CHEM 443

CHEMISTRY OF NATURAL PRODUCTS

Chapter - 1
INTRODUCTION

Introduction

- The chemistry of the Natural products include their biosynthesis, extraction, identification, quantification, structural elucidation, physical and chemical properties and reactions.
- Natural products are those chemical compounds or substances that are isolated from living organism like plants, animals, fungi and bacteria.
- They are produced by the pathway of primary or secondary metabolism.
- Metabolism is defined as series of enzyme catalyzed biochemical reaction or transformation occurring within the cells of an organism which are mainly required for its growth, development and for proper response to its environment.
- The natural products are the end of organism metabolism called metabolites, which perform different functions in animals and plant.

Introduction

- Metabolites: are the intermediate or products of metabolism, the term metabolites is usually restricted to small molecules

- Primary metabolites

  A primary metabolites is directly involved in normal Growth, development and reproduction.

  Example; carbohydrate, protein, fat and oil, alcohol e.t.c.

- Secondary metabolites

  Secondary metabolites are not directly involved in growth, development and reproduction of an organism, but they have an ecological function.

Introduction

Different sources of natural products

- **Plants**
  - Plant is one of the major source of natural products.
  - The natural products isolated from the plants depends on:
    1. Plant species: different species produces different metabolites.
    2. Variability in growing conditions: different growing condition also result different metabolites in the same species.
    3. Different part of the plants mostly contained different metabolites.
- **Microbes**
  - Bacteria and microbes are the important source of natural products.
  - The fermentation, followed by purification results some useful natural products.
  - These natural products are very useful as antibiotic.

Introduction

Different sources of natural products

- Marine organism
  - They are also important source of natural products.
  - The chemistry of marine natural products will influenced by different variables:
    1. Currents and sediments.
    2. pH levels.
    3. Atmospheric constituents.
    4. Metamorphic activity
    5. Ecology.
  - Curacin A is obtained from a marine cyanobacterium and shows potent antitumor activity.

Introduction

Different sources of natural products

- Animal
  - Animals also yield natural chemicals which are important.
  - Potent analgesic compound called epibatidine has obtained from the poisonous skin extracts of the Ecuadorium frog.
  - The snake toxin also contained some useful peptides based natural products. These peptides based natural products have specific interaction with macromolecules and cells, like bungarotoxin from cobra snake.

Introduction

Major classes of natural products

- Peptides (basically consist of amino acids).
- Fats and oils
- Vitamins.
- Terpenes (Terpenoids).
- Steroids.
- Alkaloides.
- Phenolic compounds (Flavonoids)

Introduction

Why 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.
- Natural products can be an effective bridge from tradition to modern scientific developments, including genetics, molecular biology, biotechnology, and pharmaceutical science.

Natural Products: Historical Perspective

- The use of natural products, especially plants, for healing is as ancient and universal as medicine itself.
- The therapeutic use of plants certainly goes back to the Sumerian civilization, and 400 years before the Common Era, it has been recorded that Hippocrates used approximately 400 different plant species for medicinal purposes.
- Natural products played a prominent role in ancient traditional medicine systems, such as Chinese,
- According to the World Health Organization (WHO), 75% of people still rely on plant-based traditional medicines for primary health care globally.

Natural Products: Present and Future

- An impressive number of modern drugs (~40% in use) have been derived from natural sources, many based on their use in traditional medicine.
- Nature has been a source of therapeutic agents for thousands of years.
  - Between 1983 and 1994, natural products or their derivatives, 60–80% of antibacterial and anticancer drugs were from natural origins.
  - In 2000, approximately 60% of all drugs in clinical trials for the multiplicity of cancers had natural origins.
  - In 2001, eight of the 30 top-selling medicines were natural products or their derivatives, (simvastatin, pravastatin, amoxycillin, clavulanic acid, azithromycin, ceftriaxone, cyclosporin, and paclitaxel).

Natural Products: Present and Future

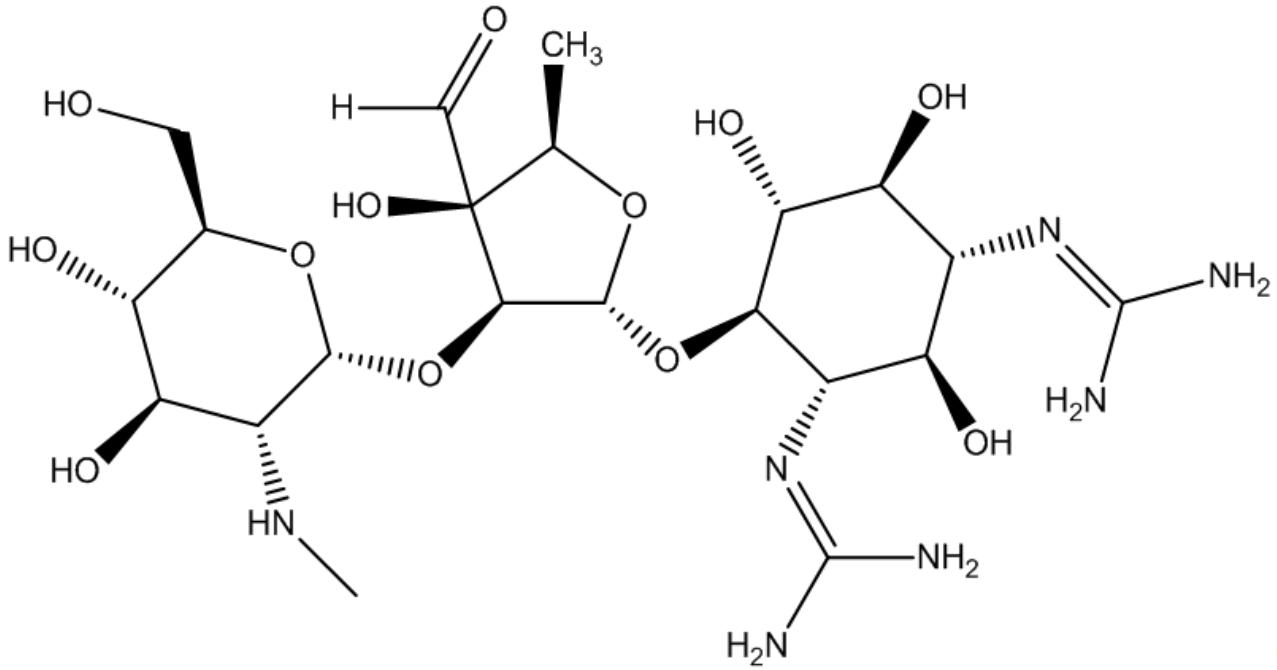
- Natural products are used directly in the ‘‘natural’’ pharmaceutical industry.
- The use of herbal drugs is once again becoming more popular in the form of food supplements and complementary and alternative medicine.

- Natural products can contribute to the search for new drugs in three different ways:
  1. By acting as new drugs that can be used in an unmodified state (e.g., vincristine from Catharanthus roseus).
  2. By providing chemical ‘‘building blocks’’ used to synthesize more complex molecules (e.g., Diosgenin from Dioscorea floribunda for the synthesis of oral contraceptives).
  3. By indicating new modes of pharmacological action that allow complete synthesis of novel analogs (e.g., synthetic analogs of penicillin from Penicillium notatum).

Natural Products: Important Fields of Applications

Healthcare

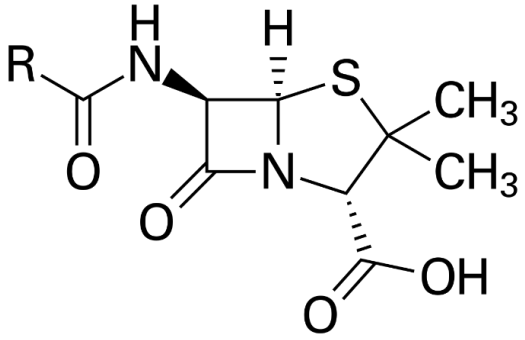
- The discovery of antibiotics,
  - In 1943, Selman A. Waksman discovered streptomycin, an active ingredient of the mold Streptomyces griseus:



Natural Products: Important Fields of Applications

Healthcare

- The discovery of antibiotics,
  - Penicillin; The Scottish bacteriologist Alexander Fleming had already discovered this material in 1928; however, its preparation proved very difficult.
  - In Britain and the USA, it was possible for the first time at the end of the Second World War to obtain penicillin on a larger scale.
  - Production in Germany was begun in 1944 by Hoechst.

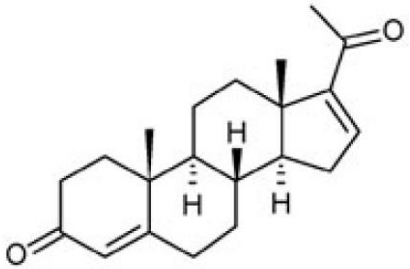


Natural Products: Important Fields of Applications

Fragrances

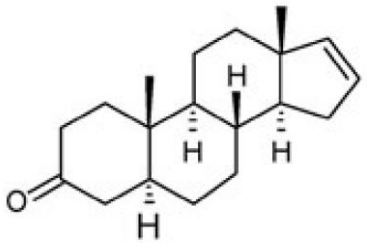
- Henry IV (1553–1610), the first Bourbon on the French throne, is believed to have written as follows:
  - 5α-androst-16-en-3-one and androsta-4,16-dien-3-one act as attractants for women.
  - Pregna-4,16-diene-3,20-dione acts as attractants for men.

Female pheromone

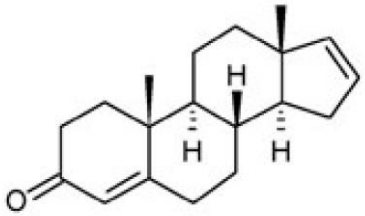


Pregna-4,16-diene-3,20-dione

Male pheromones

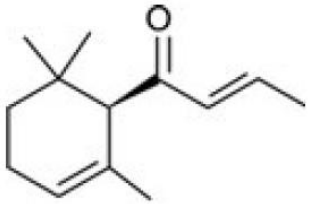


5α-Androst-16-en-3-one



Androsta-4,16-dien-3-one

- α-Damascene is responsible for the scent of roses and may be prepared on an industrial scale.

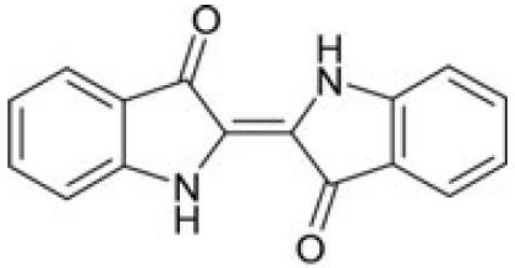


α-Damascone

Natural Products: Important Fields of Applications

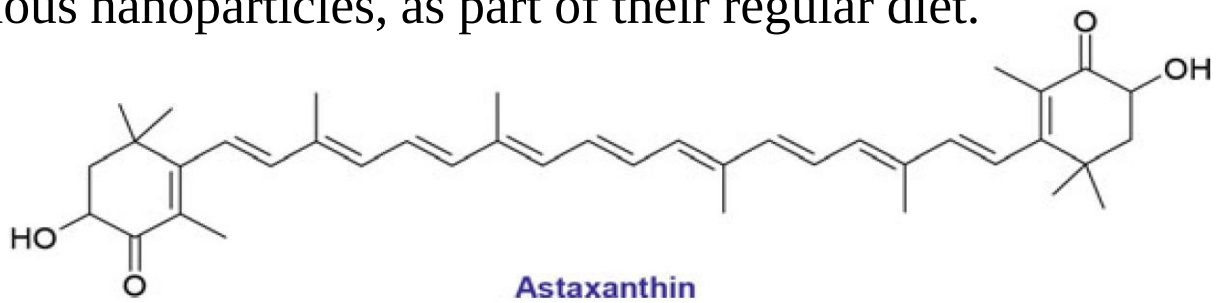
Colorants

- Indigo, a natural dye extracted from the leaves of certain plants; nowadays synthetic indigo is an essential colorant.



Indigo

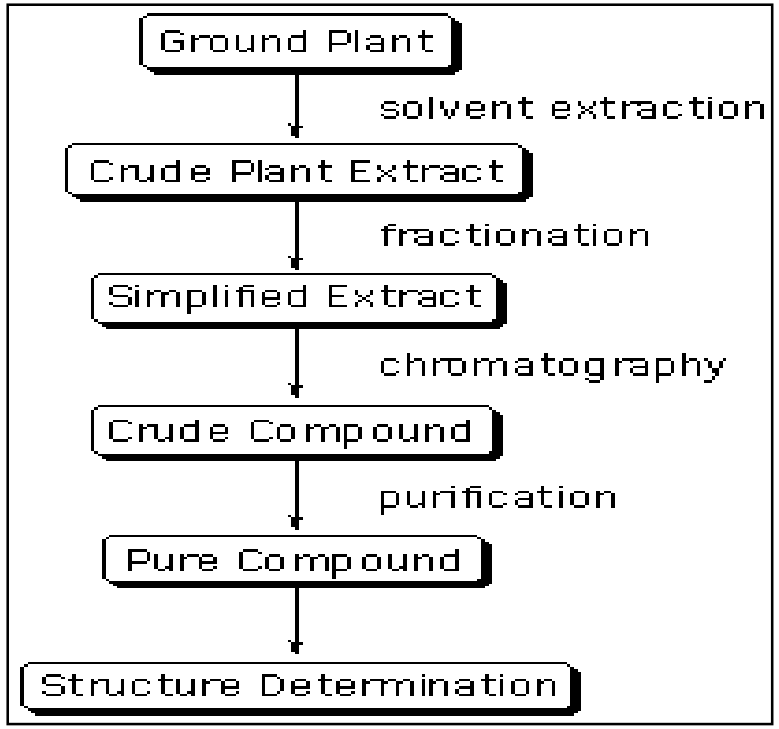
- Salmon, the farmed fish are fed the naturally occurring carotenoid dyestuff astaxanthin, in the form of amorphous nanoparticles, as part of their regular diet.



Astaxanthin

Natural Products: General isolation strategy of natural products

- Extract the dried and ground plant material with a suitable solvent.
- Concentrate the extract.
- Separate and purify each component.
- Since the concentrate contains an enormous variety of compounds, early isolations involved selective crystallization of the most dominant component in the mixture.
- Liquid natural products were distilled.
- Natural organic acids were isolated by aqueous basic extraction and natural organic bases (alkaloids) were isolated by aqueous acidic extraction.



Natural Products: Method Used in Classical Structural Elucidation

- Determination of functional groups.
- Determination of the carbon skeleton and the location of the functional groups.
- Degradation to smaller fragments (A-B-C ------> A + B + C)
- Elemental analysis (CHN).
- Reactivity (leading to new reactions)
- Stereochemistry.
- Synthesis of the smaller fragments (A, B, C) and the entire molecule (A-B-C).
- Classification of the compound into a biogenetic family of compounds.
- More modern structural elucidation and characterization by spectroscopy including NMR, MS, ESR, IR, X-ray, UV.

Natural Product Chemistry in the Chemical Industry

- Property or activity of a natural product was often used in the past without isolating the pure material and of course mostly without any idea of its chemical structure.
- Often centuries, or at least decades, passed between the first use of the natural product and the determination of its chemical structure.
- Once the structure was known, by means of targeted modifications it became possible to develop analogues with new or improved properties, new synthetic methods and reaction conditions could then be developed.
- Nowadays, the development of new syntheses is a key aspect and an important prerequisite for the industrial production of natural products.
- In 1975, James B. Hendrickson defined the " ideal synthesis" as one which: creates a complex molecule in a sequence of only construction reactions involving no intermediary refunction alisations, and leading directly to the target, not only its skeleton but also its correctly placed functionality.