



“बेटी बचाओ, बेटी पढ़ाओ”

**JAYOTI VIDYAPEETH WOMEN'S UNIVERSITY, JAIPUR**  
**Faculty of Pharmaceutical Science**

<b>Faculty Name</b>	- JV'n Dr. Parveen Parihar
<b>Course</b>	- B. Pharm (5 <sup>th</sup> sem)
<b>Session</b>	- Pharmacognosy and Phytochemistry – (Metabolic Pathway)

**Academic Day starts with –**

- Greeting with saying ‘**Namaste**’ by joining Hands together following by 2-3 Minutes Happy session, Celebrating birthday of any student of respective class and **National Anthem**

**Metabolic Pathway**

**Metabolic Pathway:**

The sum total of all the enzymatic mediated reactions occurring in the cell is collectively called metabolism. The reaction sequences occurring within organisms in an orderly and regulated way are known as metabolic pathways and the compounds formed during metabolism are called metabolites. During the process of metabolism many intermediate metabolites are formed which is used to denote the chemical pathways of metabolism.

As a result of metabolic process in plants, plant synthesizes primary plant metabolites and secondary plant metabolites.

### **Primary plant metabolites:**

These are considered as basic plant constituents like sugars, amino acids, coenzyme A, mevalonic acid and lipids. They are widely distributed in plants in large quantities; are directly involved in growth, development and reproduction; non-expensive to isolate from plant e.g starch from potato and do not possess biological or pharmacological action.

### **Secondary plant metabolites:**

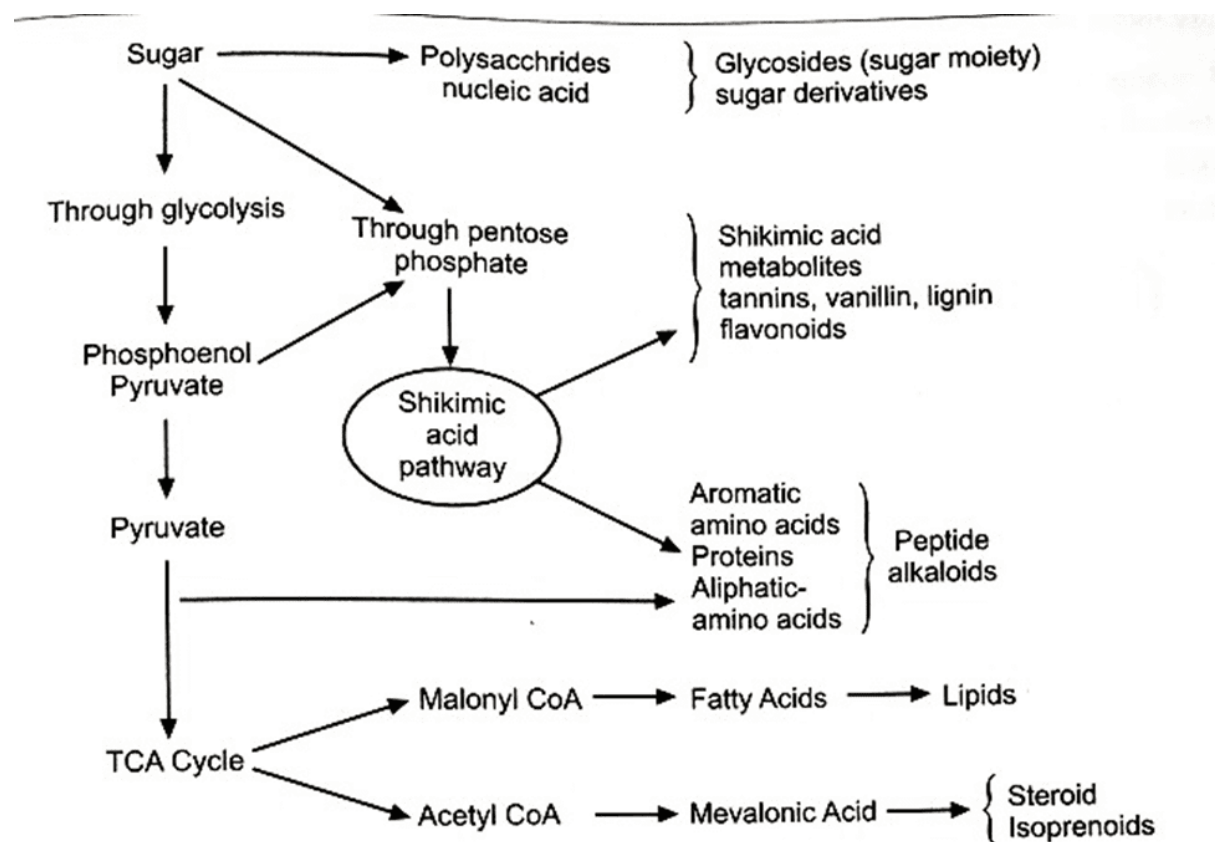
These are biosynthesized from the primary metabolites e.g- alkaloids, glycosides, tannins, flavonoids, terpenoids and volatile oils. They are more limited in distribution; restricted to taxonomic group; not directly involved in the growth and development; possess biological or pharmacological action on humans and animals; involved in chemical adaptation to environmental stress; serve as defensive, protective chemicals against microorganisms, insects and higher herbivorous animals; present in small quantities; generally expensive to isolate from plant compared to primary metabolites e.g- quinine form cinchona bark.

### **Basic Metabolic pathway**

The building blocks for secondary metabolites are derived from primary metabolism. The most important building blocks used in the biosynthesis of secondary metabolites are derived from the intermediates acetyl coenzyme A (acetyl-CoA), shikimic acid, mevalonic acid, and 1-deoxyxylulose 5-phosphate. These are utilized respectively in the acetate, shikimate, mevalonate, and deoxyxylulose phosphate pathways.

Living plants are solar-powered biochemical and biosynthetic laboratory which manufactures both primary and secondary metabolites from air, water, minerals and sunlight. The primary metabolites like sugars, amino acids & fatty acids that are needed for general growth & physiological development of plant which

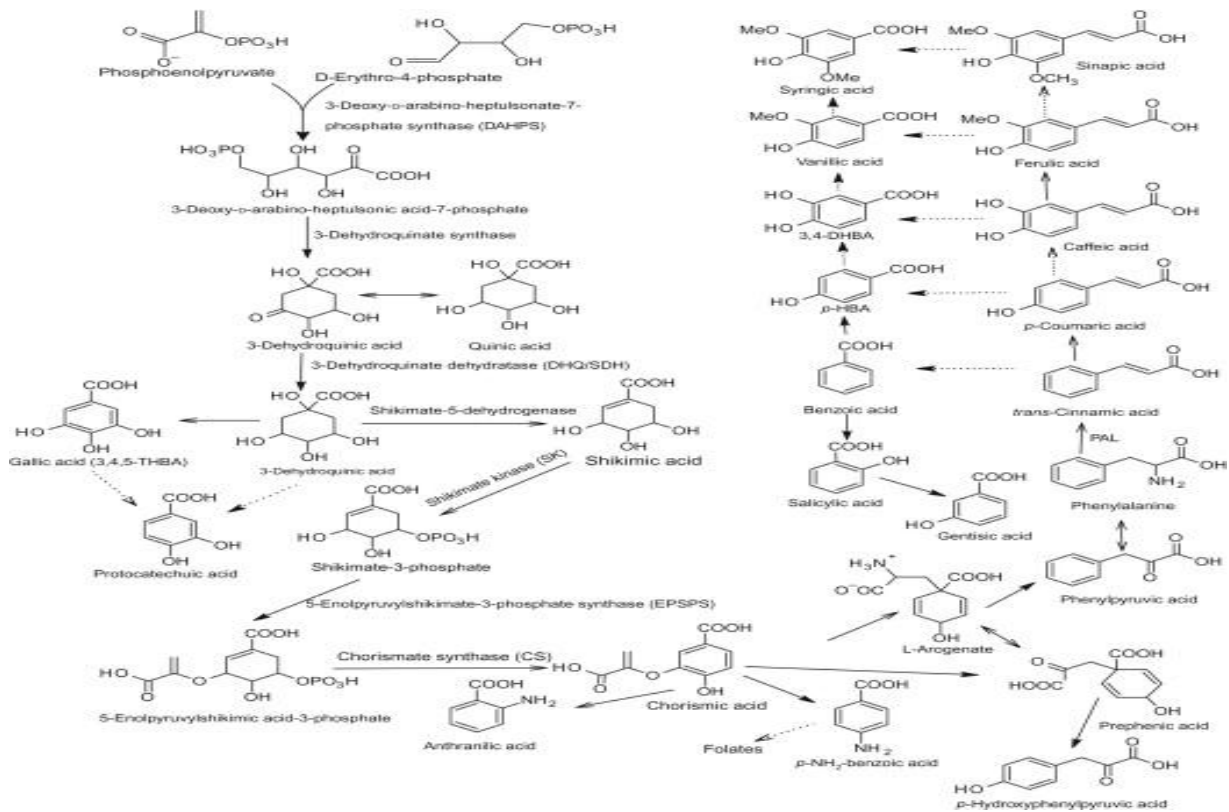
distributed in nature & also utilized as food by man. The secondary metabolites such as alkaloids, glycosides, Flavonoids, volatile oils etc. are biosynthetically derived from primary metabolites.



**Figure 1 Basic metabolic pathway**

**1.2 Shikimic Acid Pathway :** The shikimate pathway provides an alternative route to aromatic compounds, particularly the aromatic amino acids L-phenylalanine, L-tyrosine, and L-tryptophan. This pathway is employed by microorganisms and plants, but not by animals, and accordingly the aromatic amino acids feature among those essential amino acids for human beings, to be obtained from the diet.

Shikimic acid is named after the highly toxic Japanese shikimi (*Illicium anisatum*) flower from which it was first isolated



**Figure 2 Shikimic acid pathway**

- Shikimic acid pathway starts with the precursors, Erythrose 4-phosphate and Phosphoenolpyruvate coupling to form 3-deoxy-D-arabino-heptulosonic acid-7-phosphate (DAHP), a reaction catalysed by phospho-2-oxo-3-deoxyheptonate aldolase. The enzyme, 3-5 dehydroquinic acid synthase, catalysing the cyclization of DAHP to 3-dehydroquinic acid, requires cobalt (II) and nicotinamide adenine dinucleotide (NAD) as cofactors.
- The dehydroquinic acid, on reduction gives quinic acid. By dehydration of 3-dehydroquinic acid forms 3-dehydroshikimic acid, which forms shikimic acid followed by reduction. The enzymes catalysing the dehydration of dehydroquinic acid are of two kinds. Form 1, associated with shikimate dehydrogenase, is independent of shikimate concentration, while form 2 is specifically activated by shikimate.
- It has been suggested that the two forms provide a control in the

utilization of dehydroquinic acid producing either shikimic acid or protocatechuic acid.

- The formation of chorismic acid is an important branch point in the shikimic acid pathway as this compound can undergo three different types of conversion. In the presence of glutamine, chorismic acid is converted to anthranilic acid, whereas chorismate mutase catalyses the formation of prephenic acid.
- Then after anthranilic acid is converted first to phosphoribosyl anthranilic acid and then to carboxyphenylaminodeoxyribulose-5-phosphate, these reactions being catalysed by anthranilate phosphoribosyl transferase and phosphoribosyl anthranilate isomerase, respectively. Ring closure to form indolyl-3-glycerol phosphate is catalysed by indolyl-glycerol phosphate synthase. The enzyme catalysing the final reaction, that is, tryptophan synthase consists of two components; component A catalyses the dissociation of indolylglycerol phosphate to indole and glyceraldehydes-3-phosphate, whereas component B catalyses the direct condensation of indole with serine to form tryptophan.
- Tyrosine and phenylalanine are both biosynthesized from prephenic acid, but by independent pathways, which act as a precursor for the biosynthesis of phenylpropanoids. The phenylpropanoids are then used to produce flavonoids, coumarins, lignin and tannins.
- In the formation of tyrosine, prephenic acid is first aromatized to 4-hydroxyphenylpyruvic acid, a reaction catalysed by prephenate dehydrogenase. Transamination, catalysed by tyrosine aminotransferase, then gives tyrosine.

- The biosynthesis of phenylalanine involves first the aromatization of prephenic acid to phenyl pyruvic acid, a reaction catalysed by prephenate dehydratase, and then transamination catalysed by phenylalanine aminotransferase, which gives phenylalanine.

### 1.3 Acetate pathways:

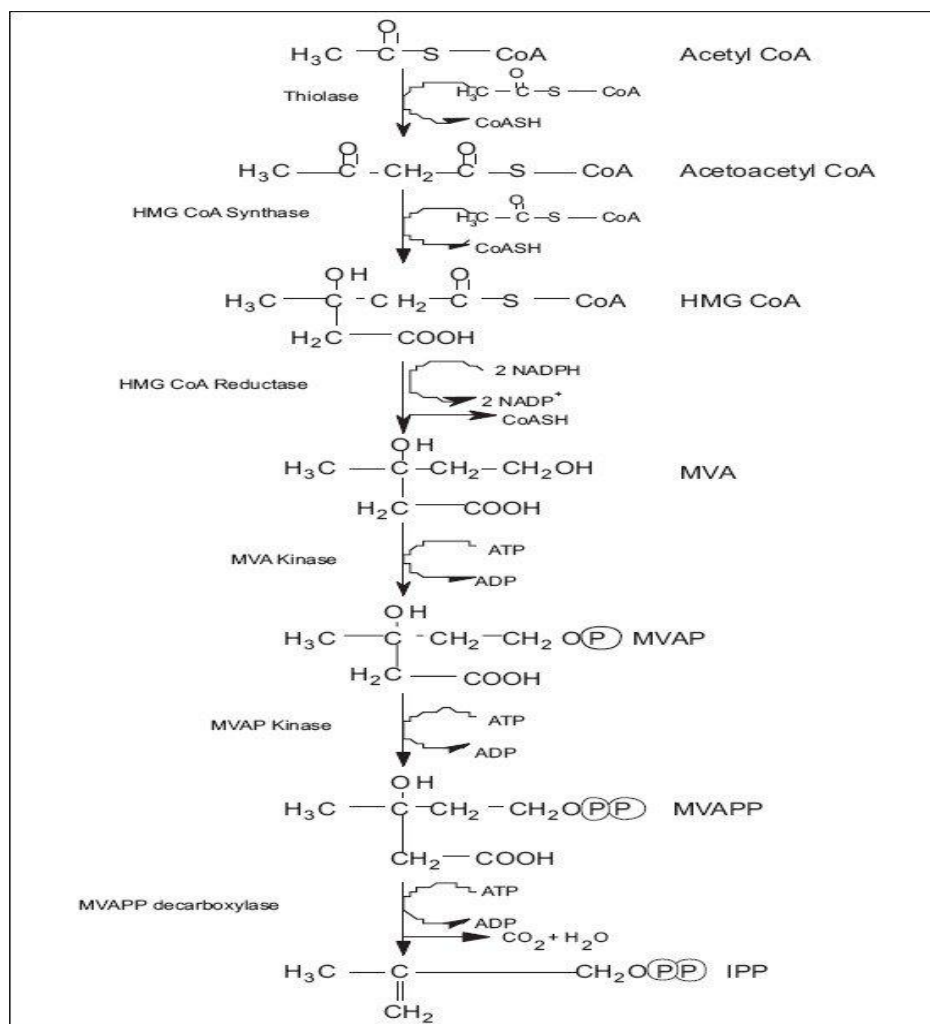
Acetate-Mevalonate Pathway:

Since a long time it was believed that acetic acid is involved in the synthesis of cholesterol, squalene and rubber-like compounds. The discovery of acetyl coenzyme A further supported the role of acetic acid in biogenetic pathways. Later, mevalonic acid was found to be associated with the acetate.

- The pathway begins with acetyl CoA molecule produced from pyruvic acid, which is the end product of glycolysis.
- First 2 molecules of acetyl CoA forms acetoacetyl CoA through Claisen condensation.
- 3rd molecule of acetyl CoA forms  $\beta$ -hydroxy  $\beta$ -methylglutaryl-CoA by aldol addition.
- Next on reduction gives rise to mevalonic acid, which is the main precursor for biosynthesis of terpenoids.
- Mevalonic acid on ATP mediated phosphorylation gives mevalonic acid diphosphate which on decarboxylation gives the 1st isoprene unit, isopentyl pyrophosphate (IPP).
- By the isomerase enzyme, the IPP gives 2nd isoprene unit Dimethyl allyl pyrophosphate (DMAPP)
- Electrophilic addition of IPP with DMAPP via enzyme prenyl transferase yield C10 unit, geranyl pyrophosphate (GPP), which is the precursor for

synthesis of monoterpenes.

- Combinations of another IPP unit with GPP give rise to form farnesyl pyrophosphate(FPP), C15 unit which acts as a precursor for the synthesis of sesquiterpene.
- Further addition of IPP unit gives C20 geranyl geraniol pyrophosphate (GGPP) to produce a range of Diterpenes.
- On further addition of IPP unit gives C25 geranyl farnesyl pyrophosphate called Sesterterpenes.
- The tail to tail addition of two FPP units yields C30 unit, triterpene. Similarly 2 units of GGPP yield C40 unit, tetraterpene.



**Figure 3 Acetate mevalonate pathway**

- **Next Topic-**
  - Pharmacognosy – (Acetate melonate pathway)
  
- **Academic Day ends with-**

National song' Vande Mataram'