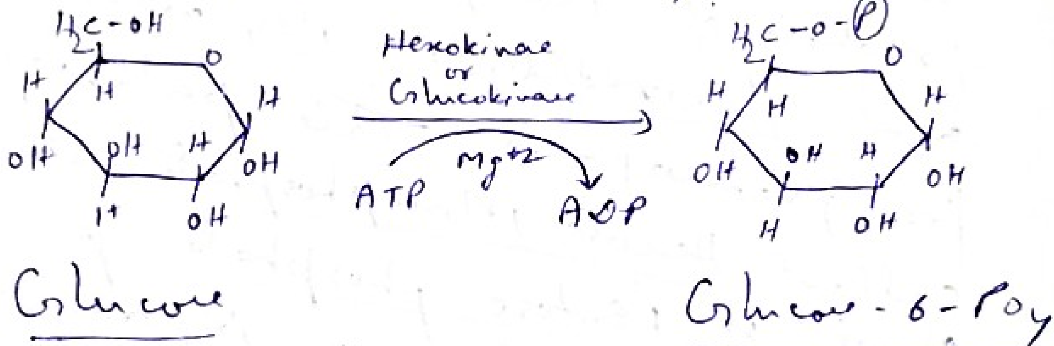
Pentose Phosphate Pathway
or
Hexose Monophosphate Shunt
(HMP SHUNT)

In normal pathway, glucose is oxidatively decarboxylated through glycolysis and kreb's cycle for ATP (Adenosine TriPO4). Synthesis. But there exists another pathway of oxidative decarboxylation of glucose, which doesnot generate reduced NAD or ATP but generate reduced NADP and ribose-5-PO4 as intermediate metabolite. The end products of this pathway are Fructose-6-PO4 and glyceraldehyde 3 PO4 which are recycled for gluconeogenesis. This pathway is called Hexose Monophosphate shunt (HMP) shunt or Pentose phosphate pathway.

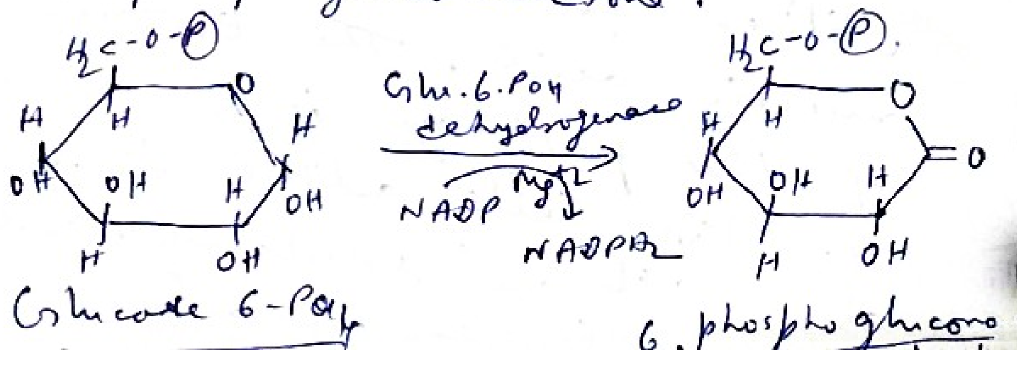
This pathway is very important for biosynthetic process in the cells. This pathway is very important as the reduced NADP generated during the pathway is used for synthesis of Fatty acids, steroids and ribose-5-PO4 is utilised for synthesis of nucleotides and nucleic acids. The enzyme system of this pathway is in the cytosol of the liver cells, adipose tissues, Mammary gland cells and steroidogenic cells of testis, ovary, placenta and adrenal cortex.

The HMP pathway though uses some early reactions of glycolysis, is entirely different from glycolysis. The entire pathway involves 8 steps —

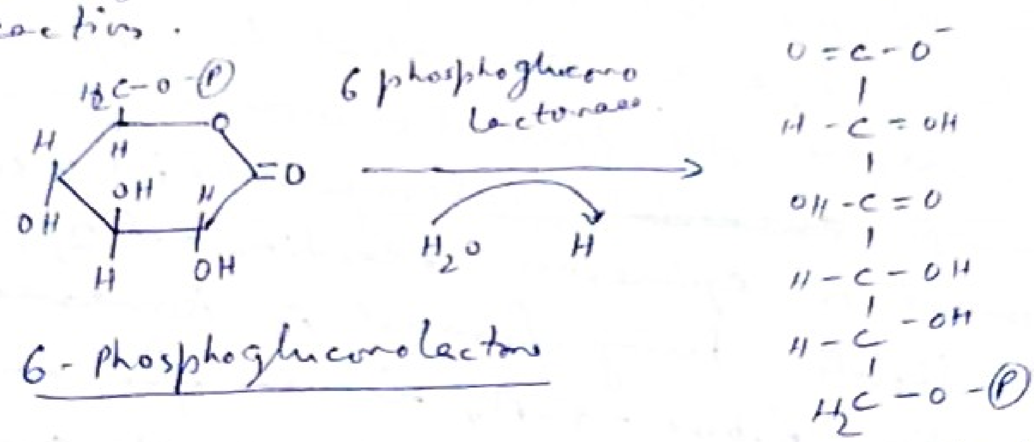
(1) Phosphorylation of glucose — The enzyme glucokinase or hexokinase, as in glycolysis, brings about phosphorylation of carbon-6 of glucose. ATP in the presence of Mg^{+2} provides both phosphate and energy for phosphorylation. Three such glucose molecules are simultaneously used in this pathway, generating three molecules of glucose-6-PO_4



(2) Dehydrogenation of glucose-6-PO_4 — Glucose-6-PO_4 is oxidised by the enzyme glucose-6-PO_4 dehydrogenase. Carbon-1 of glucose-6-PO_4 loses the hydrogen pair that goes to coenzyme $NADP^+$ resulting $NADPH_2$ and also 6-phosphogluconolactone.



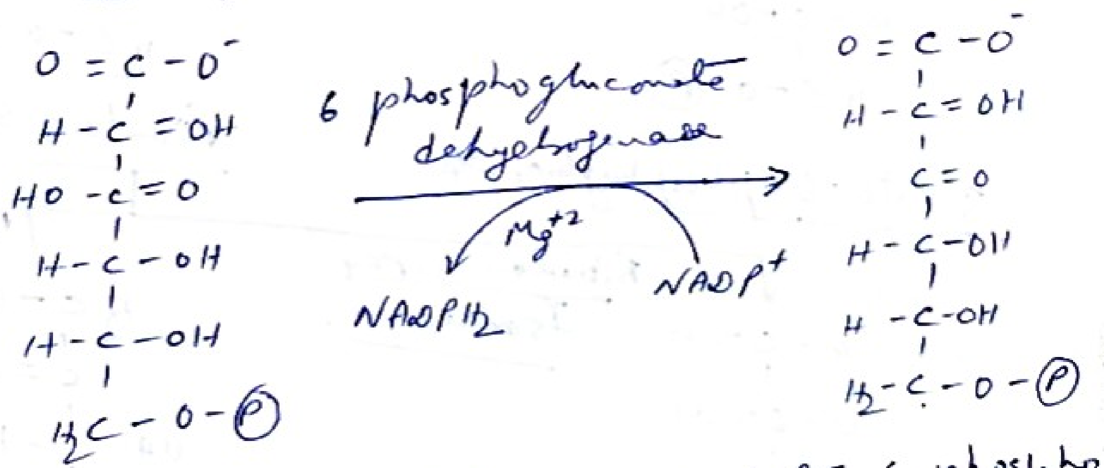
(3) **Hydrolysis of 6-phosphogluconolactone** – Hydrolysis of 6-phosphoglucono-lactone to 6-phosphogluconate is a non-enzymatic reaction, but the enzyme 6-phosphogluconolactonase enhances the rate of reaction.



6-Phosphogluconolactone

6-Phosphogluconate

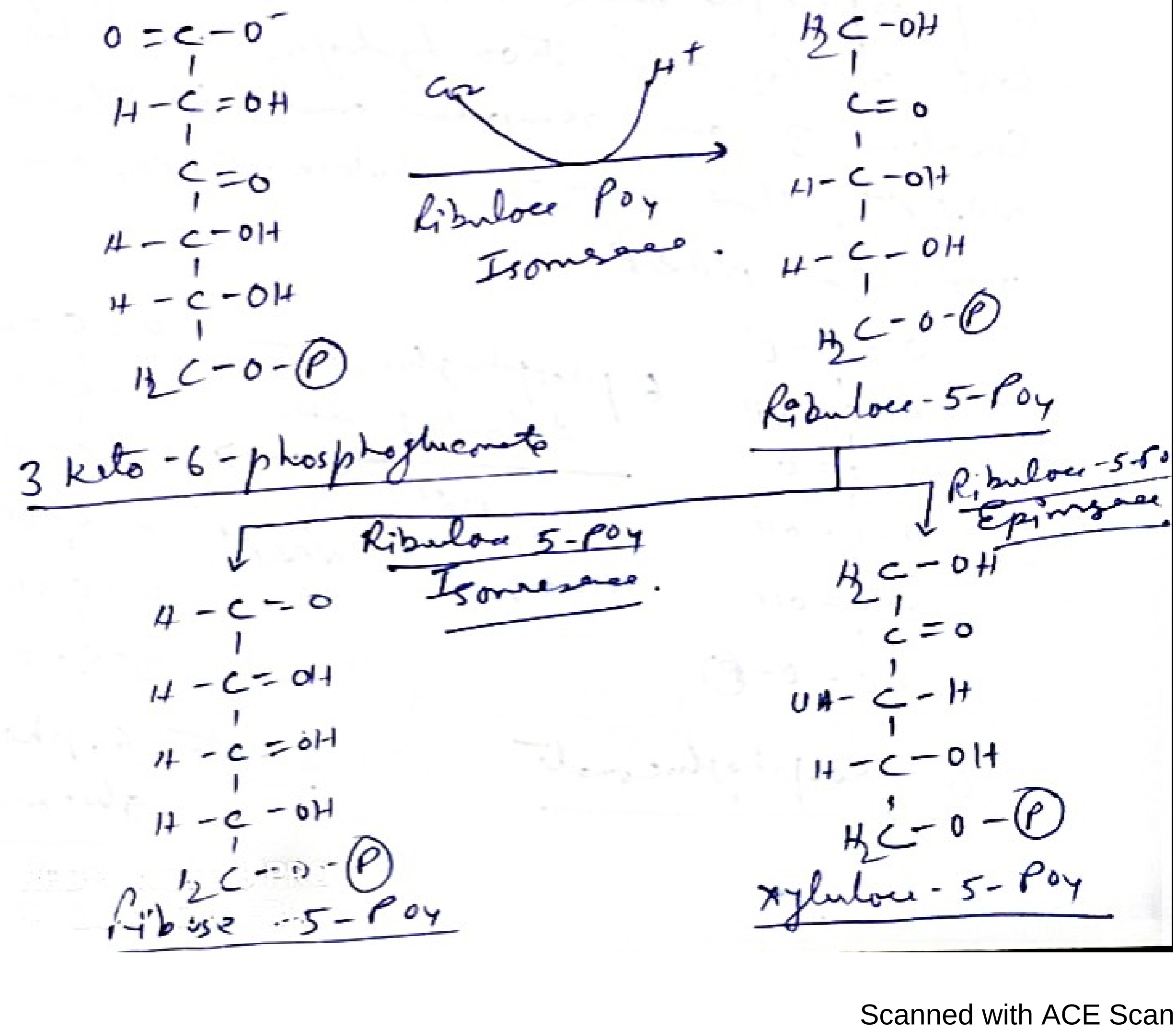
(4) **Oxidative decarboxylation of 6-phosphogluconate** – The enzyme 6-phosphogluconate dehydrogenase brings about oxidative decarboxylation of 6 phosphogluconate. The carboxyl group is lost as CO_2 and two hydrogen molecules from Carbon-3 are removed and transferred to $NADP^+$, thus forming ribulose-5-PO_4 and reduced NADP.



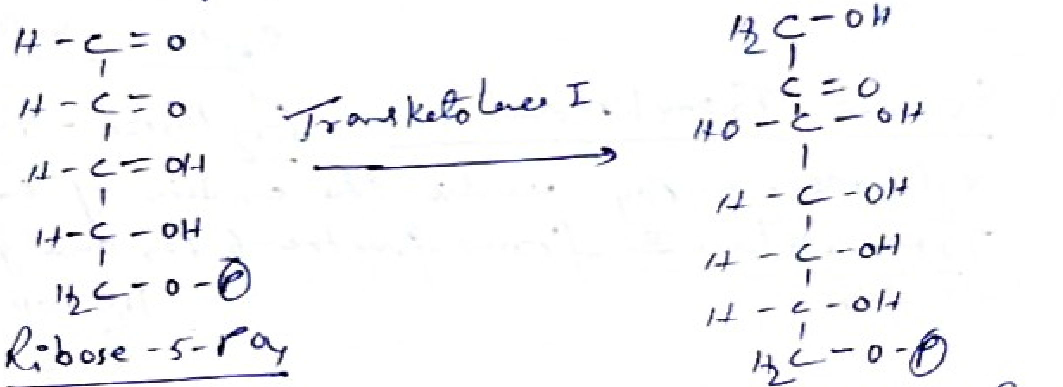
6 phosphogluconate

3 keto, 6, phospho gluconate

(5) Isomerization and Epimerization of Ribulose-5-PO_4 to Ribose-5-PO_4 and Xylulose-5-PO_4 → Out of three ribulose-5-PO_4, one is converted to ribose-5-PO_4 by the enzyme ribulose-5-PO_4 isomerase and other two are converted to xylulose-5-PO_4 by epimerase. All these conversions are mediated through enediolate intermediates; 1,2 enediolate formed is epimerase reaction and 2,3-enediolate being formed is isomerase reaction. Ribose-5-PO_4 is used for nucleotide synthesis while xylulose-5-PO_4 are used for synthesis of fructose-6-PO_4 and glyceraldehyde-3-PO_4 through transketolation and transalkylation reactions.

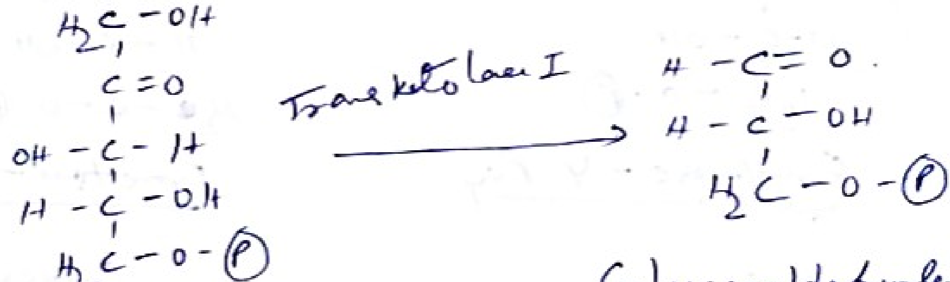


(6) <u>First Transketolation</u> – The ribose-5-PO_4 and one of two molecules of xylulose-5-PO_4 are acted upon by the enzyme <u>transketolase</u> removing a 2 carbon moiety from the former and transfers it to the latter. Thus xylulose-5-PO_4 after losing two carbons is left out as <u>glyceraldehyde-3-PO_4</u> and ribose-5-PO_4 after getting 2 carbons gets converted to <u>sedoheptulose-7-PO_4</u>. Transketolase requires thiamine pyrophosphate as coenzyme.



Ribose-5-PO_4

Sedoheptulose-7-PO_4

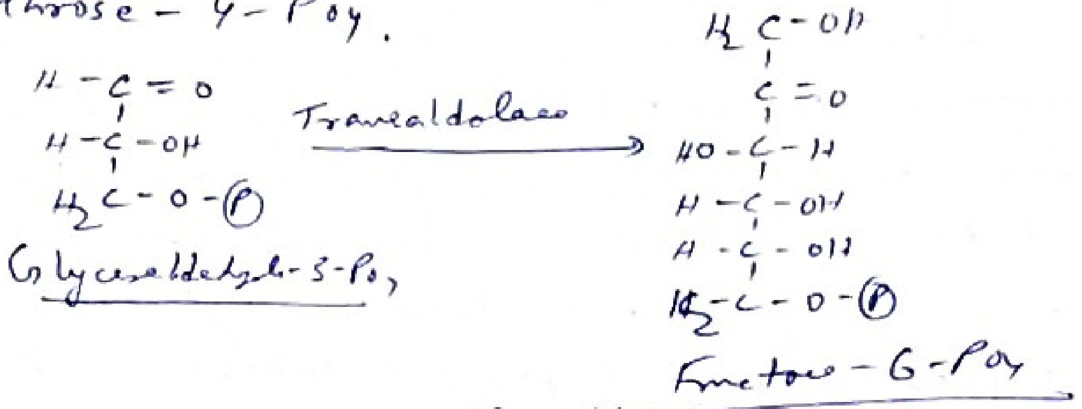


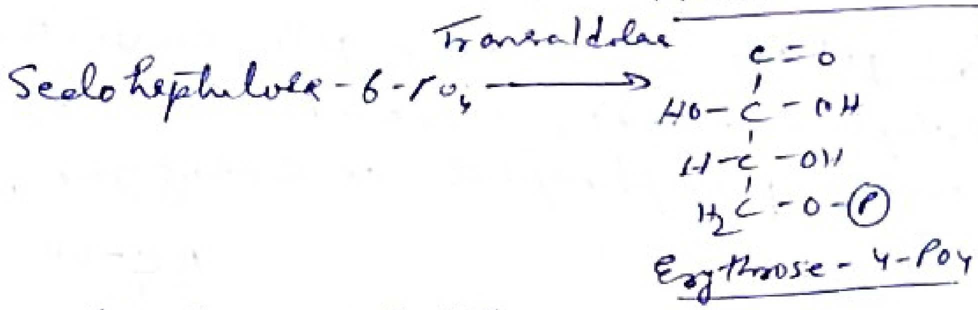
Glyceraldehyde-3-PO_4

Xylulose-5-PO_4

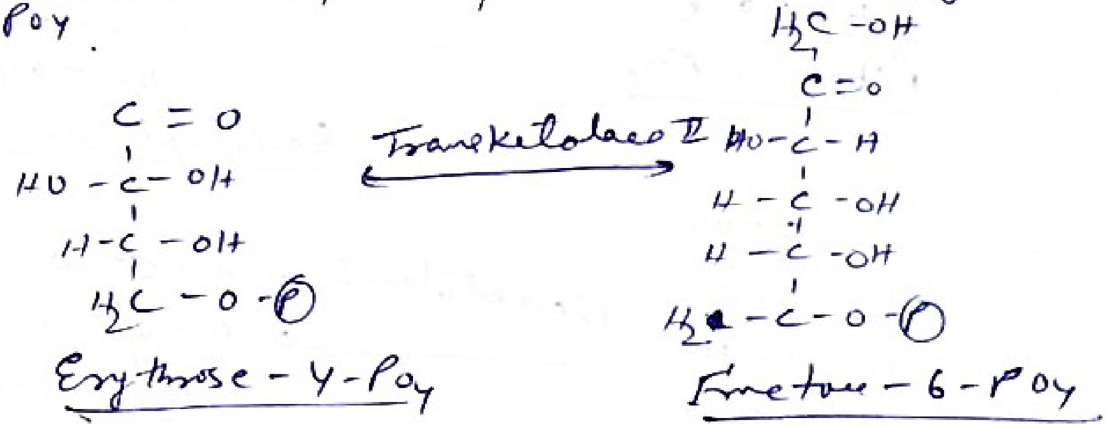
(7) <u>Transaldolation</u> – Products of transketolation <u>sedoheptulose-7-PO_4</u> and <u>glyceraldehyde-3-PO_4</u> are acted upon by the enzyme <u>transaldolase</u> that removes a 3-carbon moiety from the former and transfers it to the latter, thus forming fructose-6-PO_4. The sedoheptulose-7-PO_4

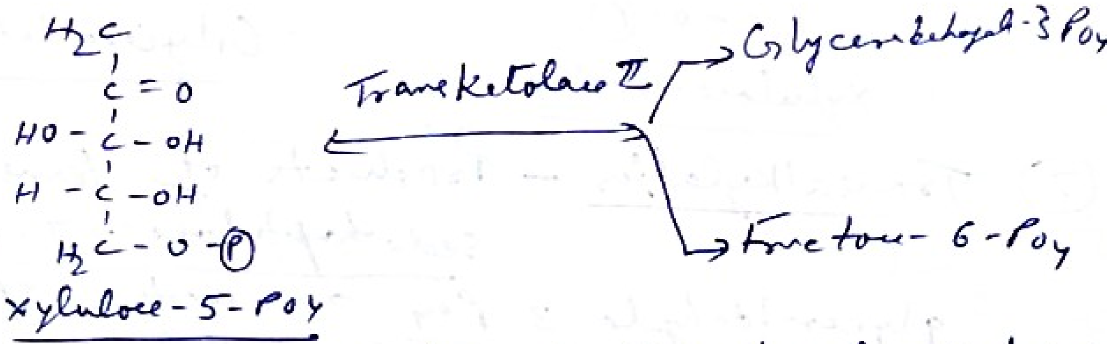
after losing 3-carbon moiety is left out as Erythrose-4-PO4.





(8) **Second Transketolation** — Erythrose-4-PO4 & xylulose-5-PO4 under the action of enzyme Transketolase II forms fructose-6-PO4 and glyceraldehyde-3-PO4.





Hence, In this pathway, 3 molecules of glucose generate two molecules of fructose-6-PO4, one molecule of glyceraldehyde-3-PO4 and two molecules of NADP, besides releasing one CO_2.