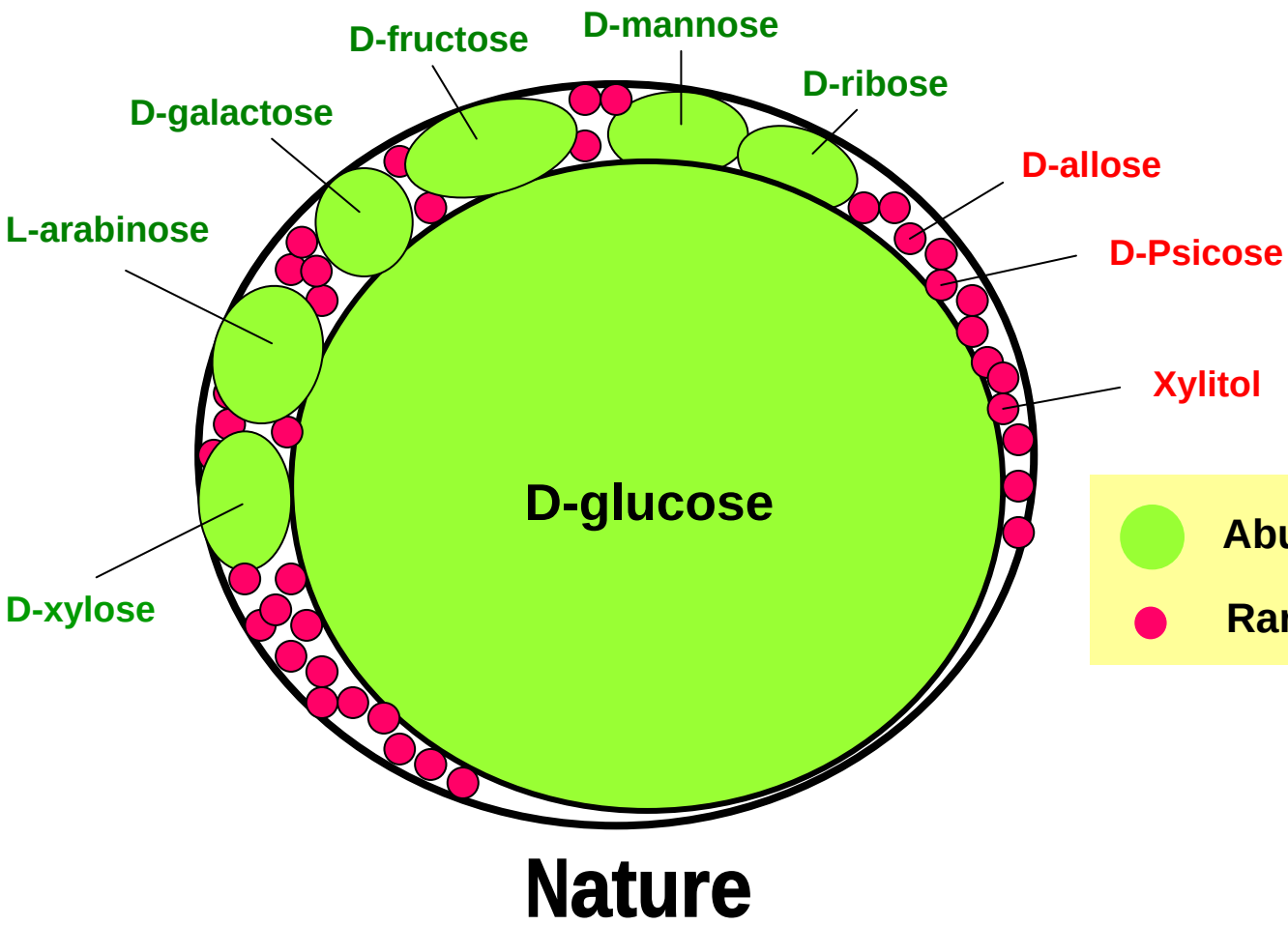
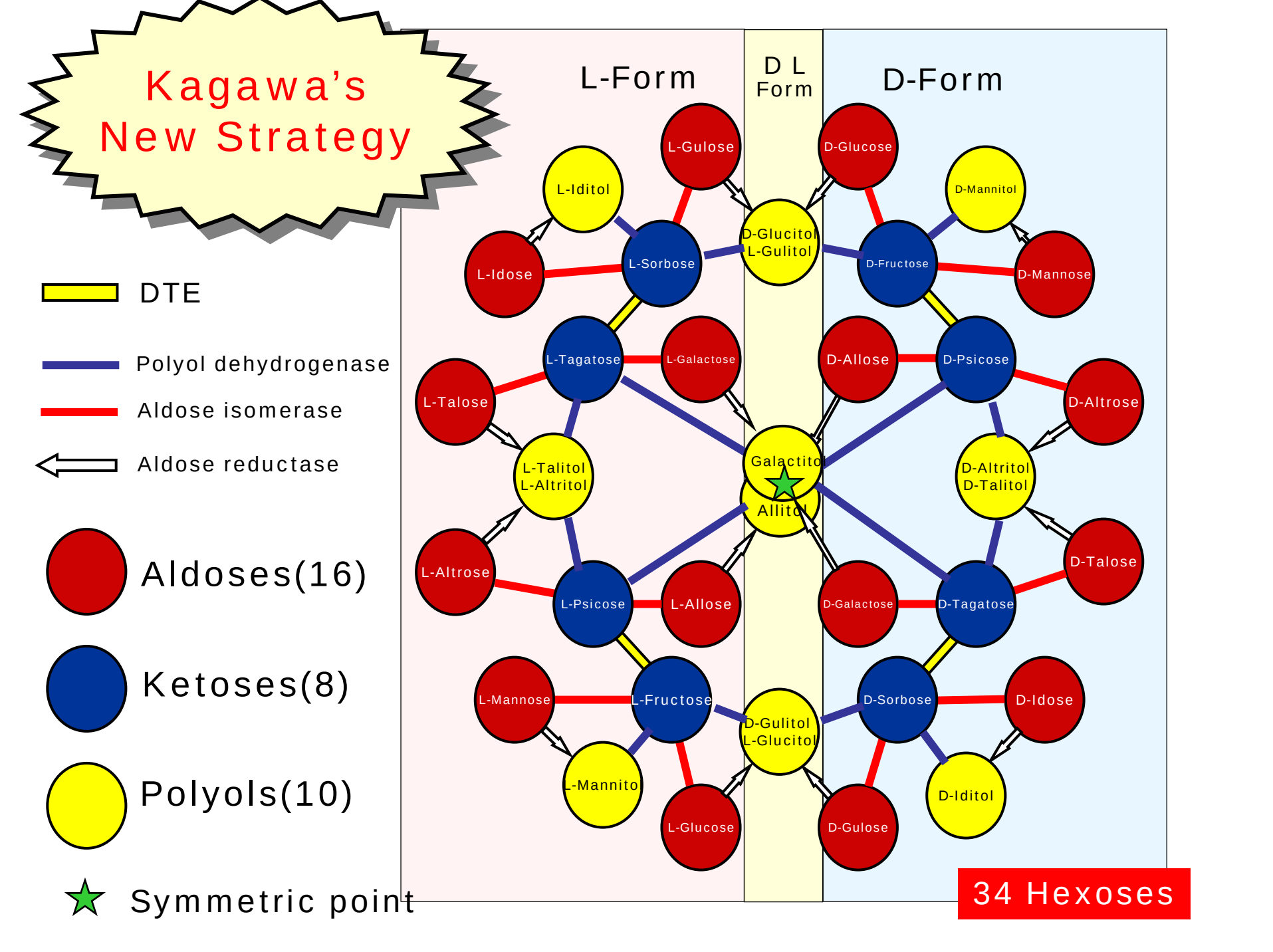
Definition of Rare Sugars

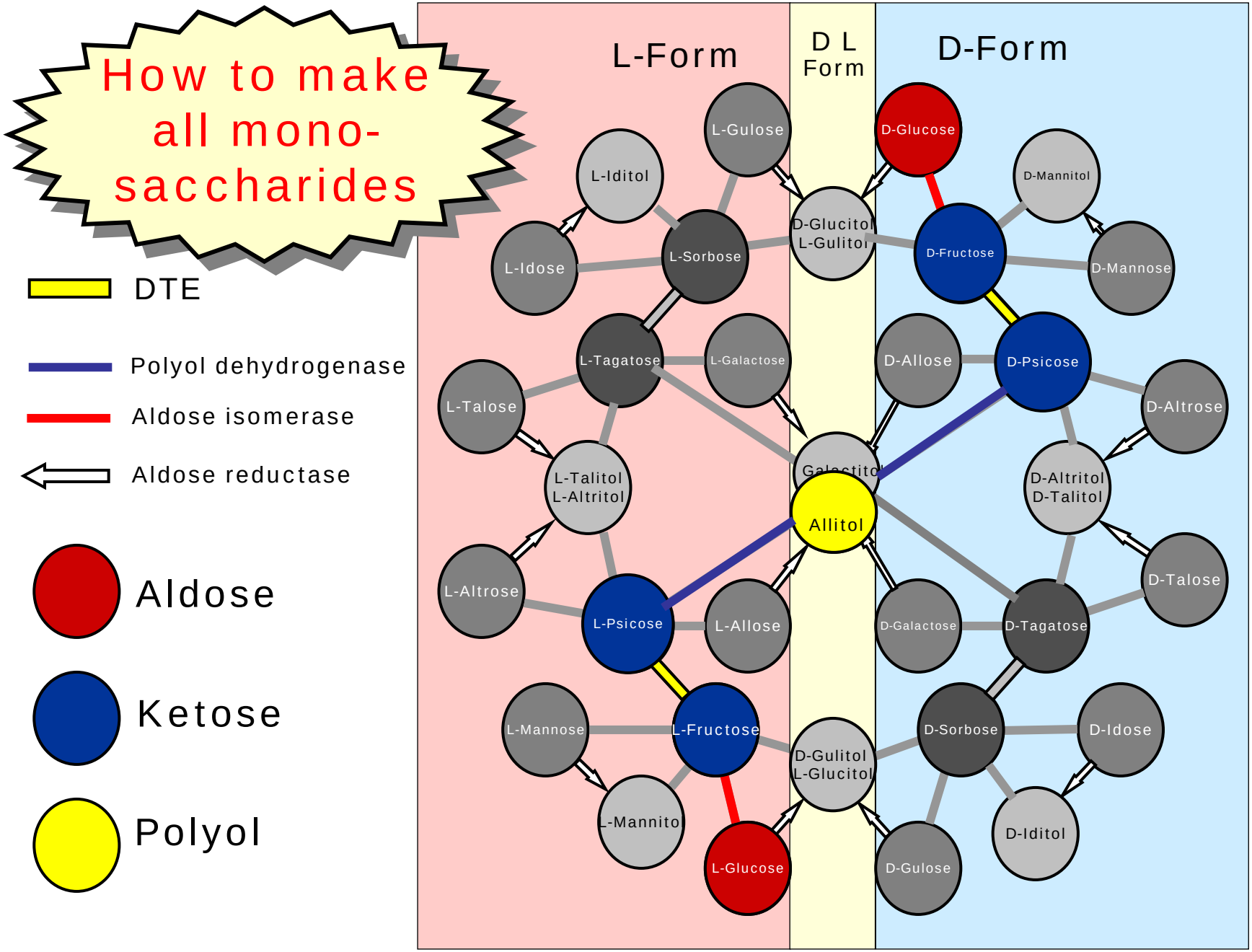
香川大学

Monosaccharides and their derivatives that are rare in nature.



International Society of Rare Sugars

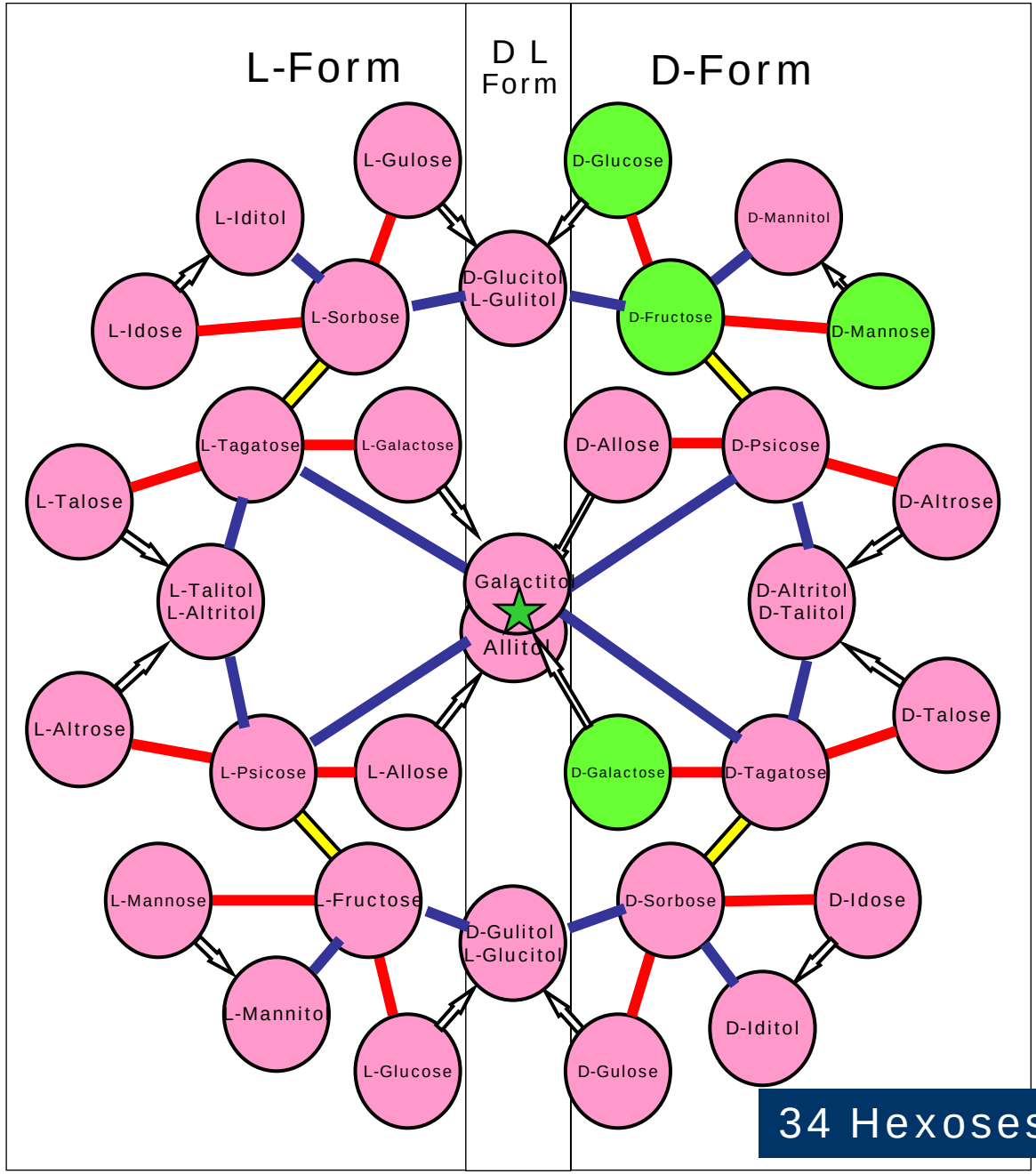

Kagawa's New Strategy
L-Form
D L Form
D-Form
DTE
Polyol dehydrogenase
Aldose isomerase
Aldose reductase
Aldoses(16)
Ketoses(8)
Polyols(10)
Symmetric point
L-Gulose
L-Iditol
L-Idose
L-Sorbose
L-Tagatose
L-Galactose
L-Talose
L-Talitol
L-Altritol
L-Altrose
L-Psicose
L-Allose
L-Mannose
L-Fructose
L-Mannitol
L-Glucose
D-Glucose
D-Mannitol
D-Glucitol
L-Gulitol
D-Fructose
D-Mannose
D-Allose
D-Psicose
D-Altrose
Galactitol
Allitol
D-Altritol
D-Talitol
D-Talose
D-Galactose
D-Tagatose
D-Sorbose
D-Idose
D-Gulitol
L-Glucitol
D-Iditol
D-Gulose
34 Hexoses

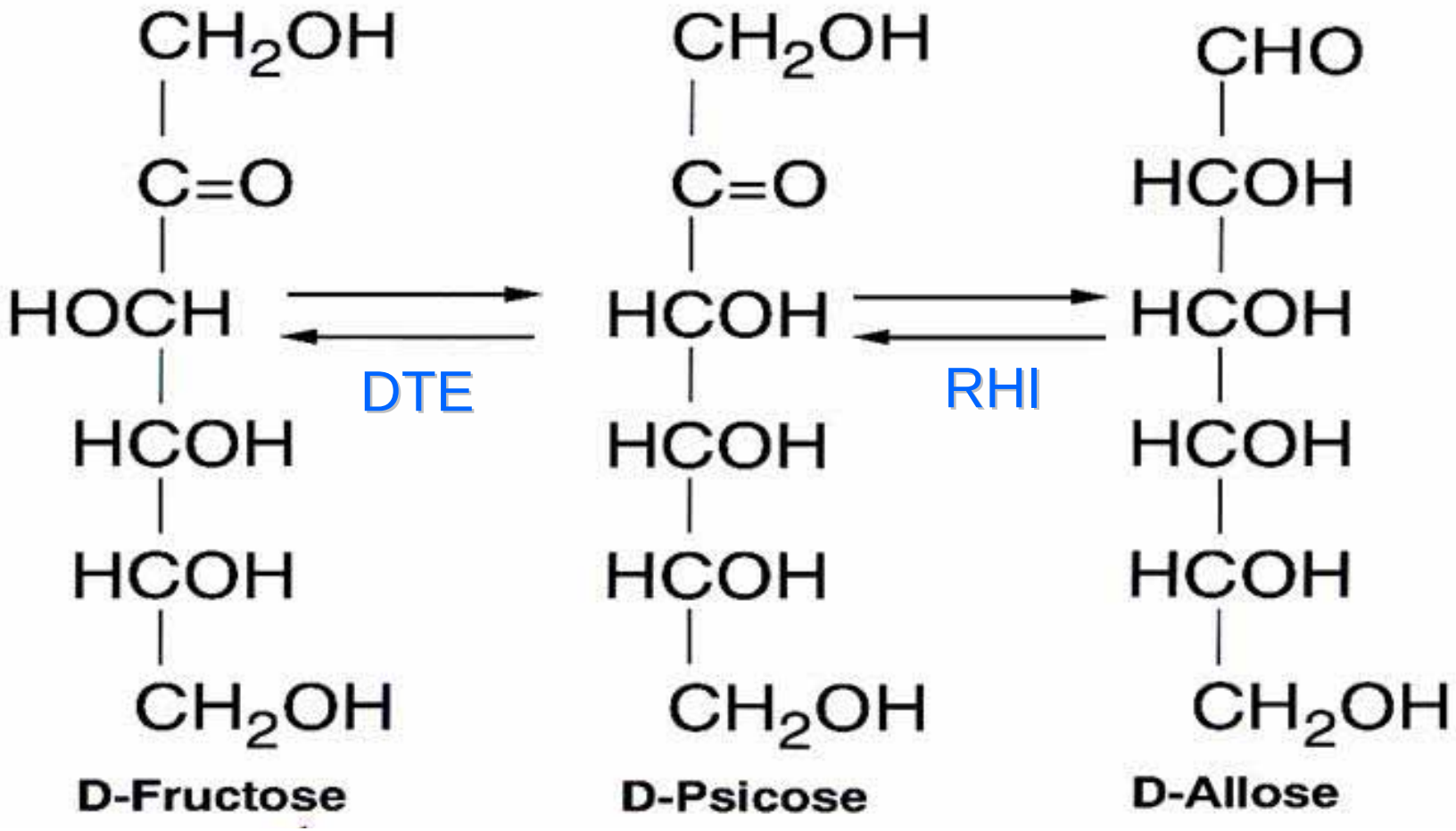

How to make all mono-saccharides
DTE
Polyol dehydrogenase
Aldose isomerase
Aldose reductase
Aldose
Ketose
Polyol
L-Form
D L Form
D-Form
L-Gulose
L-Iditol
L-Idose
L-Sorbose
L-Tagatose
L-Galactose
L-Talose
L-Talitol L-Altritol
L-Altrose
L-Psicose
L-Allose
L-Mannose
L-Fructose
L-Mannito
L-Glucose
D-Glucitol L-Gulitol
Allitol
D-Gulitol L-Glucitol
D-Glucose
D-Mannitol
D-Fructose
D-Mannose
D-Allose
D-Psicose
D-Altrose
D-Altritol D-Talitol
D-Talose
D-Galactose
D-Tagatose
D-Sorbose
D-Idose
D-Iditol
D-Gulose

Relationship between rare sugars and abundantly existing sugars

Rare sugars

Abundantly existing sugars in nature

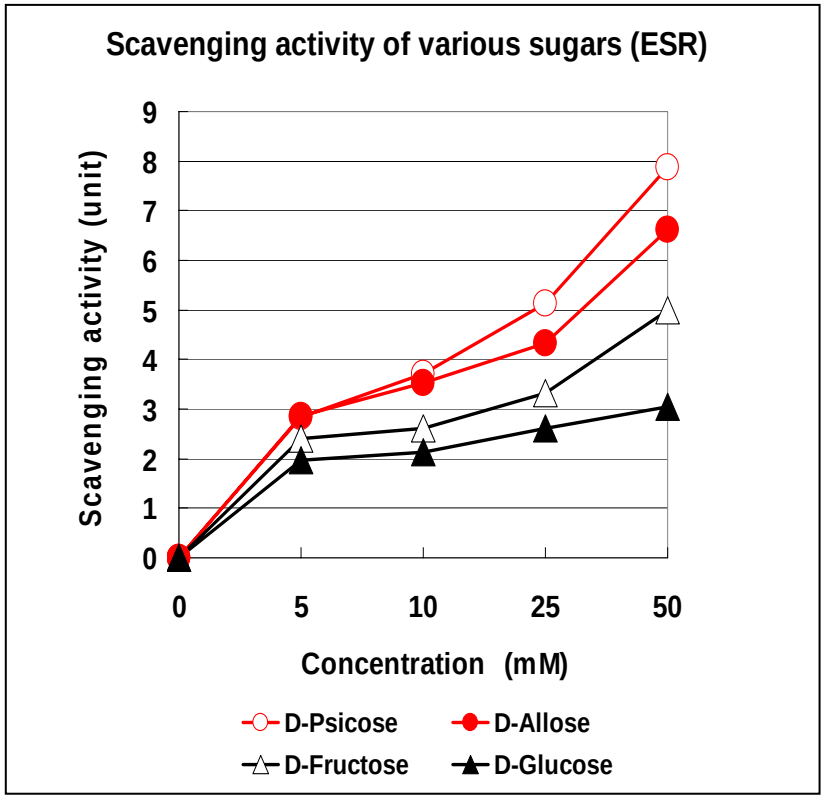


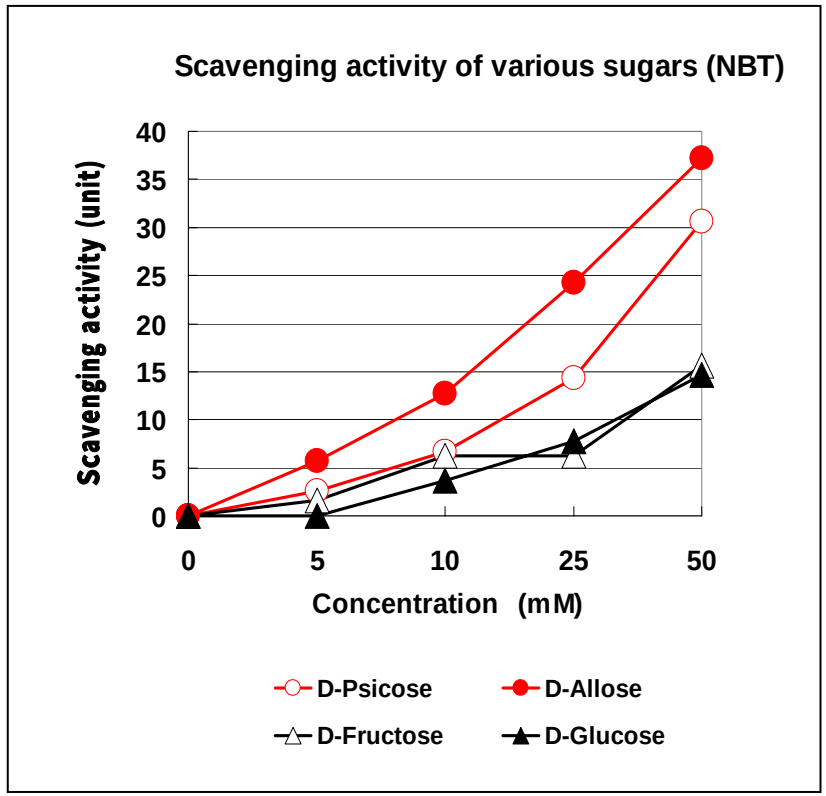


Enzymatic conversion allows to produce D-psicose from D-fructose by DTE (D-tagatose 3 epimerase), and D-allose from D-psicose by RHI (L-rhamnose isomerase). All hexoses comprise 6 carbons, 12 hydrogens and 6 oxygens with the identical molecular weight of 180.

Rare sugar : D-psicose

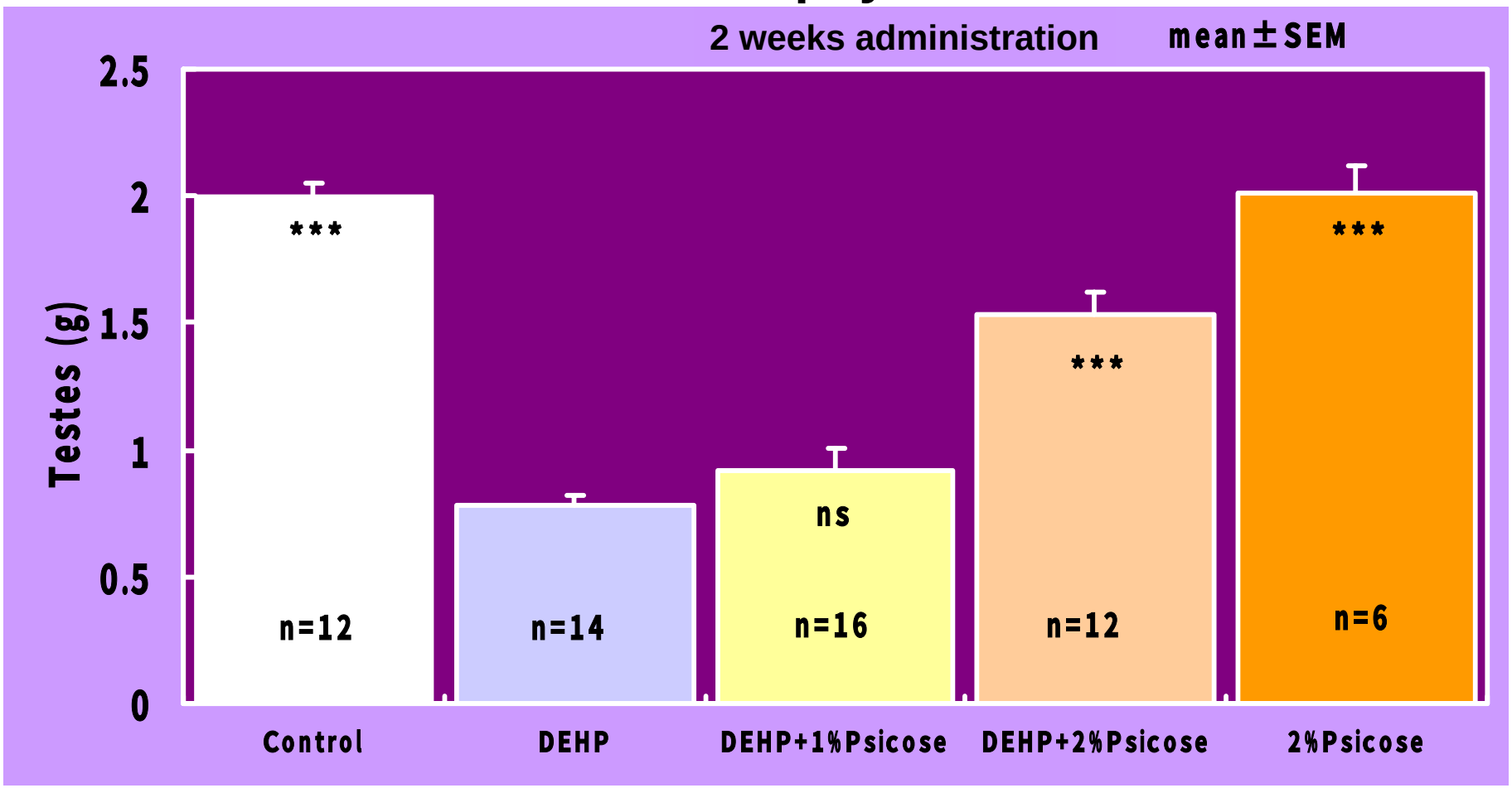
Effect of D-psicose and D-allose on ROS





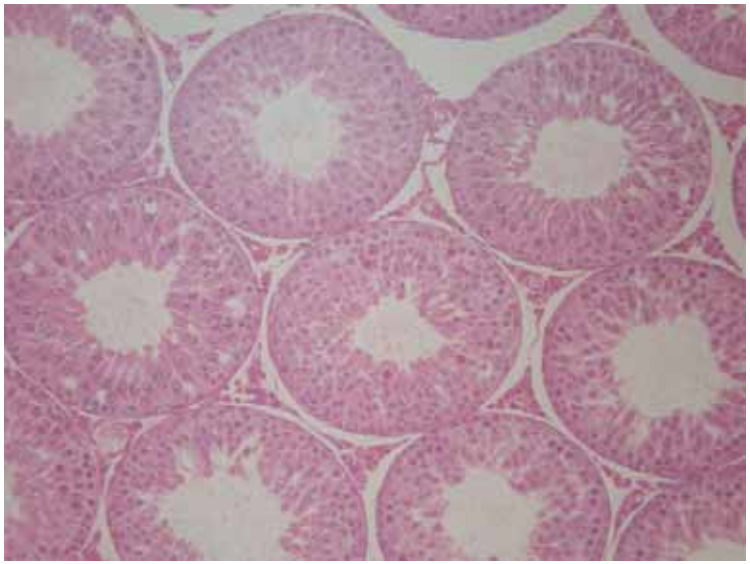
Scavenging activity of oxygen-radicals was measured by the two different methods (ESR method and NBT reduction method). D-Allose and D-Psicose showed much higher activity than D-Fructose and D-Glucose.

Supplementation of D-psicose prevents DEHP-induced atrophy of rat testis

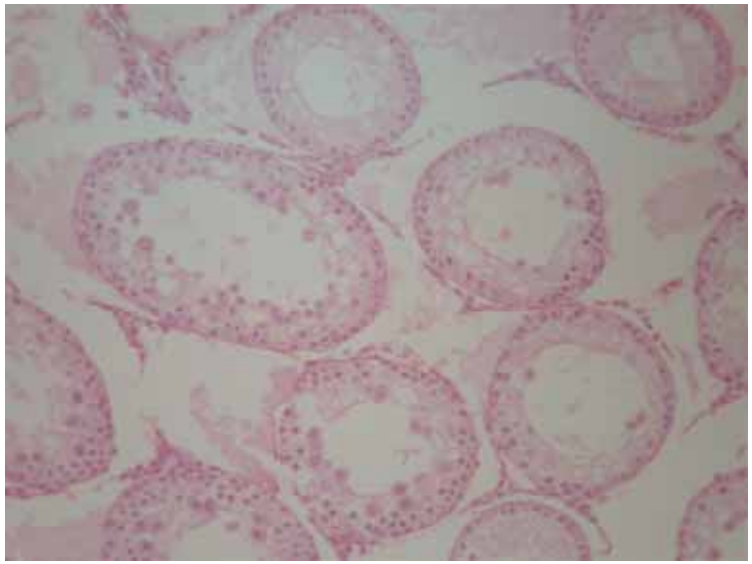


(*p<0.05, **p<0.01, ***p<0.001: vs DEHP group)

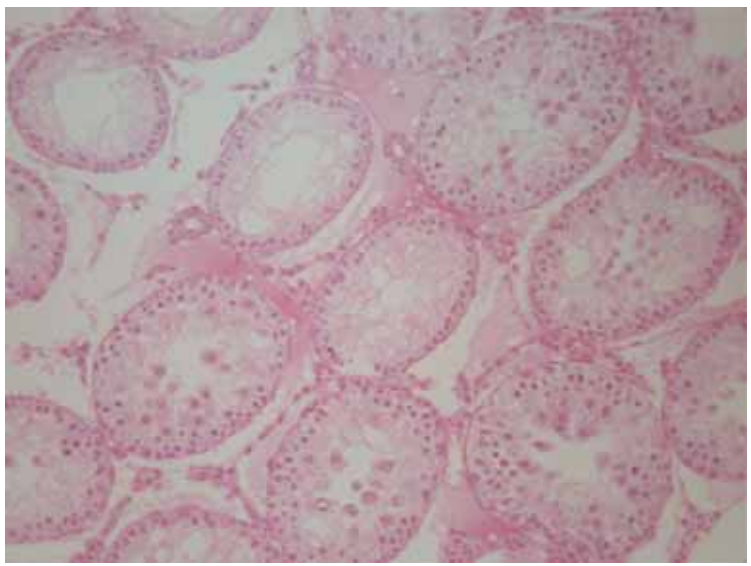
D-psicose effectively prevent DEHP-induced atrophy of rat testis.



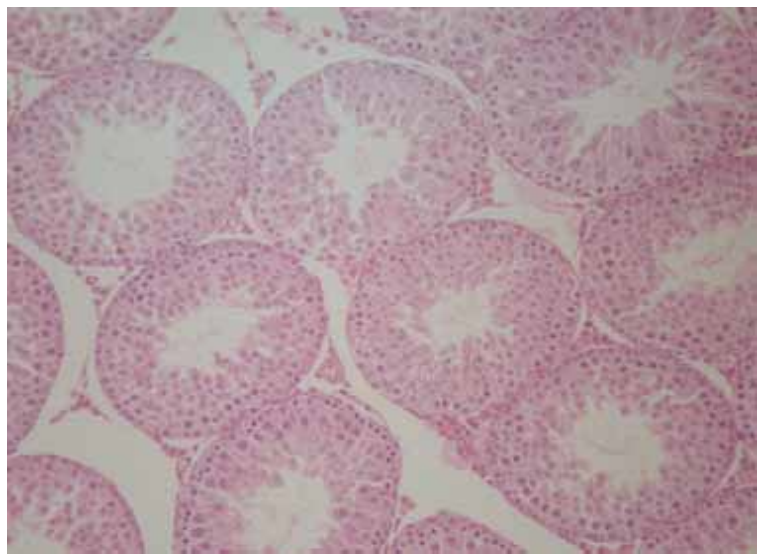
Normal testis



DEHP

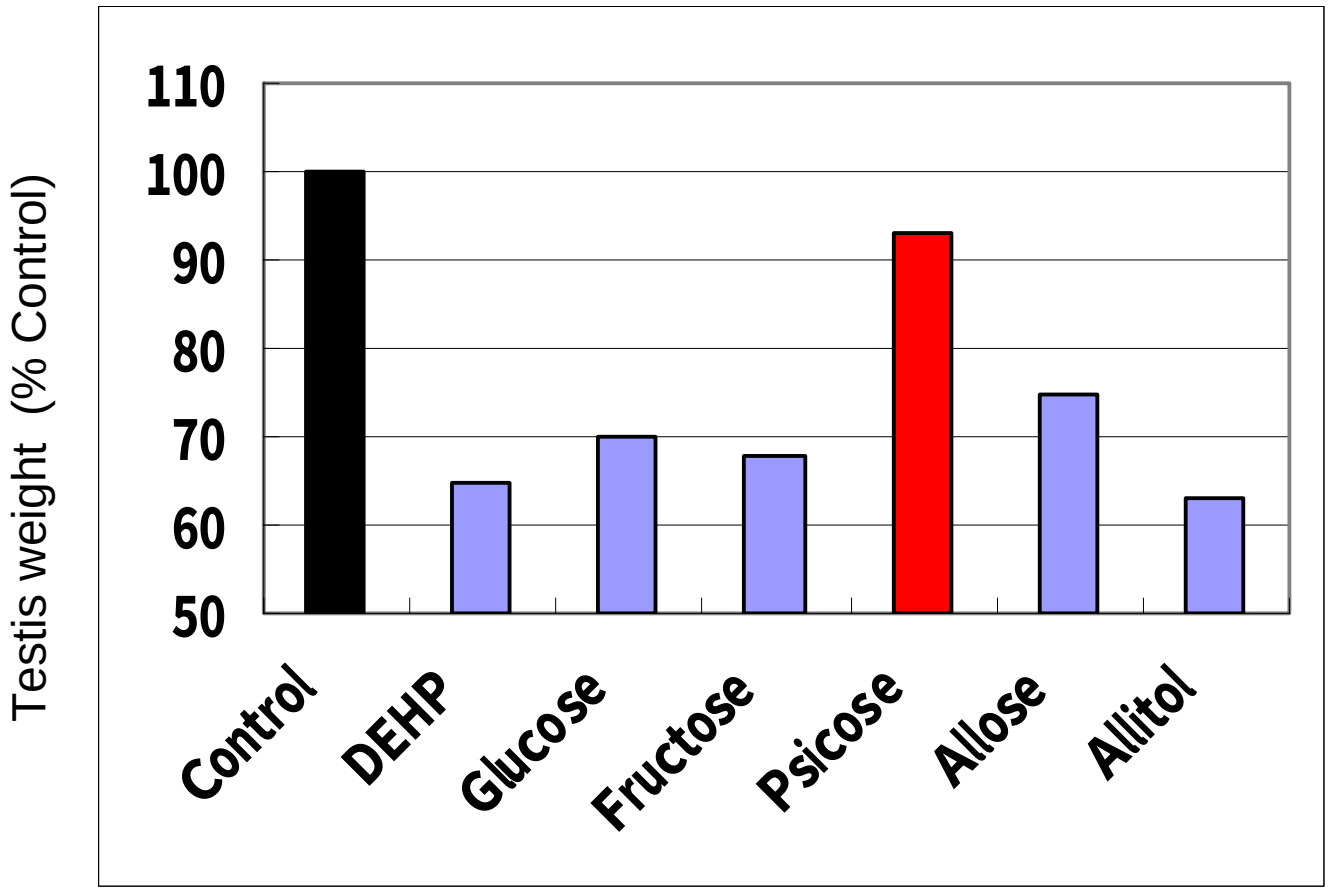


DEHP + 1% D-psicose



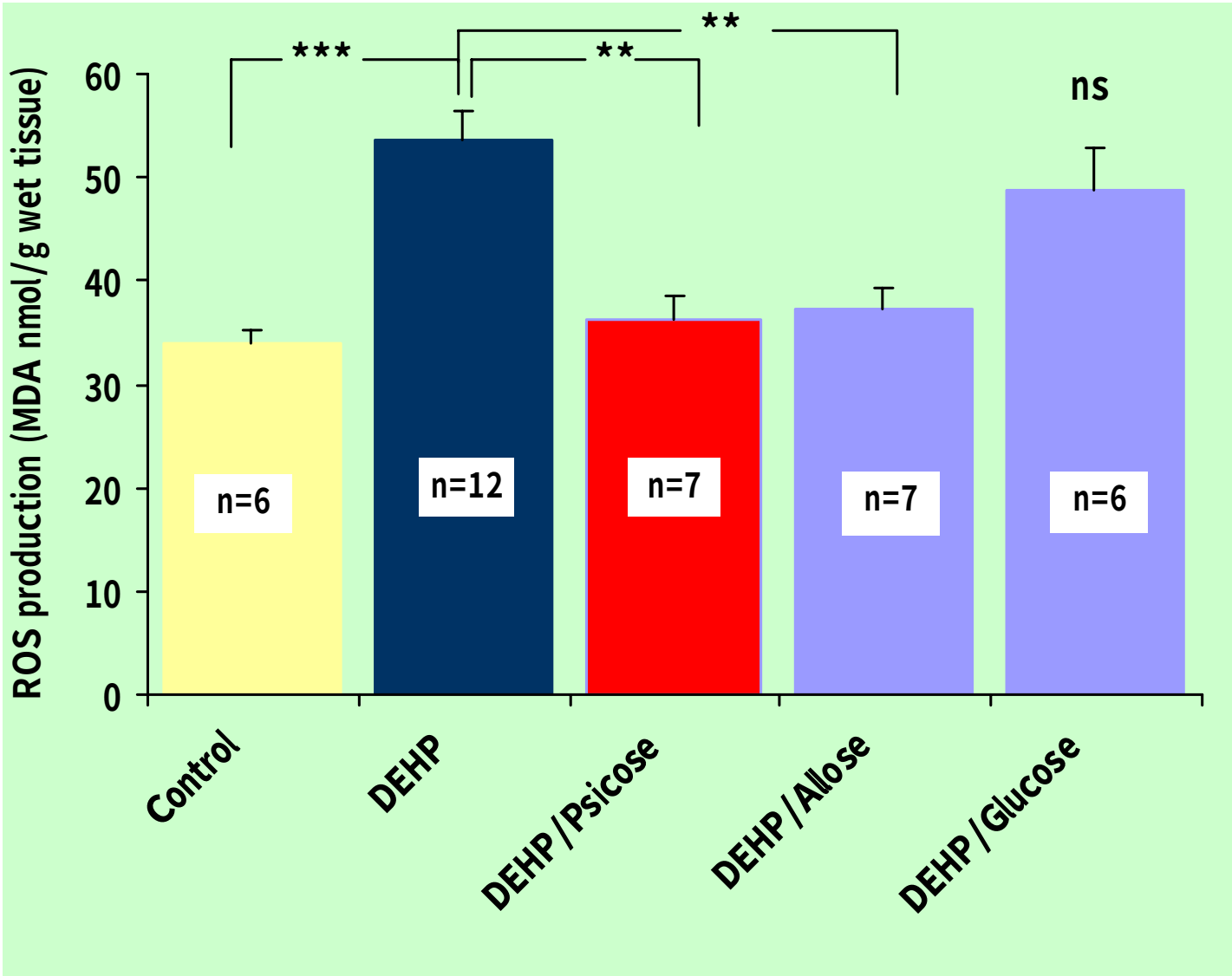
DEHP + 2% D-psicose

Effect of various monosaccharides on DEHP-induced atrophy of rat testis



D-psicose is the most potent monosaccharide inhibiting DEHP-induced atrophy of rat testis

D-psicose reduced ROS production in the testis induced by DEHP administration

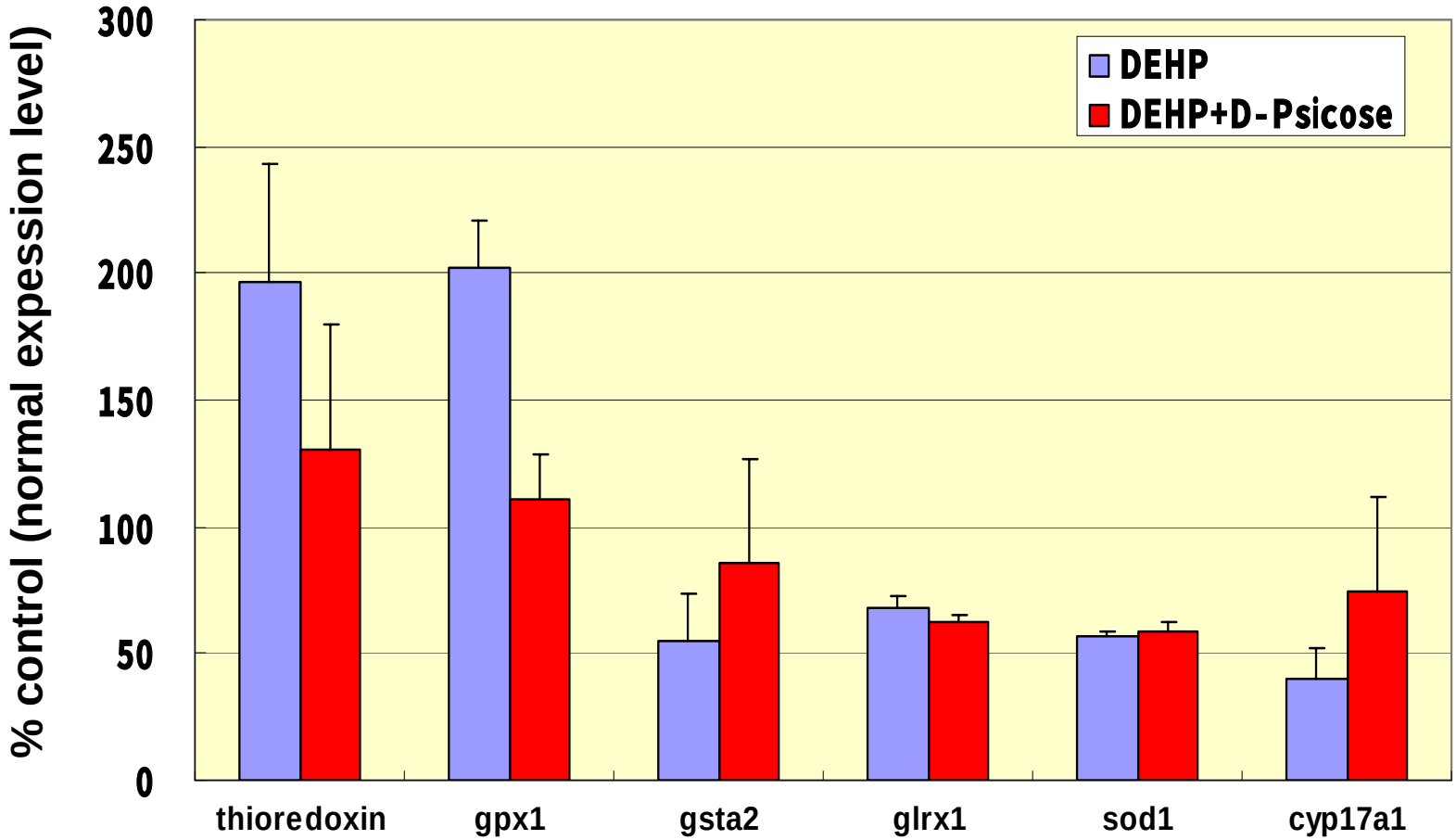


(**p<0.01, ***p<0.001: vs DEHP group)

Genes significantly altered by DEHP exposure in rat testis

Gene Name	Description	Expression change
Oxidative Stress		
Txn	Thioredoxin mRNA (NM_053800)	↑ ↑ ↑
Gpx1	Glutathione peroxidase 1 (Gpx1) mRNA	↑ ↑
Gpx2	Glutathione peroxidase 2 (Gpx2) mRNA	↑ ↑
Glrx1	Glutaredoxin 1 (thioltransferase) (Glrx1) mRNA	↓
Sod1	Superoxide dismutase 1 (Sod1), mRNA	↓ ↓
Detoxification		
Gsta2	Glutathione-S-transferase, alpha type2 (Gstα2)	↓ ↓
Steroidogenesis		
Cyp17a1	cytochrome P450, family17, subfamily a, polypeptide1	↓ ↓ ↓
Hsd11β2	Hydroxysteroid 11-beta dehydrogenase 2 , mRNA	↓ ↓
Signal transduction		
S100a9	S100 calcium binding protein A9 (calgranulin B)	↑ ↑
Transcription factors		
Atf3	Activating transcription factor 3(Atf3), mRNA	↑ ↑

Changes in gene expression in rat testis after DEHP and Rare Sugar (D-psicose) treatment



Thioredoxin, Glutathione peroxidase 1 : DEHP ↑ D-psicose ↓
Glutathion S-transferase α2 : DEHP ↑ D-psicose ↓
Glutharedoxin, SOD : DEHP ↓ D-psicose →
Cyp17a1 : DEHP ↓ D-psicose ↑

Summary of the study

1. Oral administration of DEHP, when converted to MEHP, causes an increase of ROS production in testis.
2. ROS are mainly superoxide radicals and H_2O_2.
3. ROS production mainly occurs in germ cells not in Sertoli cells.
4. Oxidative stress causes apoptosis of germ cells.
5. Vitamins C & E or D-psicose, one of rare sugars, can be used for the prevention of DEHP-toxicity.
6. Several molecular markers such as oxidative stress related genes are applicable to evaluate the toxicity.

Future projects

DEHP

1) Lower doses, longer exposure
2) Optimize the prevention method
   - Vitamins C & E
   - Rare sugars
     → other rare sugars
3) Mechanism
   - What are the effective and responsible markers?
   - Other possible mechanisms of the toxicity

Other EDCs

1) Oxidative stress could be more or less the common etiological factor for other EDCs.
2) Markers related to oxidative stress can be standardized.
3) Prevention has to be considered.

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