming generally receives credit for discovering penicillin, in fact technically Fleming rediscovered the substance. In 1896, the French medical student Ernest Duchesne originally discovered the antibiotic properties of Penicillium, but failed to report a connection between the fungus and a substance that had antibacterial properties, and Penicillium was forgotten in the scientific community until Fleming's rediscovery.


青霉素的偶然性

Fleming's serendipitous discovery changed the course of medicine

- **Accidental Discoveries** : 如果1928年的夏天不是凉快潮湿的天气, 如果某个青霉孢子没有幸运地落在弗莱明的实验培养皿上, 如果没有产生足够的青霉素? 如果弗莱明对这个意外事件漠然置之, 青霉素能否发现或者能否在20世纪40年代就造福人类, 我们都无法假设。
- 但青霉素走向临床又有一定的必然性: 社会对抗生素的迫切需求, 微生物学、病理学等基础学科的发展, 多学科的配合等都加快了青霉素的开发应用过程。
- 一个药物从实验室研究到临床应用存在很多关键因素和关键环节, 缺了哪一个都可能会导致最终的失败。意料之外而又情理之中。
- 一个偶然的发现, 一个被两次发现的发现, 一个及时的发现, 一个迅速商业化的发现, 一个划时代的发现-----带动一个学科的发展。

What if Fleming Had not Discovered Penicillin?

ABOUT PENICILLIN



From *Algebra* comes the report by the Allied Medical Commission: "There never has been a therapeutic agent to compare with penicillin in its usefulness against a wide variety of diseases, including pneumonia, blood infections, syphilis, and a host of other infectious 'ills'."

More than any *antibiotic* since its mold, penicillin is being made today as there was a year ago—and the cost has been reduced 84 per cent. Remarkable changes have occurred in the method of manufacturing since penicillin was first made at the Squibb Laboratories in 1940. But the ones used for growing the mold have been replaced by huge tanks several stories high. Production time has been cut from two weeks to three days.

Military needs come first, but production is now great enough to provide limited amounts of penicillin for civilian use. The House of Squibb is proud to have shared in the development of this new medicinal agent that now is man's greatest defender against bacterial invasion.

Through a microscope the filices and spores of Penicillium seem to look like this. Growing in a liquid medium, the mold gives out golden droplets rich in penicillin. The liquid must be concentrated over 20,000 times to obtain pure penicillin. The Squibb Laboratories were the first to obtain crystals of Penicillin from the wettable powder.



New Squibb Penicillin Building. Great tanks have replaced the glass bottles in which penicillin was grown so slowly. Instead of a few pounds, now over a ton of mold is grown each day, making possible a great increase in the production of penicillin.

SQUIBB
A name you can trust

Specialized *antibiotic* medicine. Various penicillin in an uncombined form, with ultraviolet light to sustain the oil. For over two years, Squibb has been producing penicillin for the National Research Council and for the armed forces. Today, through advanced hospitals, physicians can apply for the quantity of penicillin they need to treat infections.

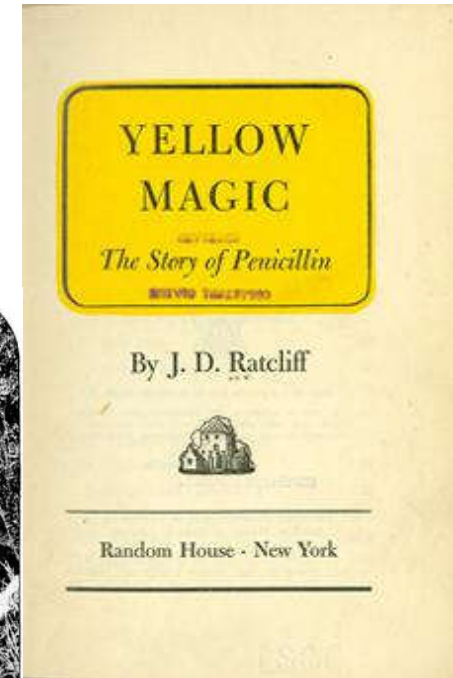


PENICILLIN, New Wonder Drug from Mold



By IRIS JOHNSON

A GREENISH BLUE mold like the one that grows on stale bread, or lends aroma and flavor to Roquefort cheese, now promises to be an important ally in helping wounded soldiers fight their way back to health.



人口学家把这段时期称为“死亡率转变的重大拐点”。青霉素和其它抗生素创造了“现代医学奇迹的奇迹”。医学延长人的寿命达20岁，其中抗生素完成了其中的10岁。 **Estimated to have saved over 200 million lives**

丘吉尔和青霉素的故事

一段因青霉素而起的传奇

科学家和政治家本是两类人，但是，青霉素却能让两类人结识。青霉素的发明者亚历山大·弗莱明与首相温斯顿·丘吉尔之间，就有着一段因青霉素而起的传奇故事。



A “wondrous fable”

医学有故事



青霉素之缘

——丘吉尔与弗莱明



各自的勋章



Sir Winston Leonard Spencer Churchill (1874-1965), 政治家、演说家及作家以及记者, 1953年诺贝尔文学奖得主, 曾于1940-1945年及1951-1955年期间两度英国首相。

青霉素故事背后的一些思考

The discovery of penicillin, one of the world's first antibiotics, marks a true turning point in human history — when doctors finally had a tool that could completely cure their patients of deadly infectious diseases.

Dr. Fleming famously wrote about that red-letter date: “When I woke up just after dawn on **September 28, 1928**, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic, or bacteria killer. But I guess that was exactly what I did.”

Why didn't Fleming make penicillin into a medicine himself?

Why the discovery of penicillin laddted 14 years?

Antibiotics fueled one of the great revolutions in modern medicine and human health

如果细致地对待身边出现的不起眼的小事，甚至有可能做出影响历史进程的事情。 “Chance favours only the prepared mind” .

Impact of Penicillin

磺胺药物和青霉素开启了现代制药工业？

It has been said that it was the creation of sulfas and penicillins that created the pharmaceutical industry, one of the largest and most profitable industries in today's world.

Drug companies existed before the 1930s, of course, but were much smaller and made such compounds as prescription medicines, aspirin, and antacid pills.

It ushered in a series of other “wonder drugs” — they became a symbol of modern therapeutics.

中国第一个抗生素:青霉素的诞生



汤飞凡



朱既明



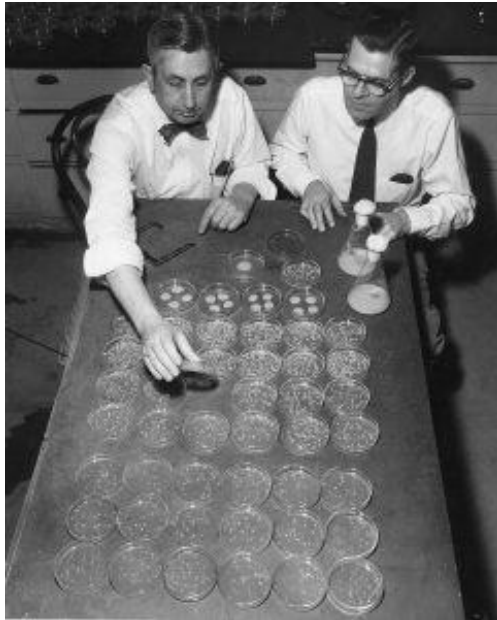
樊庆笙



童村

- 汤飞凡 (1897—1958): 医学病毒学家, 微生物学家, “衣原体之父”
- 朱既明 (1917—1998): 1980年当选为中国科学院院士 (学部委员) 中国预防医学科学院病毒学研究所研究员、名誉所长
- 樊庆笙 (1911-1998): 著名农业微生物学家, 农业教育家, 中国农业微生物学的开创者之一
- 童村 (1906—1994): 医学家、微生物学家, 我国抗生素事业的先驱者

青霉素在我国的诞生



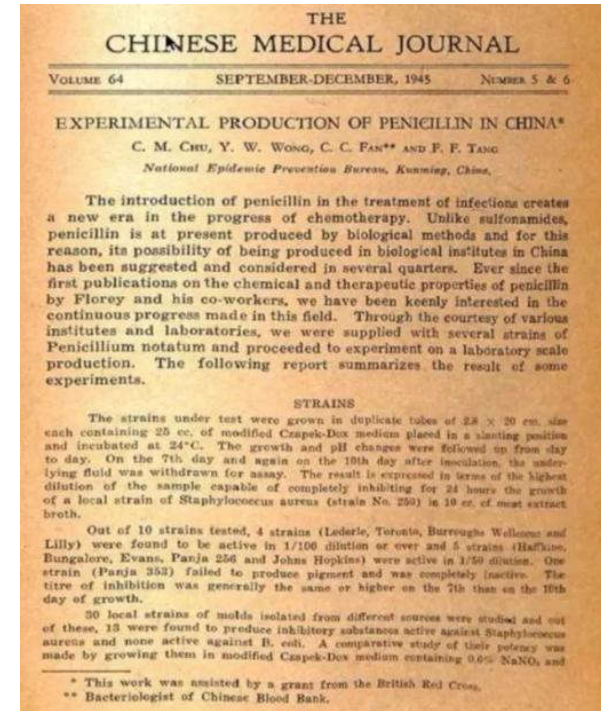
Botanists John Stauffer (left) and Myron Backus studying bacterial cultures



樊庆笙留美期间在实验室



我国最早的青霉菌株



樊庆笙1945年发表在中华医学上的论文“青霉素在中国的研制”

国产青霉素的功臣——张为申



张为申 (1909-1966)- “新中国抗生素事业奠基人”

中国抗生素之父——张为申



1959年捷克国际抗菌素会议其间合影，左起：方纲、张为申、钱恩、胥彬

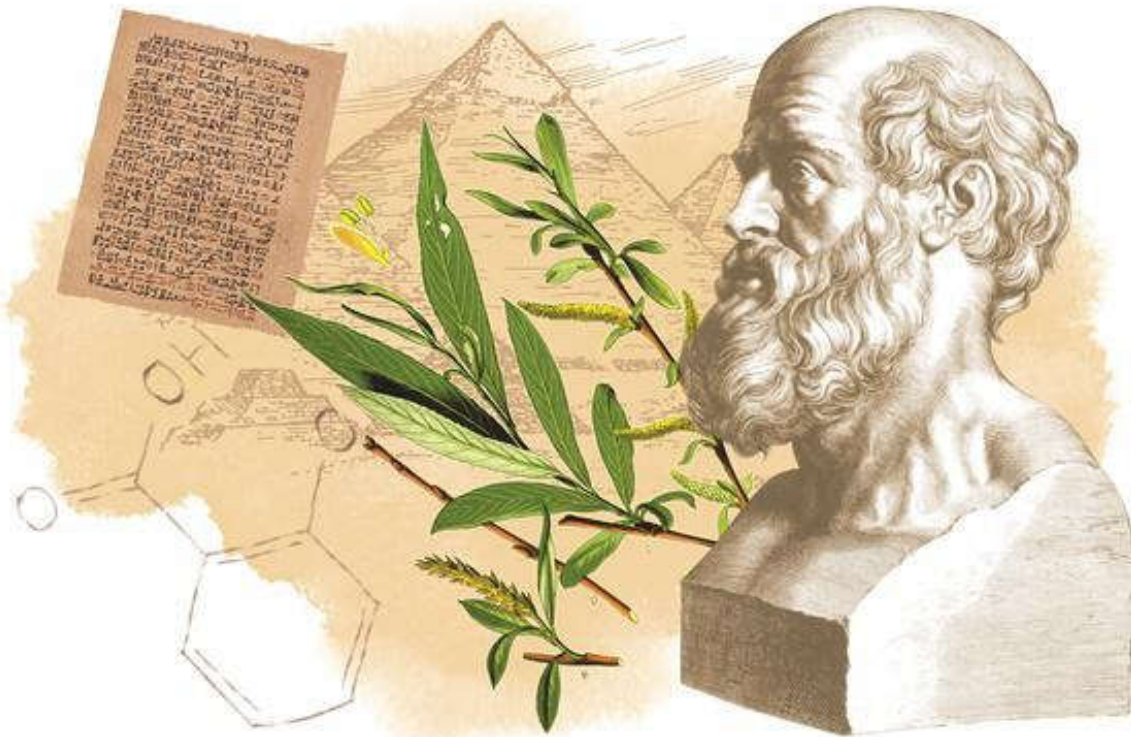
魏曦：我国微生物生态学的奠基人



魏曦 (1903—1989)



柳树皮的故事



Headache? Fever? Muscle pain?



You may have heard the phrase: “Take two aspirin and call me in the morning.”

“Take two Aspirin and call me in the morning”

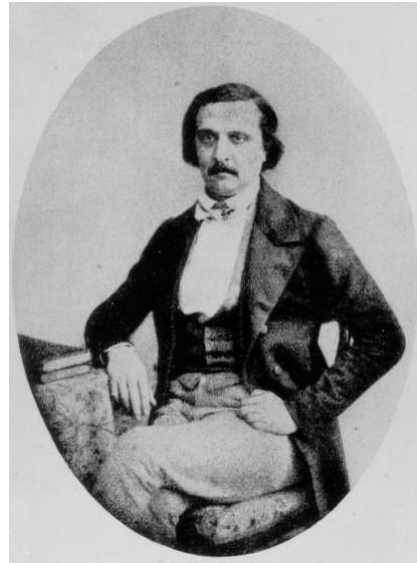
阿司匹林：早期天然产物研究最成功的范例

Aspirin®, the first blockbuster drug

德国总理认为阿司匹林和计算机、汽车并列，是德国三大支柱之一



1828年，慕尼黑药理研究所的化学家Johann A. Buchner成功从柳树皮中提取到一种淡黄色的晶体，这就是水杨苷



1853年，French chemist Charles F. Gerhardt (1816–1856) synthesized impure acetylsalicylic acid.

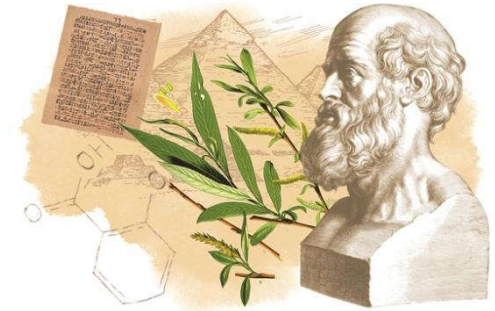


水杨酸到乙酰水杨酸（阿司匹林）只有短短一步要走，这一步，是由霍夫曼（Felix Hoffmann）完成的。
October 10, 1897

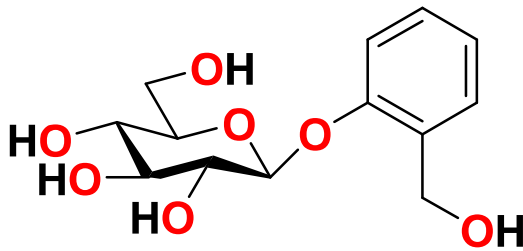
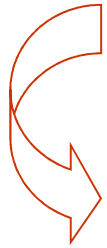
柳树皮的故事—阿司匹林



A organic compounds is recognizable by name to the average citizen.

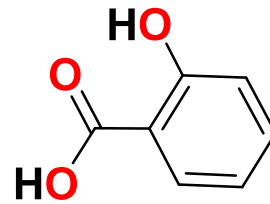


Socrates, 前469-399年
苏格拉底-西方的孔子



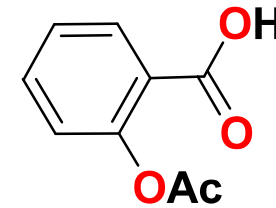
Salicin 水杨苷-前药

1826年意大利人Brugnatelli和Fontana发现柳树含有水杨苷，1829年法国化学家Henri Leroux改进了提取技术，从1.5公斤的柳皮中提取30克的水杨苷



Salicylic acid

1838年意大利
Raffaele Piria
1814 -1865



Acetylsalicylic acid
1853年法国化学家

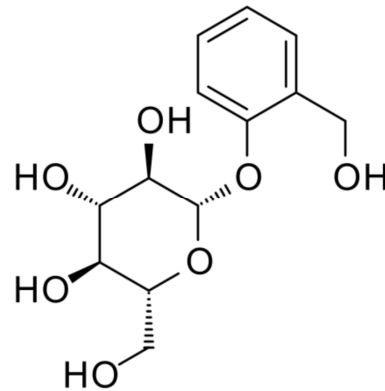
Charles F. Gerhardt
1897年合成乙酰水杨酸. 1899年上市

Salicin 水杨酸苷

The aspirin – from willow to wonder drug



**Johann Andreas
Buchner (1783-1852)**



Salicin 水杨酸苷

前药 Pro-drugs

**How White Willow Bark Benefits the Skin—
Anti-aging and Helps cleanse oily skin, smoother,
softer skin, Antioxidants**

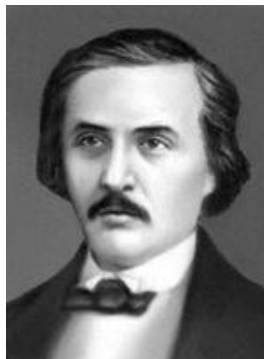
Miracle Tree: 6 Health Benefits Of Willow Bark To Get You Chomping At The Bit

20世纪最伟大的科学技术发明

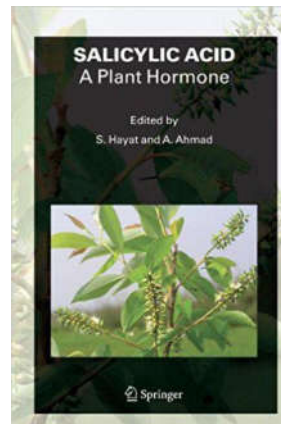
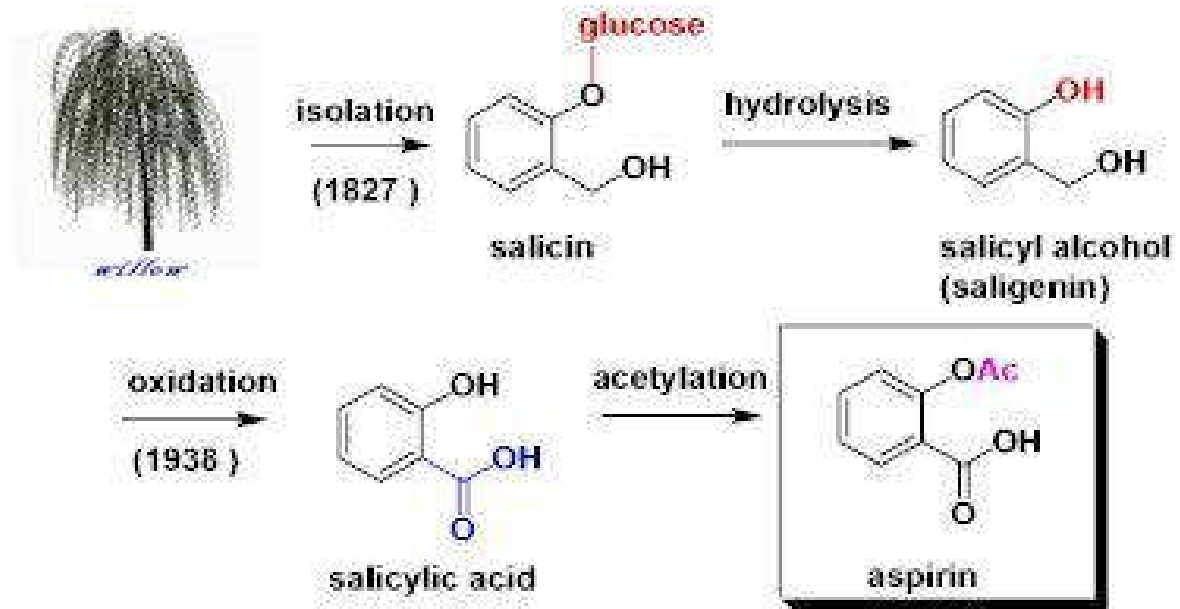
阿斯匹林列第五位



Raffaele Piria
(1814–1865)



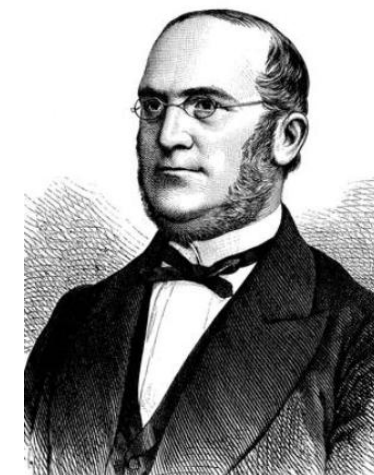
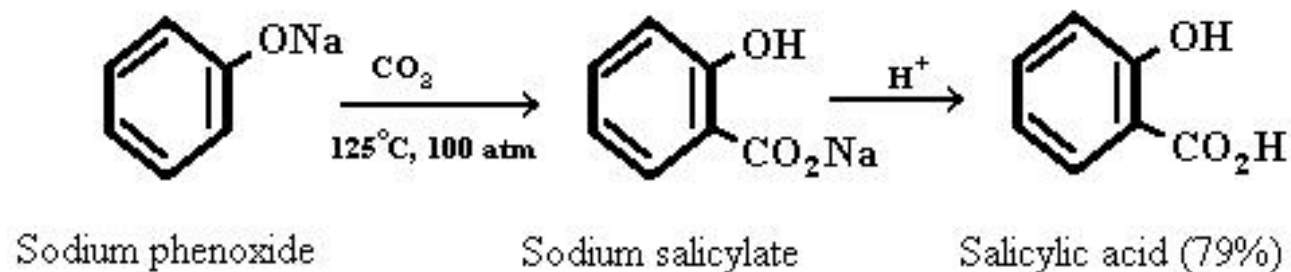
Charles Frédéric Gerhardt



前药 Pro-drugs

天使药丸

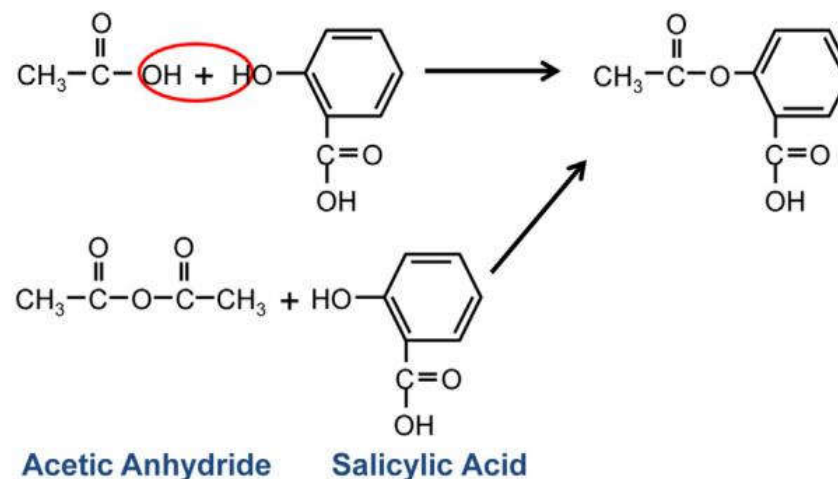
Kolbe Process for Salicylic Acid



Hermann Kolbe
(1818 – 1884)
“Synthesis”

The Kolbe Synthesis

1859

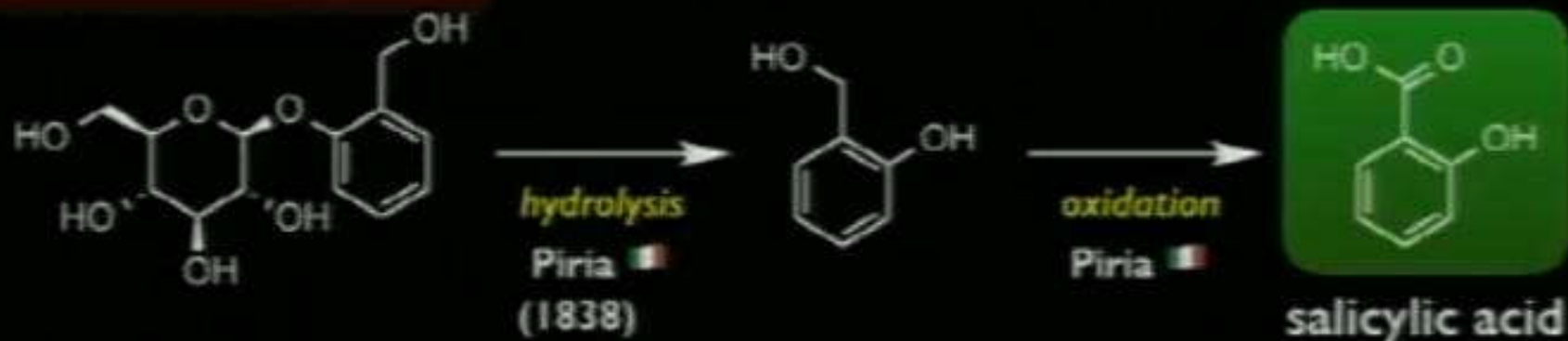


Sir John Vane
(1927–2004)

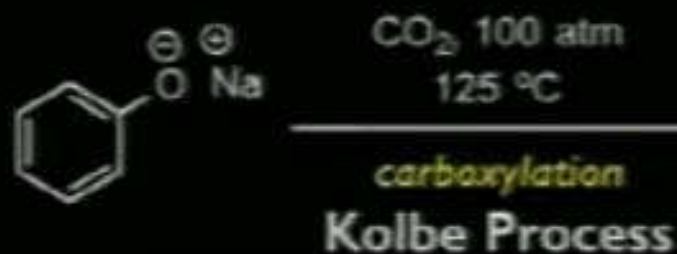
Pharmacologist John Vane elucidated its mechanism of action in inhibiting prostaglandin production in 1969 and was awarded the Nobel Prize for Medicine in 1982.

Synthesis of Salicylic Acid

from natural source



Hermann Kolbe (1859)



industrial production

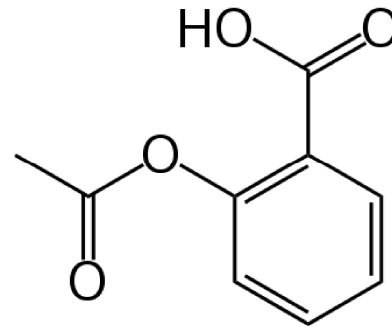
- 10% price of natural extracts
- 24,000 kg annual production

Who Synthesized Acetyl Salicylic Acid

In a chemically pure and stable form



Felix Hoffmann
(1868-1946)



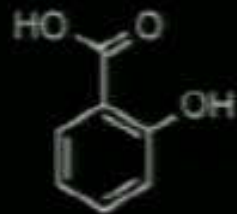
In 1897, on 10 Aug, Hoffmann synthesised aspirin (acetylsalicylic acid) by acetylating salicylic acid with acetic acid

前药 Pro-drugs



Arthur Eichengrün
(1867-1949)

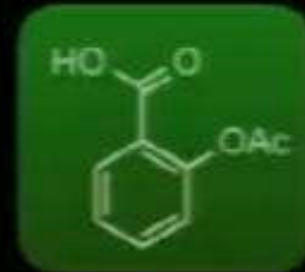
Aspirin



salicylic acid

Ac₂O, reflux

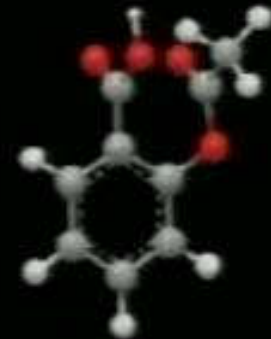
acetylation



acetylsalicylic acid (ASA)

Aspirin[®]

"miracle drug"



Side effects:

- bad taste
- irritation to digestive tract
- vomiting and ulceration

pharmaceutical
industry/
medicinal chemistry

medicinal chemistry



first made in a
pure form



Felix Hoffmann
(1897)

Bayer AG, Leverkusen, Germany

Among the 17 molecules that changed the world-aspirin was No. 4

拜耳开发阿司匹林开启了制药公司 主导药物研发的时代



拜耳公司创始人富黎德里希·拜耳及公司标志1910

每年全球要消耗2000亿片阿司匹林，相当于每个人每年吃掉20片。
德国总理将阿司匹林和计算机、汽车并列，认为是德国三大支柱之一。

The Men Who Tamed the Hangover



Advertisement for Aspirin featuring two portraits of men and various packaging. The top portrait is of Arthur Eichengrün, and the bottom portrait is of Felix Hoffmann. The text includes "Aspirin", "Bayer Tablets of Aspirin", and "The Bayer Cross Your Guarantee of Purity".

Aspirin

100 Bayer Tablets of Aspirin

BAYER

Aspirin

lets of Aspirin

and every package of genuine Aspirin bears

"The Bayer Cross"  "Your Guarantee of Purity"

Pocket Boxes of 12, Bottles of 24 and Bottles of 100

The trade-mark "Aspirin" (Reg. U. S. Pat. Office) is a guarantee that the monoacetic acid of salicylic acid in these tablets is of the reliable Bayer manufacture.



Advertisement for Aspirin featuring a nurse and various packaging. The text includes "Migraines, Névralgies, Rhumatismes", "Demandez à votre Pharmacien", "l'Aspirine", "USINES du RHÔNE", and "LABORATOIRE des PRODUITS USINES du RHÔNE".

Migraines, Névralgies, Rhumatismes

Demandez à votre Pharmacien

l'Aspirine

"USINES du RHÔNE"

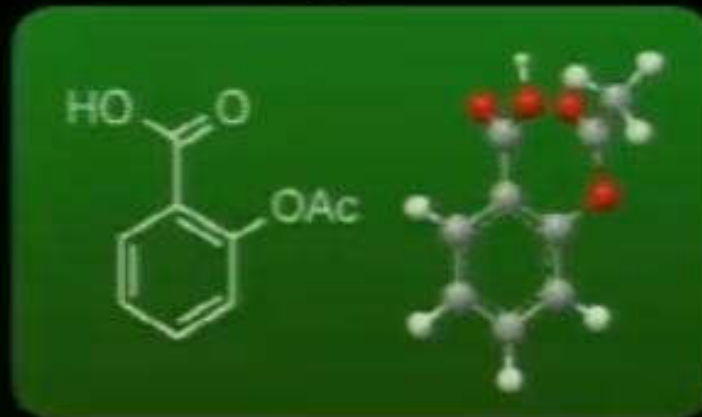
En TUBES de 20 COMPRIMÉS

LABORATOIRE des PRODUITS USINES du RHÔNE
21, Rue Jean Goujon, PARIS

Top: Arthur Eichengrün (1867-1949)
Bottom: Felix Hoffmann (1868-1946)



Aspirin

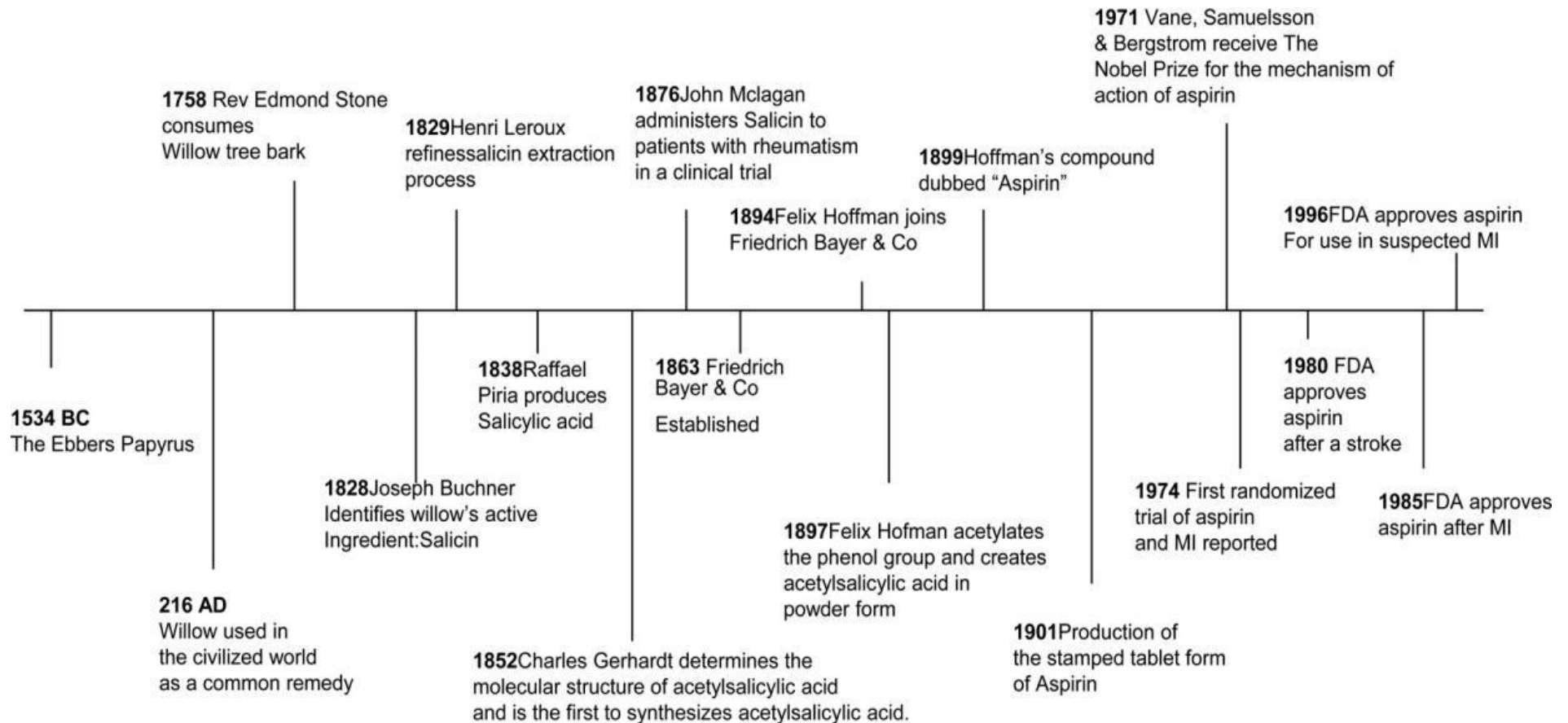


- headache
- muscle aches
- backache
- arthritis
- common cold
- toothache
- menstrual cramps
- **stroke**
- **heart attack**
- **cancer**
- **diabetes**

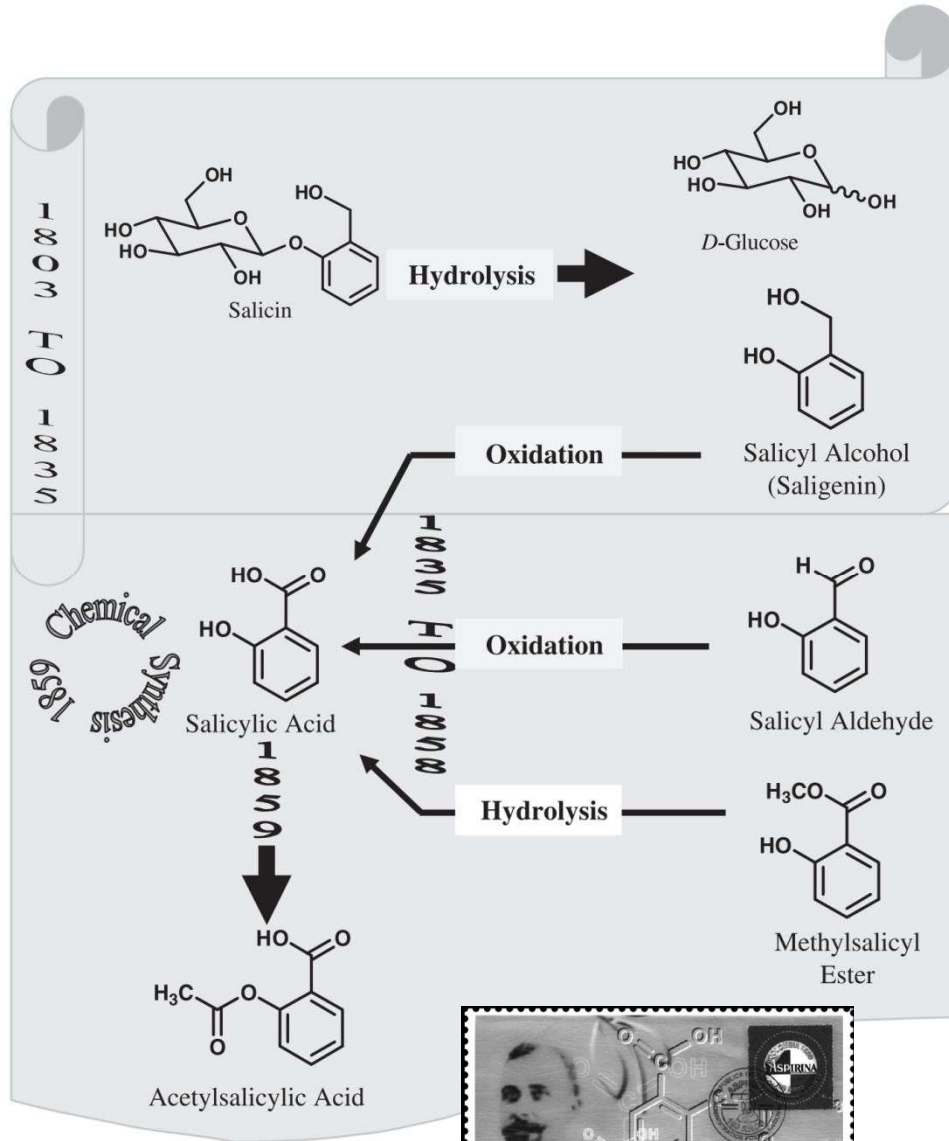


**100 billion tablets
swallowed every year!
(even in space shuttles)**

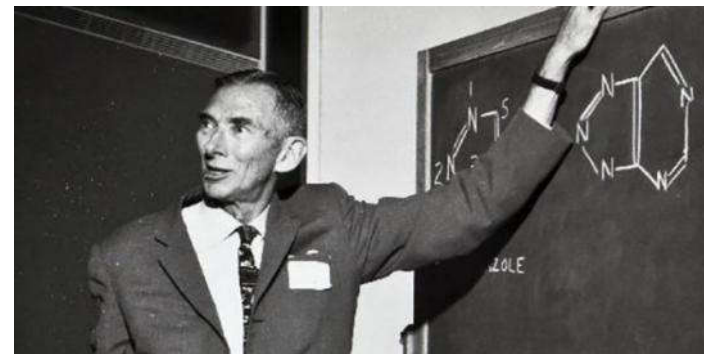
Aspirin Throughout the Ages: A Historical Review



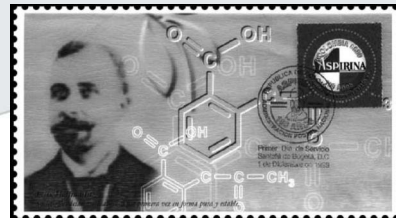
Schematic illustration of the history of aspirin discovery



Aspirin: A Pro-Drug



Adrian Albert 1907-1989
 1958年在Nature上提出“前药”的概念



Can the bark of this tree make your skin look younger?



In skin care, we use salicin and salicylic acid

Rejuvenate your skin with willow bark!

White willow bark has been used for centuries in traditional medicine to treat a range of ailments, from headaches to osteoarthritis. Now researchers have discovered that this medicinal mainstay of the ancient Greeks, Egyptians and Native Americans also has the power to make your skin smoother, firmer and younger looking!

What's its secret?

"The major component of willow bark, salicin, helps to increase the turnover of cells" and to tame the inflammation that can cause all kinds of skin aging, explains Rebecca Scritchfield, R.D.N., author of the upcoming book *Body Kindness*. "Salicin gives our skin that youthful glow," she says.

Any more benefits?

It improves wrinkles in a week! "Chronic inflammation plays a major part in aging processes," says Scritchfield. "So by removing

inflammation, you slow cellular damage." The proof: Women who used a facial serum containing 0.5% salicin (the active ingredient in willow bark) every day for 12 weeks reported significant improvements in wrinkles, roughness, pore size and radiance after one week—and fewer age spots, greater firmness overall and less sagging around the jaw after four weeks.

It turns on "youth" genes! It's well known that avoiding sun damage is a key way to avoid skin aging. Now scientists have identified another key way: revving the activity of "youth" genes, which regulate everything from collagen production to hydration to pigmentation, says Scritchfield. And topical salicin does just that, confirms recent studies reported in the *International Journal of Cosmetic Science*: It sinks into tissues where it prompts



those genes to keep doing their job instead of slowing down as they otherwise do over time.

It protects with antioxidants! Like most plant extracts, willow bark contains powerful antioxidants that help destroy the cell-ravaging free radicals responsible for visible aging, confirms Scritchfield.

Where can I get it?

Willow bark can be found in a wide range of skincare products, including: Botanics Shine Away Ionic Clay Mask (\$9.99, Ulta.com); Eminence Clear Skin Willow Bark Booster Serum (\$30, BuyNaturalSkincare.com); EtoAMD AM Therapy Facial Moisturizer (\$31.50, Dermstore.com) and Mario Badescu Peptide Renewal Cream (\$35, Nordstrom.com). Or use a DIY mask: Mix the contents of 2 willow bark capsules (such as Puritan's Pride White Willow Bark capsules, \$4.99 for 100 capsules, Puritan.com) with 1 Tbs. of honey. Apply to skin (avoiding the eye area) and relax 20 minutes.



rinse with warm water. Pat dry and apply your favorite moisturizer.

Any precautions?

Since it is chemically similar to aspirin, you'll want to avoid willow bark if you have a sensitivity to aspirin.

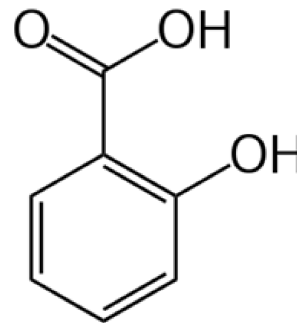
—Katie E. Kristensen

Salicylic acid clear skin

Salicylic Acid: Plant Hormone



Filipendula ulmaria, 绣线菊
commonly known as meadowsweet

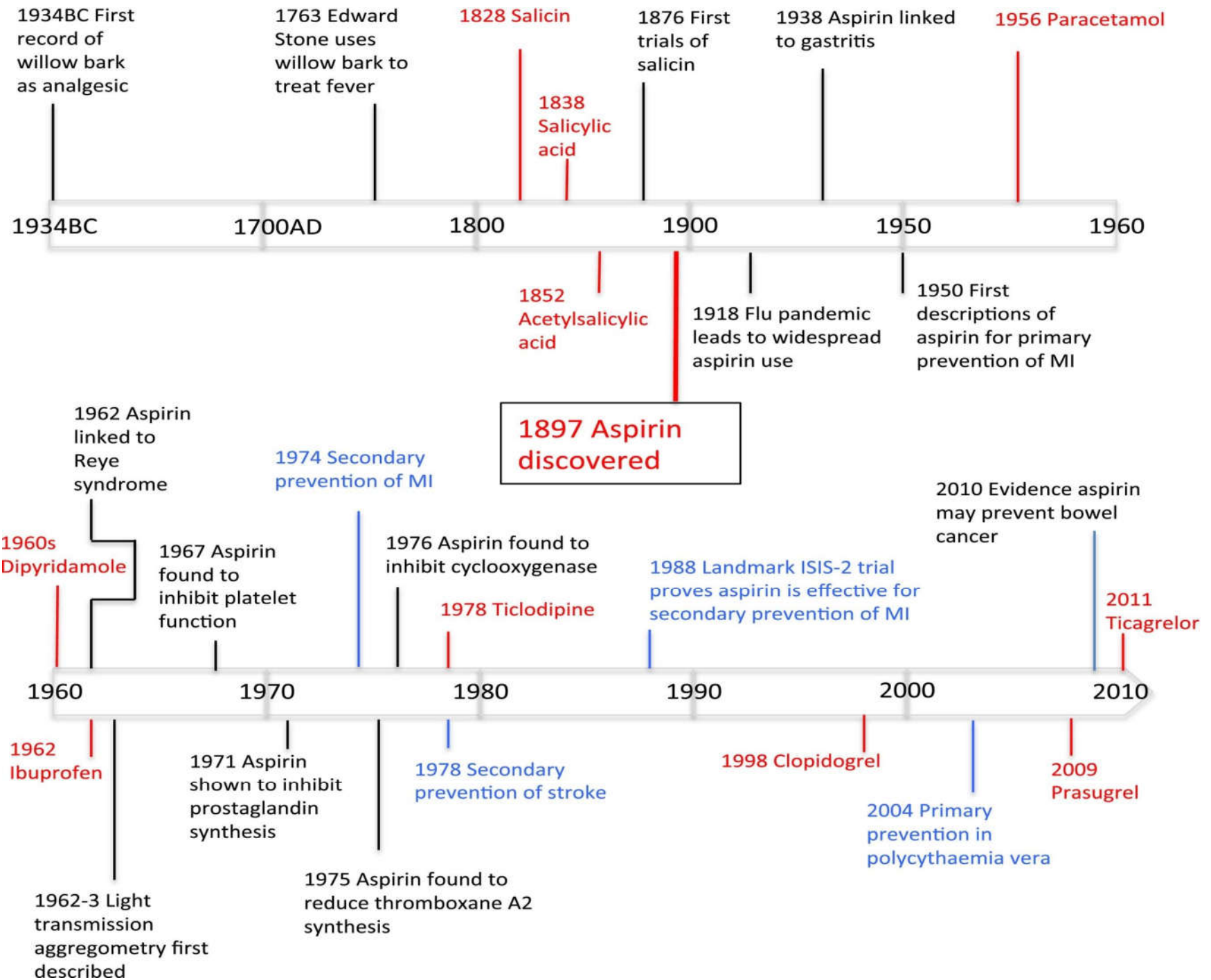


Salicylic acid as Hormone 1992



Salicylic acid was also isolated from the herb meadowsweet (*Filipendula ulmaria*, formerly classified as *Spiraea ulmaria*) by German researchers in 1839.

Aspirin remain strong in the twenty-first with widespread use as a preventive treatment for heart attacks and strokes.



Earth: Our Living Planet



Earth Day April 22

World Will Run Out of Food by 2050 Thanks to Population Boom



Earth Day April 22

“避孕药之母” 玛格丽特·桑格

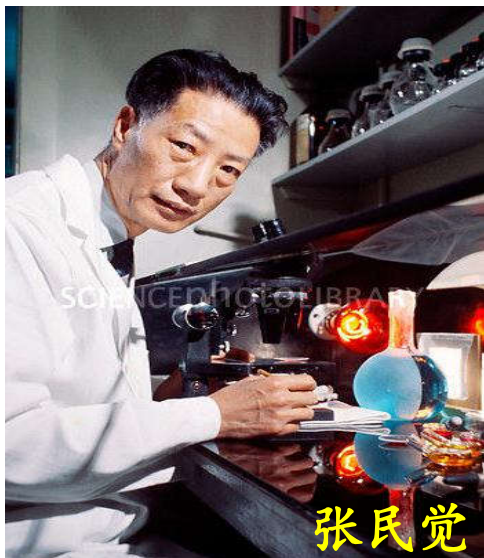


Margaret Higgins Sanger (1879-1966)

具有文化和人口学意义的避孕药是怎样问世的？

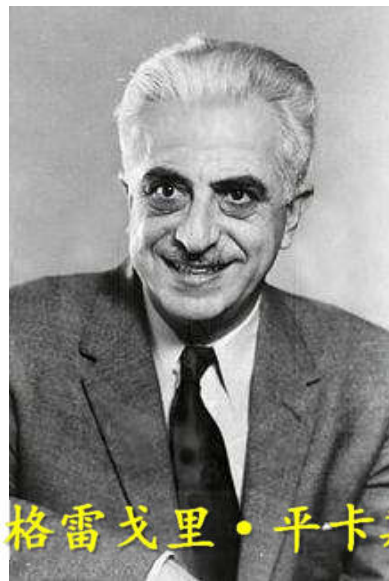
“计划生育” (family planning) 和 “避孕” (birth control)

所有明星药物之母——避孕药



张民觉 1908-1991

1954年Lasker Award获得者



格雷戈里·平卡斯

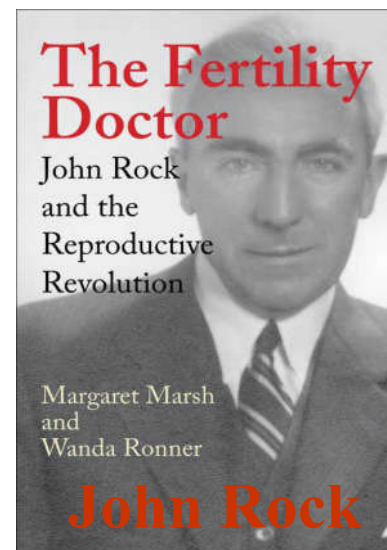
Gregory Goodwin Pincus



玛格丽特·桑格 (Margaret Sanger)



凯瑟琳 Katherine McCormick



John Rock

张明觉-与巨人同行：来自中国的“避孕药之父”



张民觉 1908-1991

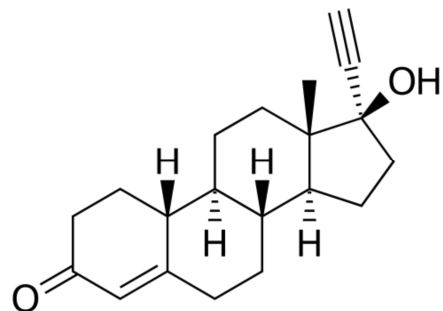


张民觉在岚县广场的雕像

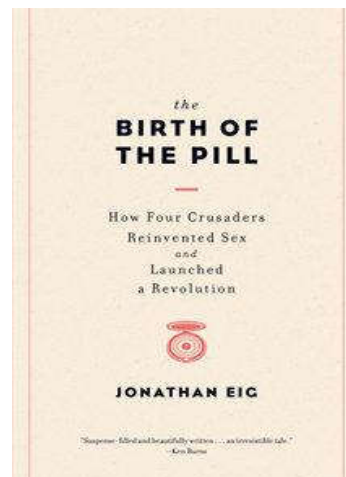
避孕药—改变了整个世界的发明



Luis Miramontes



Norethisterone (NET)



NET was synthesized for the first time by chemists Luis Miramontes, Carl Djerassi, and George Rosenkranz at Syntex in Mexico City in 1951.
2003年炔诺酮被评为影响人类历史的17个分子之一



George Rosenkranz



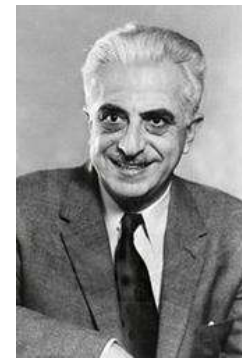
Carl Djerassi



Margaret H. Sanger



Katharine D. McCormick

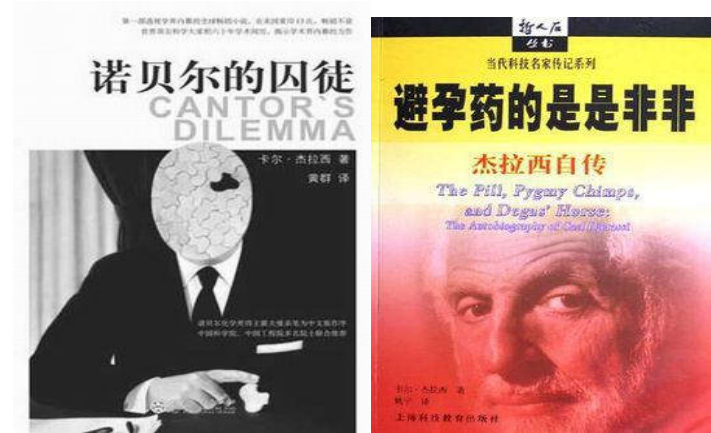


Gregory G. Pincus



张明觉

Father of the Pill- Carl Djerassi



Luis E. Miramontes

Carl Djerassi (1923 –2015) was a Bulgarian, Austrian and American chemist, **Novelist, and Playwright** best known for his contribution to the development of oral contraceptive pills. He also elucidated the structure of steroids, an area in which he published over 1,000 papers.

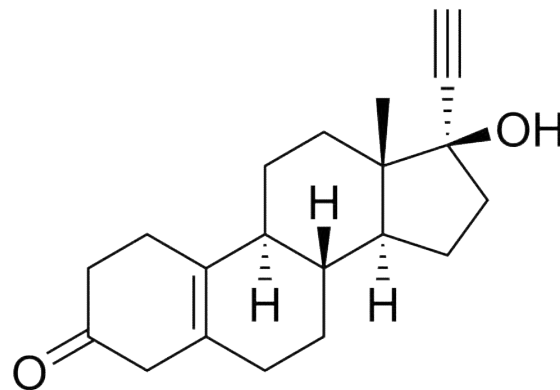
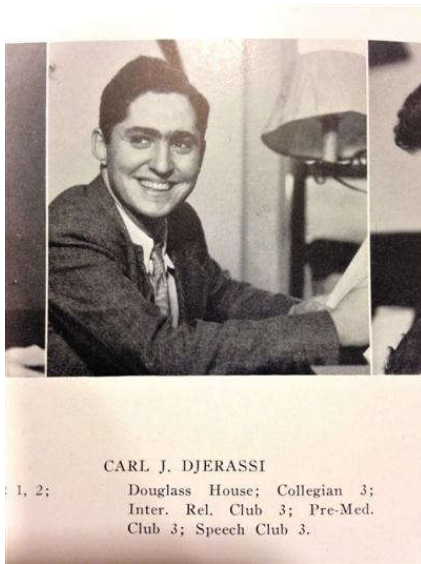
Pill 1960

Drug Name: Norethynodrel/mestranol

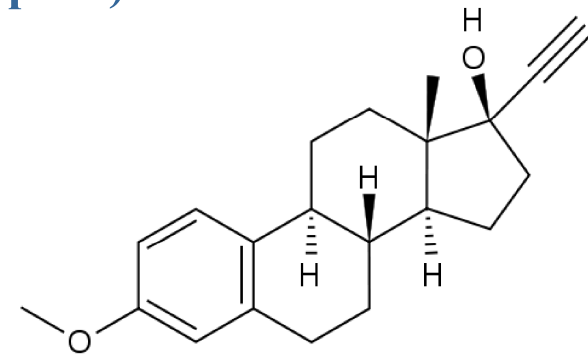
Trade Name: Enovid

Use: Hormone

Use: Birth Control (1st oral contraceptive)



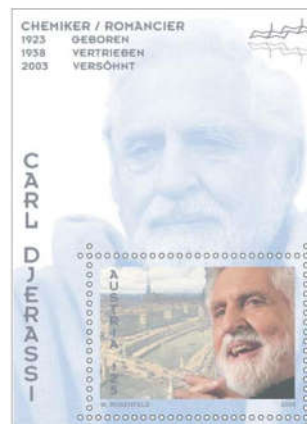
**Norethynodrel
(progestin)**



**Mestranol
(estrogen, demethylated in liver)**



Carl Djerassi获得美国国家科学奖



Diosgenin 薯蓣皂苷元与避孕药

The Chemical Father of the birth control pill

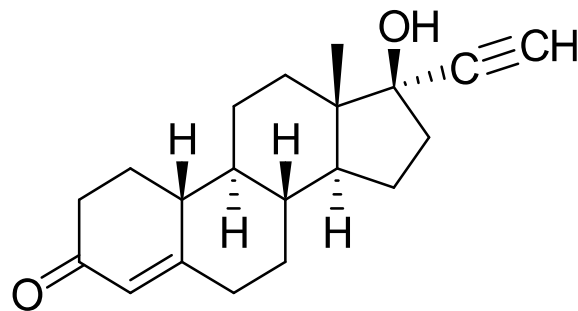
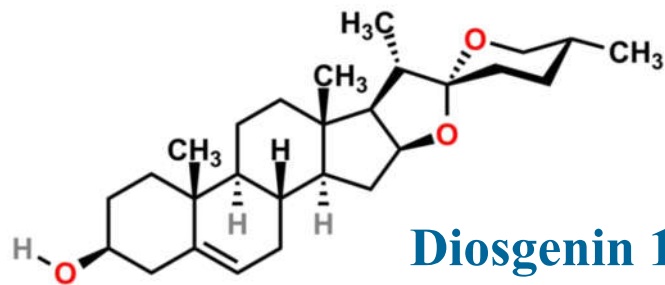


薯蓣

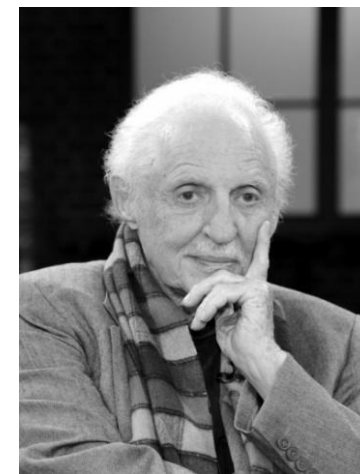
Dioscorea opposita Thunb



李铤 教授



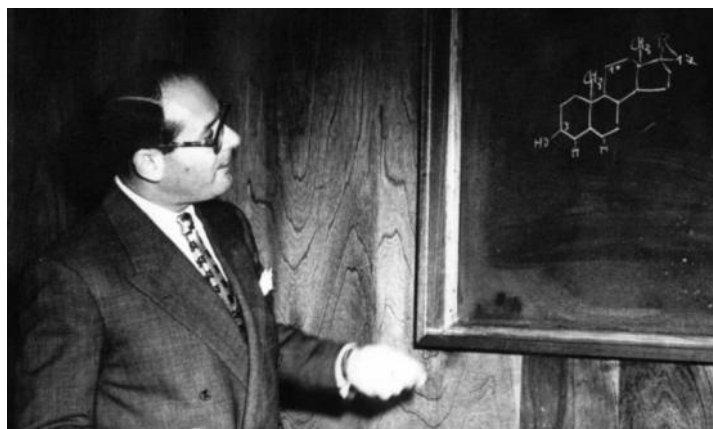
炔诺酮 Norethisterone 1951



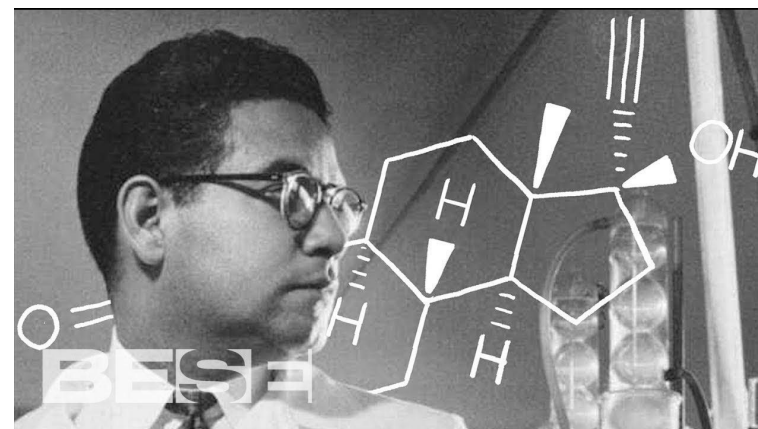
卡尔·翟若适
Carl Djerassi

“避孕药之父”：企业家、小说家、剧作家、诗人、收藏家，堪称一位全能型的天才，他也因此被誉为二十世纪的“文艺复兴式人物”。作为化学家，他一生发表科研论文1200余篇，

Hidden Figuras—George Rosenkranz and Luis E. Miramontes Cárdenas



George Rosenkranz 1916-2019



Luis E. Miramontes Cárdenas

Mexico's President Vicente Fox awarded Rosenkranz the "Condecoracion Eduardo Liceaga," the country's highest award for contributions to the health field. He was president and CEO of Syntex for 25 years and transform his fortunes, and that of the company itself and changed woman's lives.

George Rosenkranz-A Creator of the Pill



Dr. George Rosenkranz

who changed the world with the pill



Dr. George Rosenkranz
1916-1919

