

Chemistry, biochemistry and health benefits of cyclitols from carob pods



Cyclitols as a group can be commonly found in most plants

Leguminosae family are the major natural source of this compound.

Ceratonia siliqua L. (Carob), contains much higher amounts of D-pinitol than any other legume



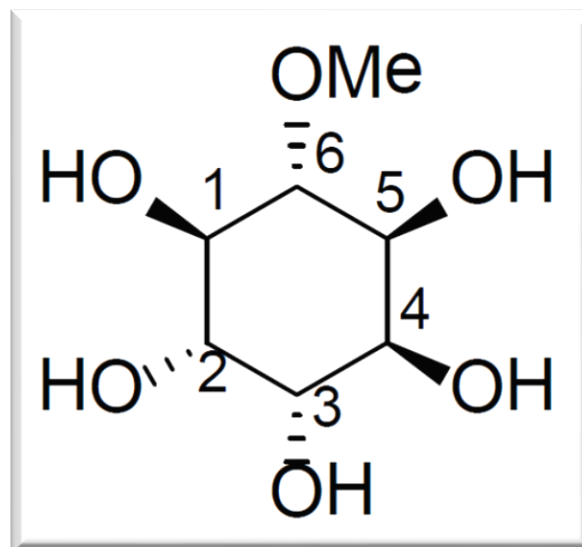
Can fix three times more CO₂ than other common woody crops.

Half of the water requirements.

Resistant to eroded soils and fires.

D-pinitol is the 3-O-methyl ether of D-chiro-inositol, that is to say the (1R,2S,3R,4S,5S,6S)-6-methoxycyclohexane-1,2,3,4,5-pentaol.

Methylated cyclitols (cyclohexane-1,2,3,4,5,6-hexaols): 9 isomers, only 5 naturally occurring: myo-, chiro-, scyllo-, muco-, neo-inositol



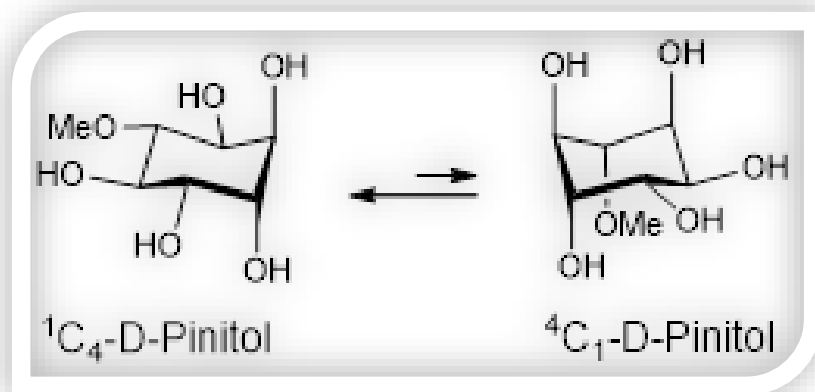
White to off-white solid: melting point of 186-187 °C.
Very soluble in water and slightly soluble in ethanol.
Specific rotation in water is $[\alpha]_D = + 65^\circ$ (c 0.4, H₂O)

Most plausible
conformation
of D-Pinitol in
water

1C_4 -like geometry
(scheme 1, left).

Energetically
favoured versus a
 4C_1 -like (scheme
1, right)

More than 98% of
the molecules in
solution.

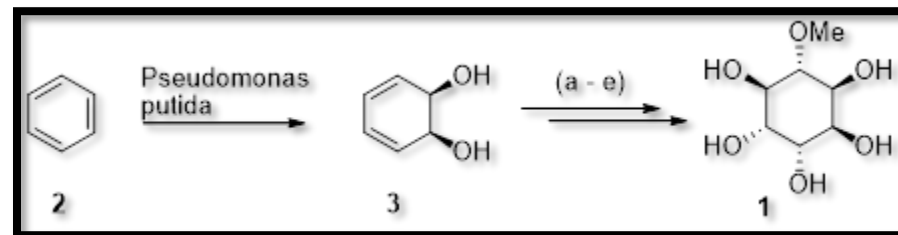


In agreement with experimental data obtained from single-crystal X-ray diffraction analysis

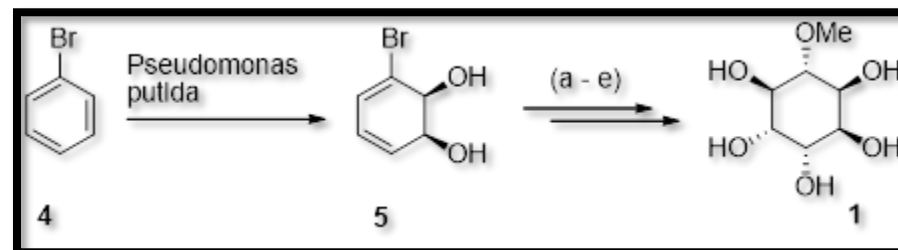


Synthetic D-Pinitol

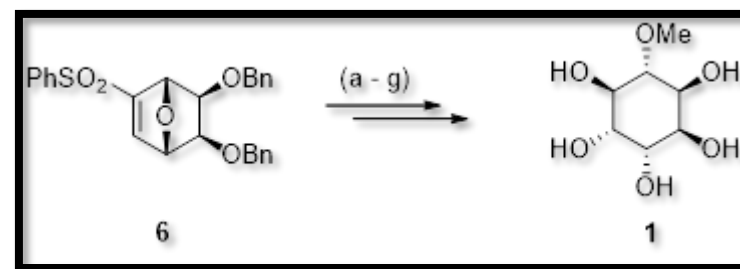
Ley et al: 49%
overall yield
from benzene.

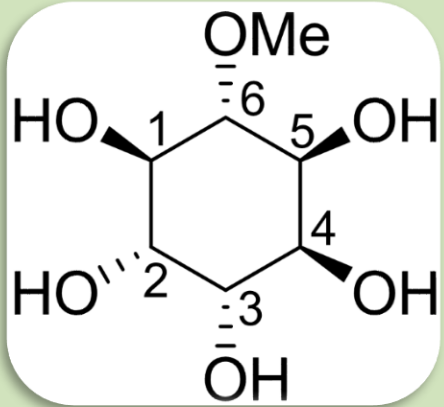


Hudlicky et al:
56% yield.



Aceña et al:
10% yield.





Pharmacological potential of D-pinitol as a result of its multifunctional properties

- **Anti-cancer.**
- **Anti-diabetic.**
- Antioxidant.
- Hepatoprotective.
- Immunosuppressor.
- Inhibitor of osteoclastogenesis.
- Anti-aging.
- Creatine retention promotor.



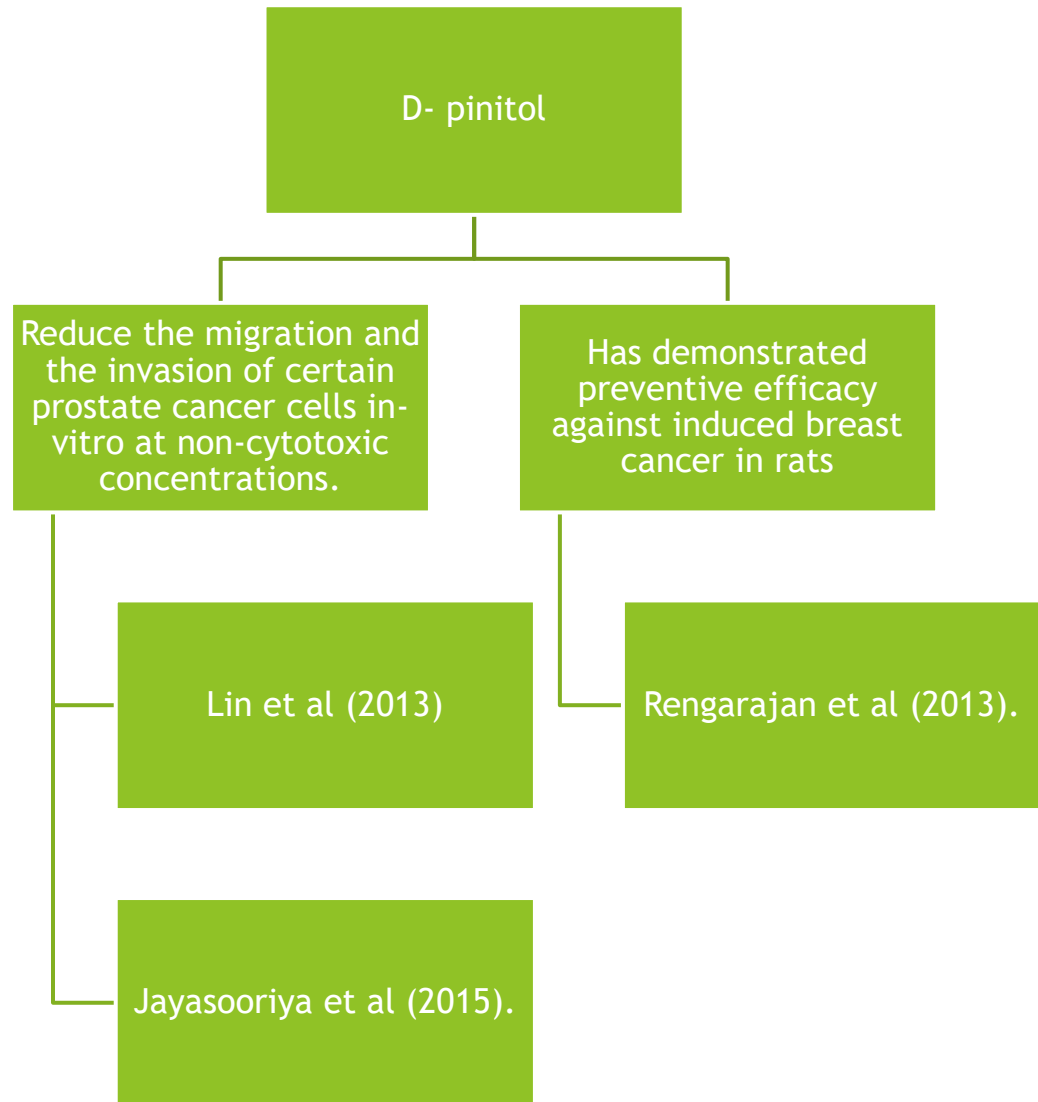
Cancer

- Enormous public health problema.
- Leading cause of mortality.
- Breast cancer is the most diagnosed cancer in women.
- Prostate cancer is the most diagnosed cancer in men.
- Cancer metastasis is the major cause of mortality for patients with cancer.

Considerable lesser risk of cancer exists in those people who regularly ingest fruits and vegetables: attributed to their combination of phytochemicals.

- Chemoprevention through dietary intervention is an emerging option to reduce the incidence of certain cancers.
- National Cancer Institute has highlighted a number of foods for which there are evidences that associate them to a reduced risk of cancer.
 - Soybean: rich in D-Pinitol.





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D-Pinitol is an effective blocker of the Nuclear factor kappa B (NF- κ B) pathway

Inhibition of TNF-induced cell invasion.

Down-regulation of gene products that prevent apoptosis and promote inflammation and tumour metastasis.

Diabetes mellitus is a chronic complex disease with a high number of complications associated.

- Every year 6.8% of the world's population die due to complications of diabetes.
- Its prevalence is expected to increase throughout the world from 171 million in 2000 to 366 million in 2030.

Primary complications:
Abnormally high levels of blood glucose.

- Deficiency in insulin secretion.
- Insulin receptor or postreceptor events, leading to the disturbance in the metabolism of carbohydrates, proteins and fats

Secondary complications:
Progression and aggravation of oxidative stress.

- Glucose autoxidation.
- Protein glycation.
- Formation of advanced-glycation-endproducts (AGEs).



Expert's opinion on
diabetes mellitus
from World Health
Organization (WHO)

Second Report. World
Health Organ. Tech.
Rep. Ser. 1980, 646, 1-
80.

Prioritizing the
evaluation of the
effectiveness of plants,
and natural compounds
derived from them, in
this condition.

D-Pinitol

Insulinomimetic properties.

Capacity to reduce hyperglycaemia.

Regulates metabolic complications associated to diabetes mellitus.



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The ability of D-Pinitol to reduce hyperglycaemia can not be attributed to:

- Increased insulin concentrations.
- Neither to the augmentation of the insulin action.



D-Pinitol may act via a post-receptor pathway of insulin action affecting glucose uptake

D-Pinitol exerts an insulin-like effect on glucose transport independently of insulin, acting downstream in the insulin signalling pathway



PI3K/Akt pathway is one of the primary signalling pathways whose dysregulation is implicated in a number of human diseases including cancer, diabetes, cardiovascular and neurological diseases.



It is thought that **D-Pinitol relieves insulin resistance** through the **PI3K/Akt pathway**, thereby reducing the concentration of blood glucose by up-regulation of glycogen synthesis.



In concordance with the **structural similarity of D-Pinitol with inositol phosphates**, known to be involved in the signalling of insulin via the PI3K/PKB pathway



Inositol phosphates

Group of mono- to polyphosphorylated inositols.

Play crucial roles in diverse cellular functions.

THANK YOU VERY
MUCH FOR YOUR
ATTENTION

