PharmacognosyII

Lec. 1 **3rd stage 1st semester** **Year 23-24**

Lecturer: Dr. Jamel Fani

Introduction general biosynthesis pathways of secondary metabolites

Primary metabolites: molecules that are essential for growth and development of an organism. Examples: 1- Carbohydrates. 2- Proteins. 3- Lipids. 4- Nucleic acids. 5- Hormones.

Secondary metabolites: molecules that are not essential for growth and development of an organism.

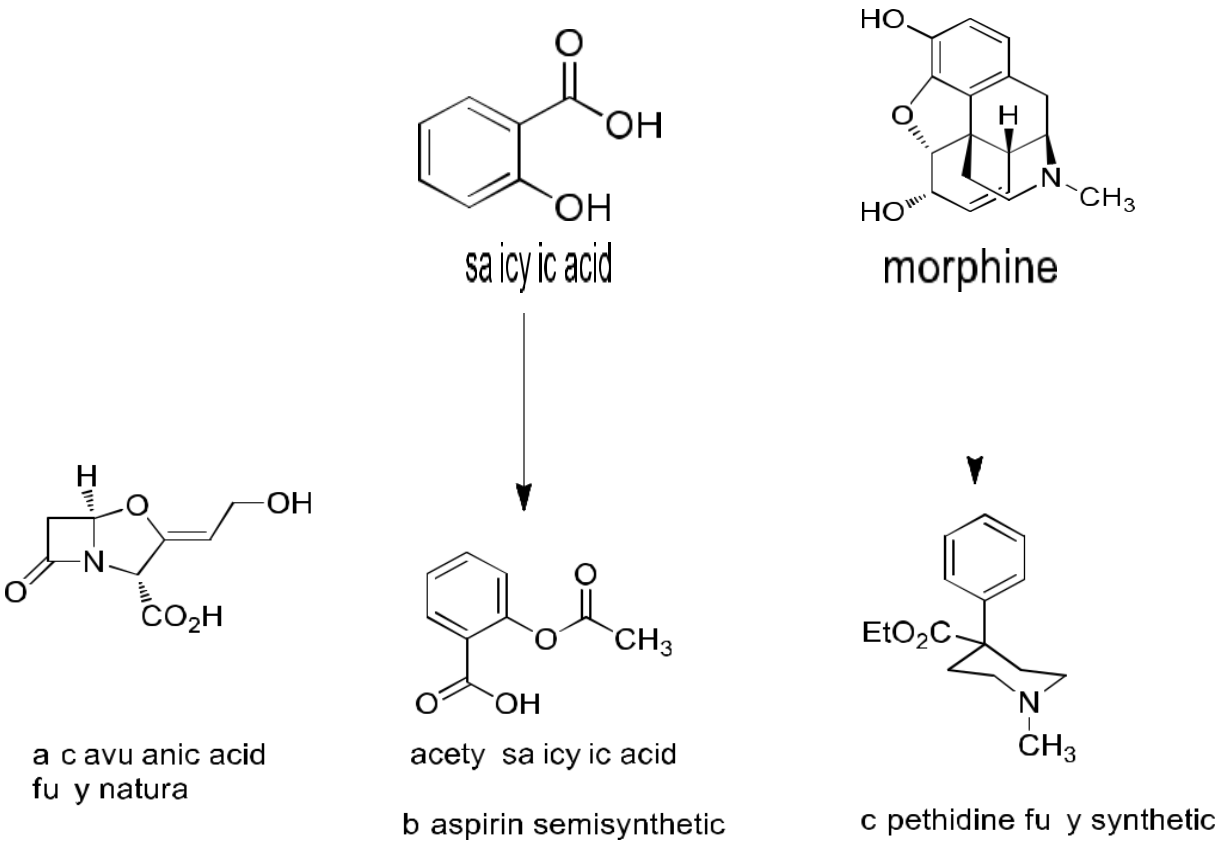
Secondary metabolites are:

- Biosynthetically derived from primary metabolites. They are more limited in distribution being found usually in specific families.
- Chemically warefare to protect plants from the attacks by predators and pathogens.
- Important for abiotic stresses
- Medicine
- Industrial additives

Natural products: are defined as organic compounds in the molecular range 100-2000. The term is also applied to bulk substances from nature, such as crude plant material, food stuffs, resin and exudates from plants or extracts (alcoholic or water) of plant material. The term can be extended to pure single compound of natural occurrence, for example, morphine.

Historically, natural products form the basis of medicine, and even now, many of the compounds that are medicinally important are derived from natural sources. It is highly likely that these compounds produce by the plant as defense mechanism to protect the plant or animal from attack (**phytoalexins**).

Medicinal agents can be purely natural compounds (eg. clavulanic acid from bacteria), or semisynthetic compound like aspirin (acetyl salicylic acid derived from salicylic acid from the tree Salix, or a compound that is totally synthetic based on natural compound like pethidine from morphine (Figure **1**)



There are different approaches to discover a new drug lead compound:

In the **ethnobotanical** approach, knowledge of the use of a particular plant by an indigenous people is used to direct a search for a drug lead, for example, ethnobotanists used the plant curare which contains the alkaloid tubocurarine to hunt the animal for food. The plant acts as a muscle relaxant which kills the animals by paralysis of the muscles required to breathe.

In **random** approach, the plants are collected regardless of any previous knowledge of their chemistry or biological activities.

Another approach is the **chemotaxonomic** approach relies on the fact that some families contain the same type of compounds. A good example of this is the family Solanaceae which is rich sources of the alkaloids of the tropane type.

Polyketides

Natural products form a group of therapeutically important compounds, comprising many antibiotics (tetracycline and erythromycin), fatty acids, anthrone purgative glycosides and anthracyclic antituomor agents.

The biosynthesis of these compounds begins with (Figure **2**) the condensation of one molecule of malonyl coenzyme A with one molecule of acetyl coenzyme A, to form the simple polyketide acetoacetyl-CoA. In this Clasien reaction, the acidic carbon (between the two electron withdrawal group carbonyl) is the nucleophile that attacks the electropositive (electron deficient) center (the carbonyl group).

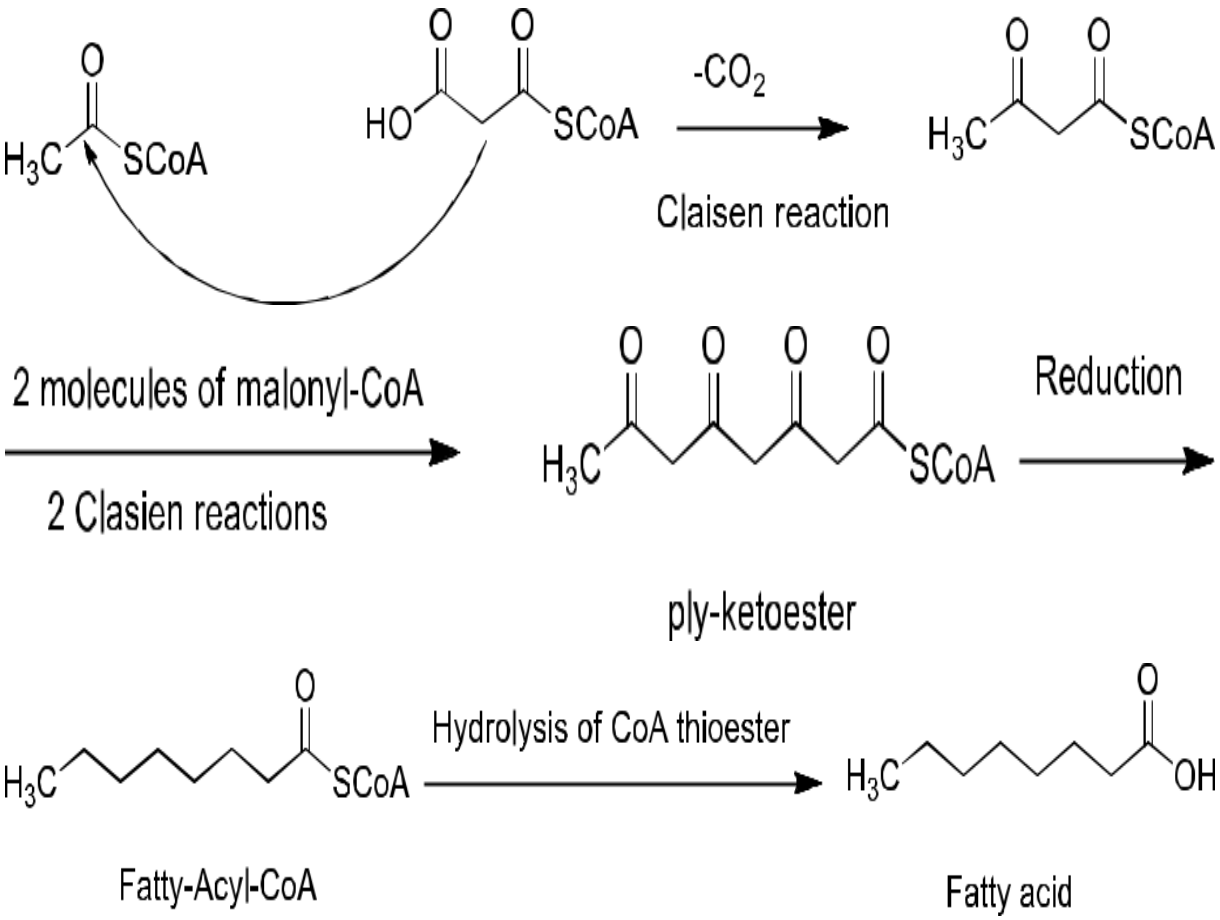


Figure 2

Polyketide is the source of the tetracycline member of compounds (Figure **3**), C-10, C-11, C-12 and C-1 are oxygenated, indicating that the precursor of these types of compounds is a poly-β-ketoester.

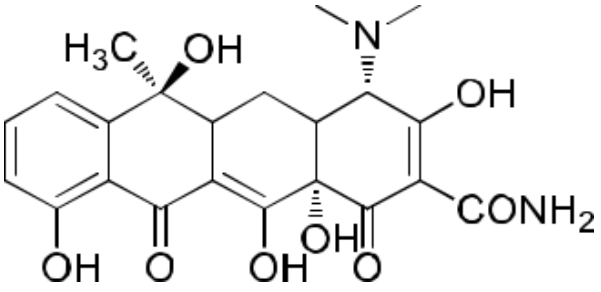


Figure 3: tetracyc ine

A further group of polyketide-derived natural products is the statins (lower cholesterol by inhibiting the formation of mevalonic acid which is the key intermediate in the synthesis of cholesterol), the macrolide antibiotic erythromycin and griseofulvin.

Shikimic acid derived natural products

Shikimic acid is the precursor for many natural products and aromatic amino acids (Figure **4**)

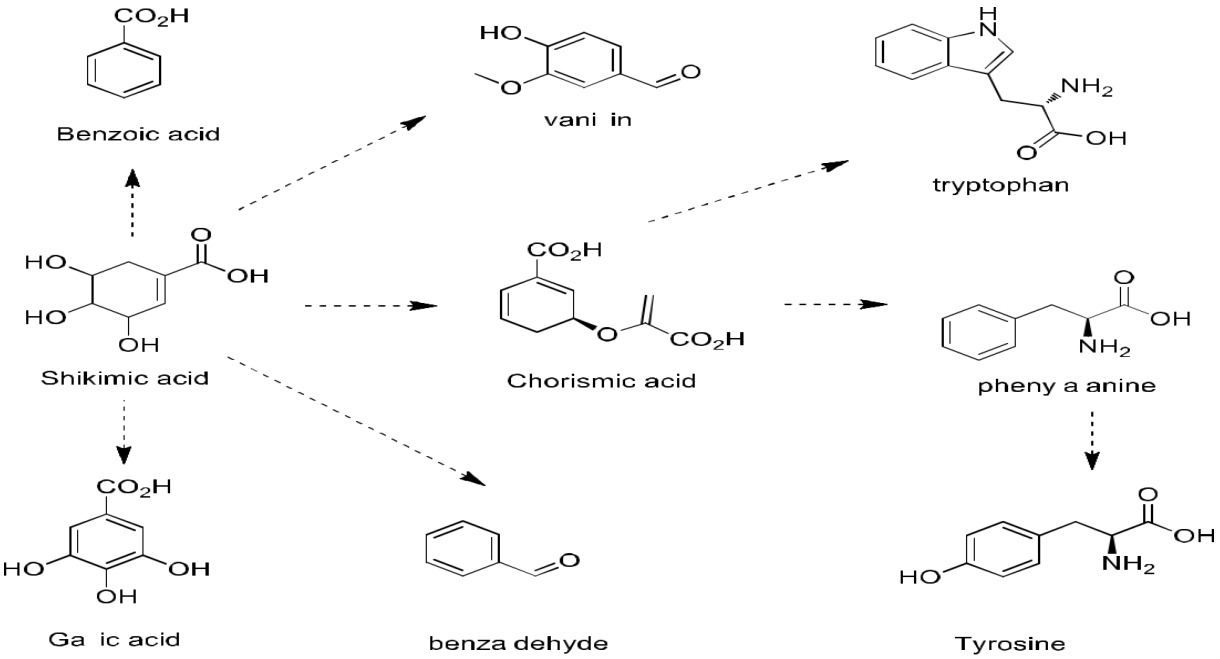


Figure 4: Shikimate pathway

A number of natural product groups can be constructed from the amino acid phenylalanine, in particular phenylpropenes, lignans, coumarins and flavonoids. Cinnamic acid is the precursor of aromatic compounds.