Secondary Metabolites: other functions?

Secondary metabolites are also facilitators of micronutrient uptake:

- an Arabidopsis mutant, which is deficient in the 2-oxoglutarate-dependent dioxygenase Feruloyl-CoA 69-Hydroxylase 1 and thus no longer able to produce coumarins, was found to suffer from iron deficiency under alkaline conditions;
- young maize benzoxazinoid mutants that do no longer produce and excrete benzoxazinoids were found to suffer from iron deficiency.

The use of plant metabolites started..

2600 BC, and in the following 4000 years, secondary metabolites originating from plants were used mainly for medicinal and poison purposes as well as food.

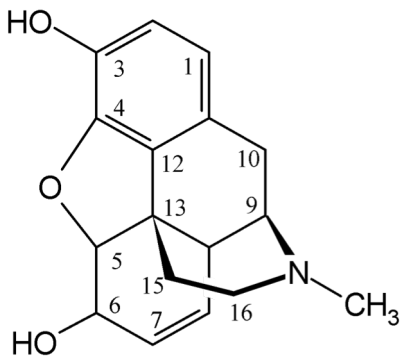
Morphine was the first natural product isolated from the opium poppy (*Papaver somniferum*) in 1806 and it opened a new era in secondary metabolite research.

Papaver somniferum

Morphine

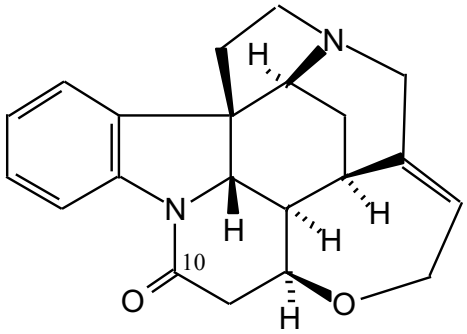
(aromatic alkaloid from opium, *Papaver somniferum*)

Isolation: 1806, Sertürner
Structure: 1925, Robinson
Synthesis: 1954, Ginsberg
Biogenesis: 1959, Leete

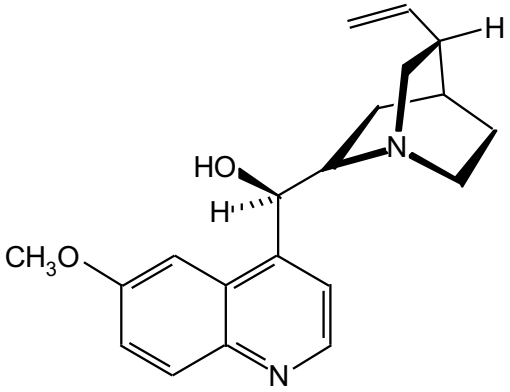


Some milestones in natural products chemistry

Nux vomica



Strychnine



Quinine

Cinchona pubescens

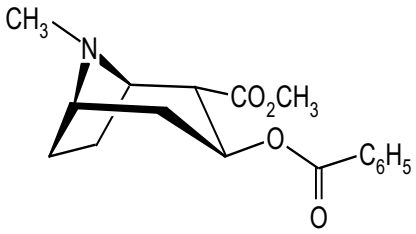
Strychnine
(aromatic alkaloid from *Strychnos nux-vomica*)

Isolation: 1818, Pelletier & Caventou
Structure: 1946, Robinson
Synthesis: 1954, Woodward
2001, Eichberg

Quinine
(quinoline alkaloid from *Cinchona* species)

Isolation: 1820, Pelletier & Caventou
Synthesis: 1944, Woodward

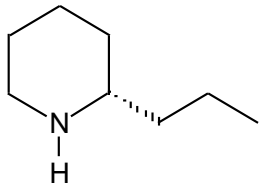
Some milestones in natural products chemistry



Cocaine

Cocaine
(aliphatic alkaloid from *Erythroxylon coca*)

Isolation: 1859, Niemann
Synthesis: 1923: Willstätter



Coniine

Coniine
(aliphatic alkaloid from hemlock, *Conium maculatum*)

Isolation: 1886, Ladenburg
Structure: 1926, Koller

Erythroxylon coca

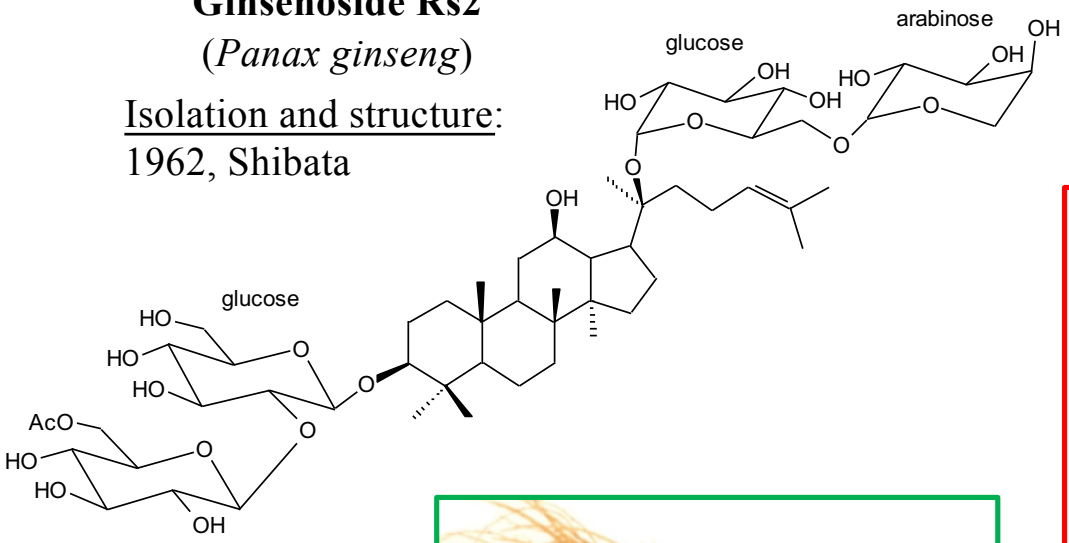
Conium maculatum (cicuta)

Some milestones in natural products chemistry

Ginsenoside Rs2

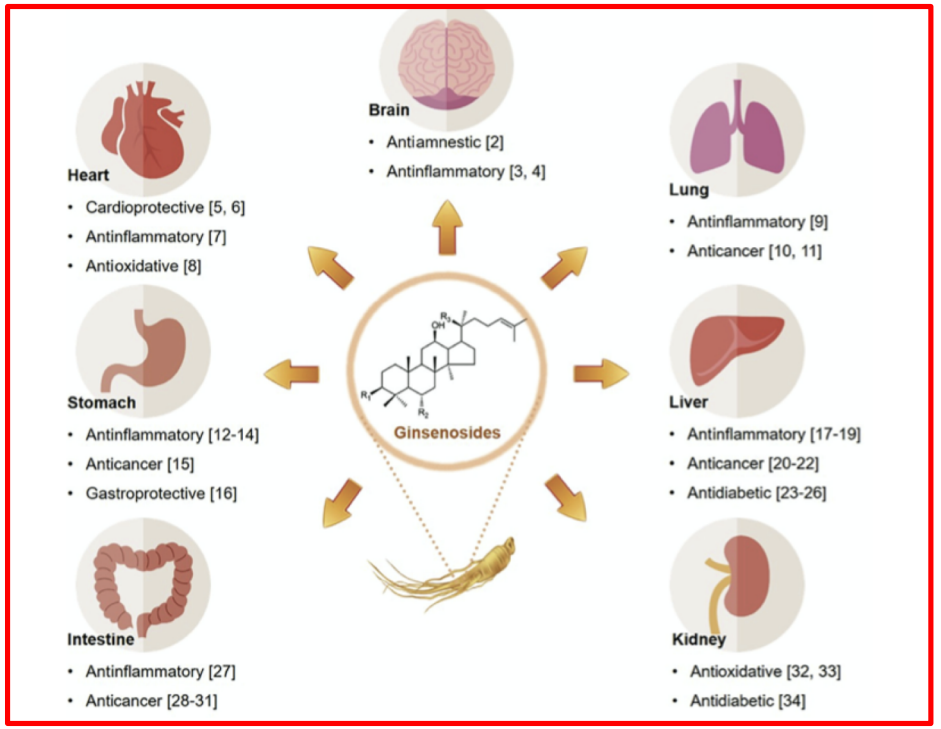
(*Panax ginseng*)

Isolation and structure:
1962, Shibata

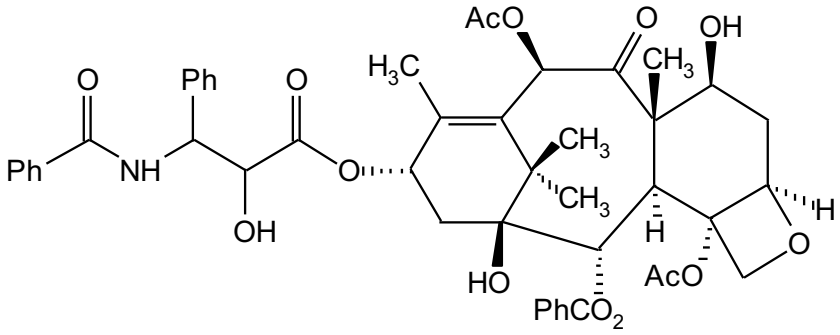


triterpene with a steroid structure

https://doi.org/10.1016/j.jgr.2018.06.001



Some milestones in natural products chemistry



Taxol

(antitumor diterpene from Pacific yew, *Taxus* species)

Isolation: 1971, Wani *et al*.

Structure: 1971, Wani *et al*.

Taxol -Paclitaxel

- Available (1992 in the US, 1993 in Europe).
- Today, more than 30 years after the first research and 10 years after its introduction into clinical practice, taxol has received the approval of the registration authorities of 75 countries for the treatment of 3 forms of cancer (breast, ovary and lung) and continues to be the subject of new research.

- 1958: the discovery. The National Cancer Institute (NCI) starts a program to examine 35,000 botanical species in order to find an active ingredient against cancer cells. One of the samples examined came from the Californian coast of the Pacific was **the bark of the yew tree** (Yew or ***Taxus brevifolia***), often referred to in ancient traditions as **'the doctor of the forest'**.

- 1971: isolated principle, compound 17 as an active anticancer drug. Development is suspended due to difficulties relating to the extraction and processing of the compound.

- 1979: the mechanism discovered. Susan Horwitz of the Albert Einstein College of Medicine in New York discovers the mechanism of action of taxol: **The antitumor drug Taxol stabilizes microtubules and reduces their dynamicity, promoting mitotic arrest and cell death.**

- 1989: clinical trials. 30% of ovarian cancer patients treated with taxol at the Johns Hopkins Oncology Center respond positively to treatment. The National Cancer Institute invites pharmaceutical companies to collaborate in trials.

- 1990: The National Cancer Institute begins phase III of the study to compare the effectiveness of taxol with respect to that of traditional drugs.

- 1991: The National Cancer Institute chooses Bristol-Myers Squibb as its partner for the production and commercialization of the new anticancer drug.

Why study Natural Products?

- Natural products are the source of the most complex and fascinating chemical structures.
- Natural products represent **biological diversity**.
- Natural products are expressions of the genome.
- Natural products **represent natural biological activity**, whether as single compounds or as complex mixtures.
- Natural products are part of the **natural wealth of the country**, and can be an important source of livelihood, from **agriculture** and **food**, **pharmaceuticals**, **fine chemicals industry**, **cosmetics** and **nutraceuticals**
- Natural products can be an effective bridge from tradition to modern scientific developments, including genetics, molecular biology, biotechnology, and pharmaceutical science.

The market for natural products is huge

- Pharmaceuticals
- Traditional herbal medicines:

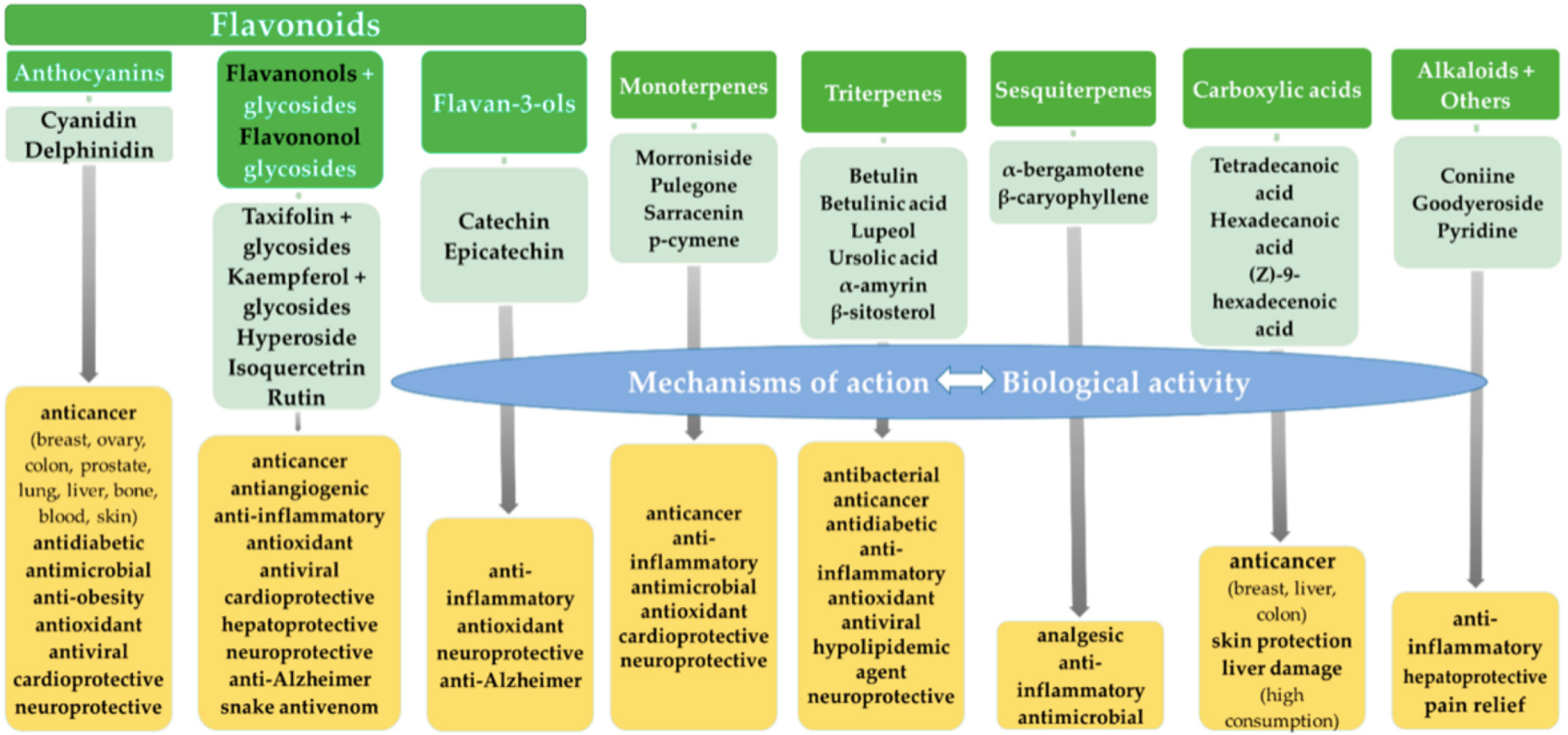
US and Europe: gingko biloba, St. John's wort, ginseng, garlic*, echinacea, saw palmetto, soya*, kava-kava, golden seal, aloe*, gotu kola* (*also grown in the Philippines)

India, China, Japan: Ayurverda, TCM, Kampo

Philippines: lagundi, sambong, ampalaya, banaba, malunggay

- Beverages: tea (e.g., green, chinese), herbal teas, coffee
- Food supplements and health products
- Fats and oils
- Herbs and spices, food flavor ingredients
- Perfumes and scents
- Essential oils, others …

Secondary Metabolites with Biomedical Applications from Plants of the *Sarraceniaceae* Family



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