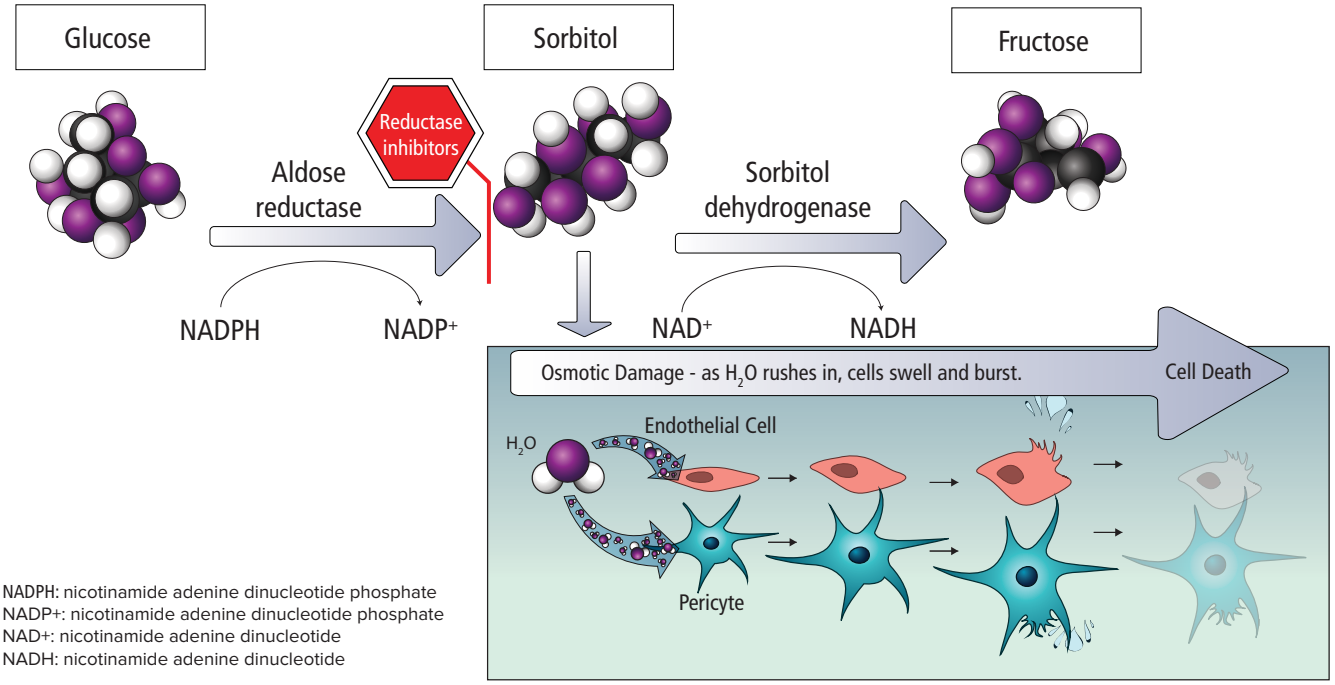
# MODULE 6.6
## Polyol Pathway

The polyol pathway, also called the sorbitol-aldose reductase pathway, metabolizes excess glucose in diabetes. The enzyme aldose reductase converts glucose to intracellular sorbitol, the first step in the pathway, using nicotinamide adenine dinucleotide phosphate (NADPH) as a cofactor.[1,2] In this process, NADPH is converted to nicotinamide adenine dinucleotide phosphate (NADP+). Sorbitol, incapable of crossing cellular membranes, accumulates in the cell and is then oxidized to fructose by sorbitol dehydrogenase, producing nicotinamide adenine dinucleotide (NADH) from nicotinamide adenine dinucleotide (NAD+).[3]

As NADPH levels in the cell fall in this process, the antioxidant capability of the cell is affected.[2,3] NADPH is a cofactor required for regenerating intracellular glutathione, which is an important scavenger of reactive oxygen species. NADPH also promotes the production of nitric oxide, an important vasodilator. Therefore, the depletion of NADPH increases oxidative stress on the cell.

The buildup of sorbitol is thought to contribute to osmotic damage to retinal endothelial cells and pericytes.[1] Also, the fructose produced in the polyol reactions can be converted into strong glycating agents that can lead to the production of advanced glycation end products (AGEs), thereby triggering activation of the AGE and protein kinase C pathways.[2,3]

## Polyol Pathway




NADPH: nicotinamide adenine dinucleotide phosphate
NADP+: nicotinamide adenine dinucleotide phosphate
NAD+: nicotinamide adenine dinucleotide
NADH: nicotinamide adenine dinucleotide

### References

1. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet*. 2010;376(9735):124-136.

2. Tarr JM, Kaul K, Chopra M, Kohner EM, Chibber R. Pathophysiology of diabetic retinopathy. *ISRN Ophthalmol.* 2013;2013:343560.

3. Wu Y, Tang L, Chen B. Oxidative stress: implications for the development of diabetic retinopathy and antioxidant therapeutic perspectives. *Oxid Med Cell Longev.* 2014;2014:752387.