

The Major Therapeutic Discoveries

Introduction:

The major therapeutic discoveries represent a set of innovations that transformed the management of diseases and significantly increased life expectancy.

The 19th century was the century of discoveries and revolutions.

Medicine and therapeutics experienced spectacular progress, far more significant than during all previous centuries combined.

I. The Major Therapeutic Discoveries

I.1. Pain Medications

I.1.1. Opioids (Morphinics)

German pharmacist Friedrich Sertürner isolated morphine in **1806** from opium derived from the opium poppy (*Papaver somniferum*) — **the first pure alkaloid ever extracted from a plant**. Morphine became the first modern reference analgesic for acute and chronic pain, revolutionizing pain management in medicine and surgery.

Robiquet isolated **codeine** in **1832**, also from opium — an ether derivative of morphine.

George Merck isolated **papaverine** in **1848**, another alkaloid from opium.

I.1.2. Aspirin – Acetylsalicylic Acid

In the early 19th century, research into the extraction of salicin from willow bark came to fruition.

In **1853**, Charles-Frédéric Gerhardt had already synthesized acetylsalicylic acid (aspirin) from salicylic acid.

In **1897**, Félix Hoffmann, a German researcher, synthesized acetylsalicylic acid in a form better tolerated by the stomach and gave it to his father, who suffered from rheumatism.

In **1899**, Bayer filed the patent for **Aspirin®**.

I.1.3. Paracetamol

Key dates — Synthesis of paracetamol in the 19th century:

1845: Charles Gerhardt performed the first synthesis of acetanilide by acetylation of aniline — a direct precursor molecule to paracetamol. Unexploited at the time.

1878: Morse synthesized N-acetyl-para-aminophenol, i.e., paracetamol itself. This is the first documented chemical synthesis of the molecule.

1893: Joseph Von Mering isolated paracetamol as a derivative of phenacetin and published the first clinical study (December 1893). The molecule was deemed toxic and abandoned.

I.2. Cardiac Glycosides (Digitalics)

1844: Eugène Homolle and Théodore-Auguste Quevenne isolated an active powder from digitalis (foxglove), which they named "digitaline."

1868: French pharmacist Claude-Adolphe Nativelle succeeded in isolating crystallized digitaline, which was purer, more stable, and more accurately dosable. This step marked the beginning of true therapeutic standardization.

I.3. Antibiotics

1877: Pasteur and Joubert observed that a culture of anthrax bacillus grew poorly when in contact with other aerobic saprophytic bacteria, suggesting an antagonistic interaction between microorganisms.

1889: Vuillemin introduced the term "antibiosis" to describe this struggle between living organisms (one microorganism inhibiting another).

The 19th century laid the theoretical foundations; the true therapeutic antibiotics would be discovered and used later in the 20th century:

- The discovery of penicillin by Fleming (1928):

On September 3, 1928, Scottish bacteriologist Alexander Fleming observed in his laboratory that a mould of the genus *Penicillium* lysed colonies of *Staphylococci* on a culture dish, and identified the responsible antibacterial substance, naming it penicillin — though he was unable to purify it or produce it in sufficient quantities.

It was not until 1940–1941 that Howard Florey and Ernst Chain, at Oxford, developed a purification method enabling the first clinical trials.

Industrial production was launched in the United States in 1943, in the midst of World War II, revolutionising military medicine.

- Sulfonamides: the first anti-infective chemotherapy (1935):

Gerhard Domagk introduced "Prontosil" into therapeutics — the first commercialised sulfonamide.

Sulfonamides represent the first synthetic molecules used as anti-infective agents.

- Streptomycin and tuberculosis (1944):

Selman Waksman discovered streptomycin in 1944. It was the first antibiotic active against tuberculosis, later complemented by isoniazide (1951) and rifampicin, which remains a cornerstone of antituberculous treatment.

- Expansion of the antibiotic arsenal (1940–1980):

The following decades saw the discovery of a considerable number of new antibiotic families (tetracyclines, macrolides, aminoglycosides, chloramphenicol, etc.).

I.4. Anticancer agents:

1. Before the 19th century:

For centuries, surgery was the only treatment available for accessible cancers.

2. 19th century: scientific foundations

In the 19th century, anticancer agents in the modern sense did not yet exist; the major advances mainly concerned the nascent field of radiotherapy at the very end of the century.

1895: Wilhelm Conrad Röntgen discovers X-rays.

From 1896, physicians began using X-rays to treat skin tumours.

1896: Becquerel discovers natural radioactivity.

1898: Marie and Pierre Curie isolate radium and polonium, paving the way for brachytherapy.

1899: First documented cures of skin cancers by X-ray radiotherapy (Stenbeck and Sjögren).

3. 20th century: chemotherapy

1909–1910: Paul Ehrlich introduces the concept of the "magic bullet" (Salvarsan), inspiring the idea of molecules selectively targeting diseased cells.

1940s: Discovery of nitrogen mustards (mustard gas → cytotoxics), the first genuinely anticancer chemotherapeutic agents.

1950s: Development of methotrexate, the first antifolate, and the beginning of systematic chemotherapy for leukaemias.

1970s: Introduction of anthracyclines (doxorubicin), taxanes (paclitaxel), and platinum salts (cisplatin).

1990s–2000s: Revolution of targeted therapies and monoclonal antibodies, followed by immunotherapy in the 2010s.

Conclusion

- The 19th century laid the foundations of modern pharmacology: isolation of active principles, chemical synthesis, microbial theory, and the first physical cancer therapies.
- Studying the major therapeutic discoveries of the 19th century allows us to understand how modern pharmacy was built: a discipline at the crossroads of chemistry, biology, clinical practice, and scientific innovation.
- Many innovations of the 19th century were still in their infancy: antibiotics and anticancer chemotherapy would develop mainly in the 20th century, but their scientific foundations were well prepared in the preceding century.