SAMYANG

Nexweet® Allulose

Nutrition Information Datasheet

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Nexweet® Allulose

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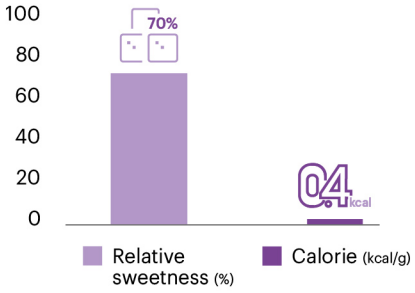
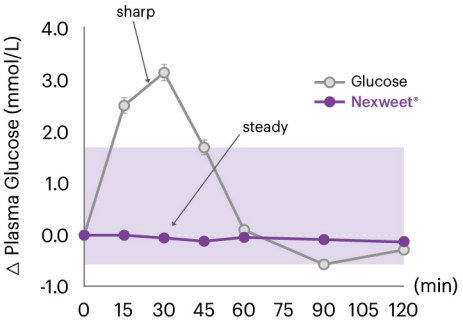
01 Characteristics

Almost zero calorie sweetener with 'No added sugar' claim



*Sucrose relative sweetness = 100

Lower blood glucose curve



* Glycemic response research report SUGiRS (2023)

The most sugar-like sweetener

- ✓ Activates 100% of sweetening sensation with its full agonist molecule
- ✓ Optimizes the sweet taste with its enhancing, masking, and modifying properties

02 Product lineup

	Nexweet® Allulose 95L	Nexweet® Crystalline Allulose
Type	Syrup	Crystalline
D-Allulose (dry basis, %) (AOAC 980.13)	≥ 95.0	≥ 99.0
Dry Solids (brix, %) (AOAC 932.14c, 941.14)	68.0 ~ 70.0	≥ 99.0
pH (in 10% solution) (Potentiometric method)	3.0 ~ 7.0	3.0 ~ 7.0

03 Health functionalities

1. Improves glucose metabolism by alleviating insulin resistance
2. By regulating oxidative stress, maintains the function of beta cells and insulinemic function
3. Alleviates adiposity by improving adipokine levels and lipid profiles
4. Maintains intestinal barrier integrity by enhancing the tight junction proteins
5. Inhibits the growth of cavity-inducing bacteria and does not induce dental caries

04 Application

Certifications

FDA GRAS APPROVED NO.828 · FSSC 22000 · HALAL · NON GMO Project VERIFIED nongmoproject.org · KETO CERTIFIED · HACCP MFDS · ISO

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1 Overall Status

1) Introduction

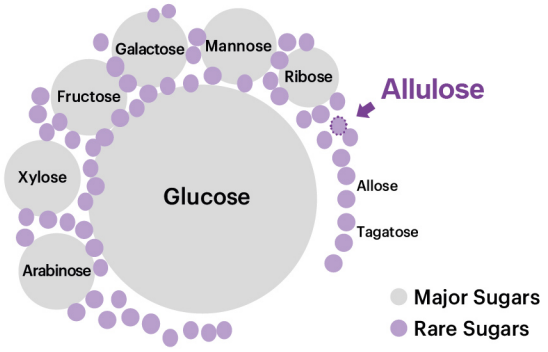
Nexweet® Allulose

Allulose is a sweet ingredient found in figs and grapes, known as the leading next-generation sweetener due to its sugar-like sweetness and almost "zero" calorie content. This rare sugar occurs naturally in small amounts in various sources such as sugar beets, figs, and raisins. Although allulose naturally exists in trace amounts, it is a safe sugar component that has been consumed for an extended period, as it is found in fruits or processed foods (▲Figure 1).

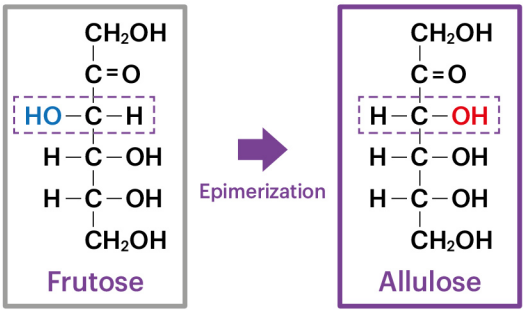
Mass production of allulose is possible using enzyme technology. Its molecular structure closely resembles that of fructose, as it is an epimer with a modified -OH group position at the C3 carbon. When applied to processed foods, Allulose exhibits properties similar to fructose. Samyang achieved successful commercialization of Allulose through its proprietary enzyme technology (▲Figure 2).

Notably, allulose became the first sugar substitute to be exempt from mandatory labeling for 'Total sugars' and 'Added sugars' according to the 2019 announcement by the U.S. Food and Drug Administration (FDA). Unlike zero-calorie sweeteners such as sucralose, erythritol, and stevia, which are classified as food additives, allulose is considered a general food raw material. This distinction allows for more versatile use across various food categories, making it an optimal choice for reducing sugars.

▲Figure 1. Composition in natural sweeteners



▲Figure 2. Allulose: C3 epimer of fructose



▲Table 1. Sweetener comparison chart

	Sweeteners approved as food additives		Plant, fruit based high intensity sweeteners		Natural sugars	Sugar alcohols		
Sweeteners	Sucralose	Aspartame	Steviol glycosides	Monk fruit	**Allulose**	Xylitol	Maltitol	Erythritol
Calories (kcal/g)	0	0	0	0	**0.4**	2.4	2.1	0
Sweetness Intensity (SI)*	600	200	200 ~ 400	100 ~ 250	**0.7**	~1	0.8 ~ 0.9	0.6 ~ 0.7

* SI of sucrose: 1

1 Overall Status

1) Introduction

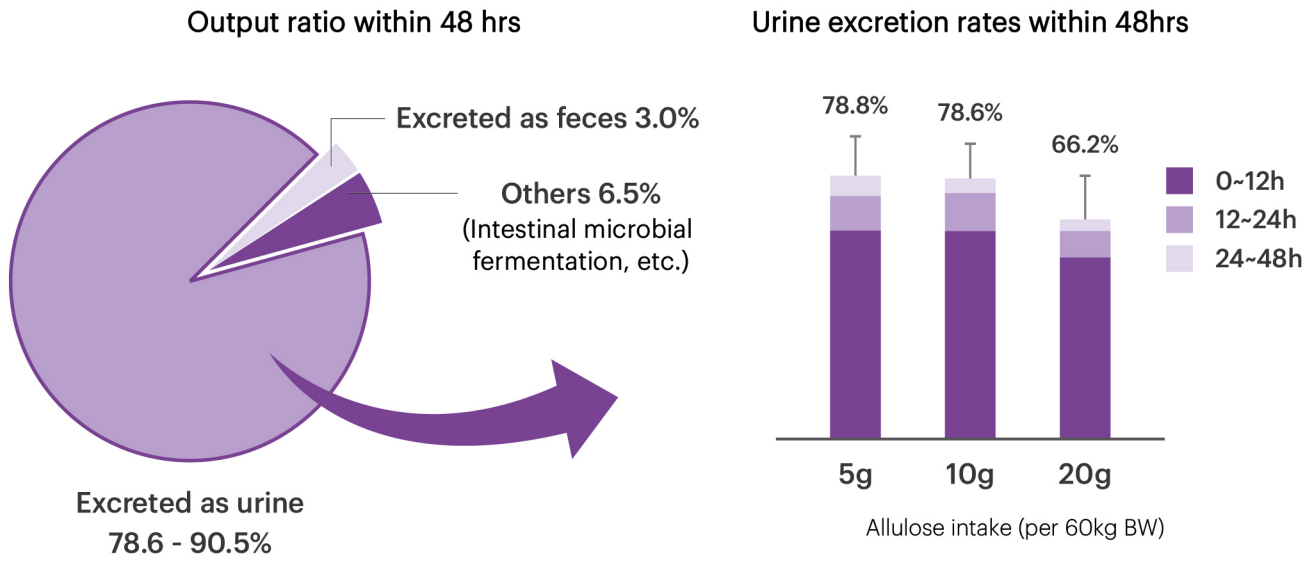
Safety

Allulose, a sugar substitute, received initial FDA approval in 2012 under the designation 'Generally Recognized As Safe (GRAS)' and has been in use for over a decade. Under FDA guidelines, allulose is suitable for consumption by individuals of all ages. In 2018, Samyang obtained GRAS (GRN 828) status from the US FDA for Nexweet® Allulose, produced using the proprietary enzyme technology.

Low-calorie sweetener

Allulose has almost no calories as it is not metabolized during digestion. While approximately 80% of allulose is absorbed in the small intestine, it is not utilized as energy and is excreted through urine. A minor portion of allulose that goes unabsorbed in the small intestine undergoes fermentation by microorganisms in the large intestine, contributing to a caloric value of approximately 0.2 to 0.4 kcal/g. The remaining portion is excreted through feces (Iida et al. 2010).

▲Figure 3. Output after ingestion of Allulose



Iida, Tetsuo et al. "Failure of d-psicose absorbed in the small intestine to metabolize into energy and its low large intestinal fermentability in humans." *Metabolism: clinical and experimental* vol. 59,2 (2010): 206-14. doi:10.1016/j.metabol.2009.07.018
https://doi.org/10.1016/j.metabol.2009.07.018

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1 Overall Status

2) Product Lineup

	Nexweet® Allulose 95L	Nexweet® Crystalline Allulose
Type	Liquid	Crystal
D-Allulose (%, Dry basis) [AOAC 980.13]	≥ 95.0	≥ 99.0
Dry Solids (Brix%) [AOAC 932.14c, 941.14]	68.0 ~ 70.0	≥ 99.0
pH (in 10% solution) [Potentiometric method]	3.0 ~ 7.0	3.0 ~ 7.0

Certifications

FSSC 22000 · HALAL · NON GMO Project VERIFIED nongmoproject.org · HACCP MFDS · KETO CERTIFIED

3) Regulatory Status

- Generally Recognized as Safe Affirmation # 693, #828

4) Labeling

- “Allulose”, “D-Allulose”, “D-Psicose”

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1 Overall Status

5) Nutritional Information

(Per 100g product)

Nutrient	Nexweet® Allulose 95L	Nexweet® Crystalline Allulose
Total Calories	39.4 kcal	40 kcal
Calories from Fat	0 kcal	0 kcal
Total Fat	<0.1 g*	<0.1 g*
Saturated Fat	0 g	0 g
Trans Fat	0 g	0 g
Cholesterol	0 g	0 g
Sodium	0 g	0 g
Total Carbohydrate	73.8 g	99.8 g
Total Sugars	0.8 g	0 g
Added Sugars	0 g	0 g
Dietary Fiber	0 g	0 g
Other Carbohydrate	73.0 g	99.8 g
Protein	<0.1 g*	<0.1 g *
Calcium (Ca)	0 g	0 g
Sodium (Na)	0 g	0 g
Iron (Fe)	0 g	0 g
Potassium	0 g	0 g
Ash	<0.1 g*	<0.1 g *
Vitamin A (as retinol)	0 g	0 g
Vitamin C	0 g	0 g
Vitamin D	0 g	0 g

* Analysis result value means a value less than LOQ or LOD (Limit of Quantification / Detection)

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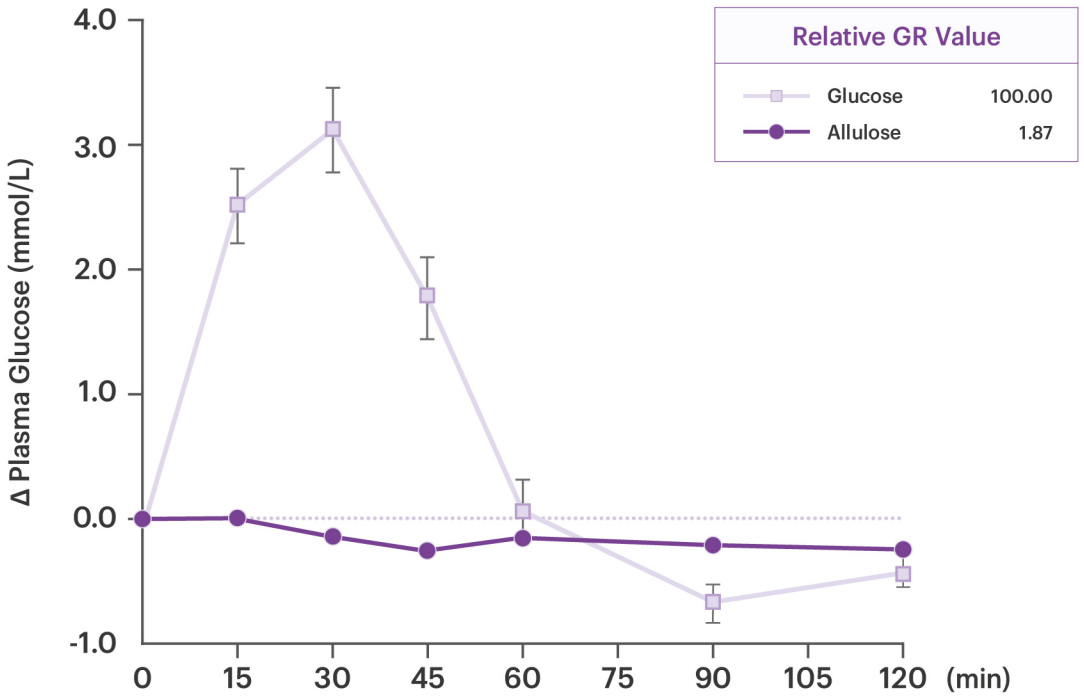
2 Low glycemic response

Nexweet® Allulose shows a low level of glycemic response.

The relative postprandial glycemic response (GR) value was measured using the modified method of ISO 26642:2010. In human (n=10), the GR value is measured after consuming the aqueous solutions containing 25 g of Nexweet® Crystalline Allulose or glucose each. For Nexweet® Crystalline Allulose, the GR value is about 1.87, compared to 100 for reference food (glucose).

▲Figure 4. The average plasma glucose concentration curves after Allulose or glucose intake



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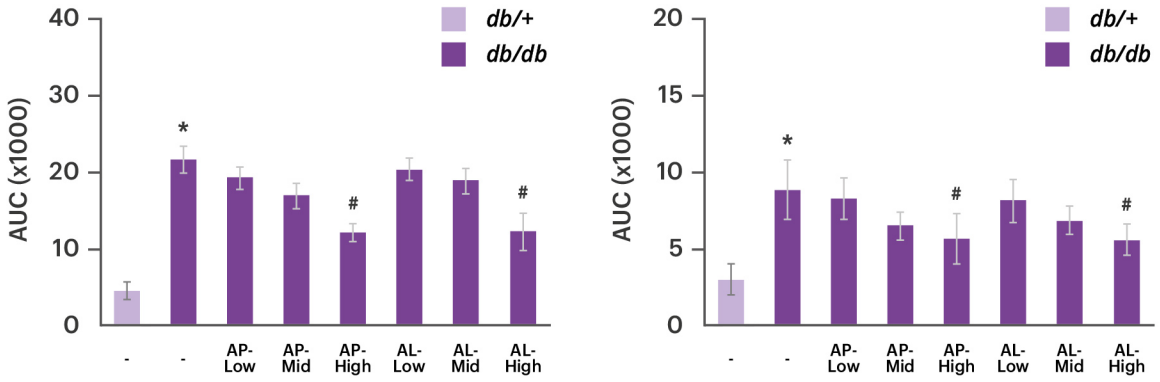
3 Improves glucose metabolism

Nexweet® Allulose has the effect of regulating glucose metabolism.

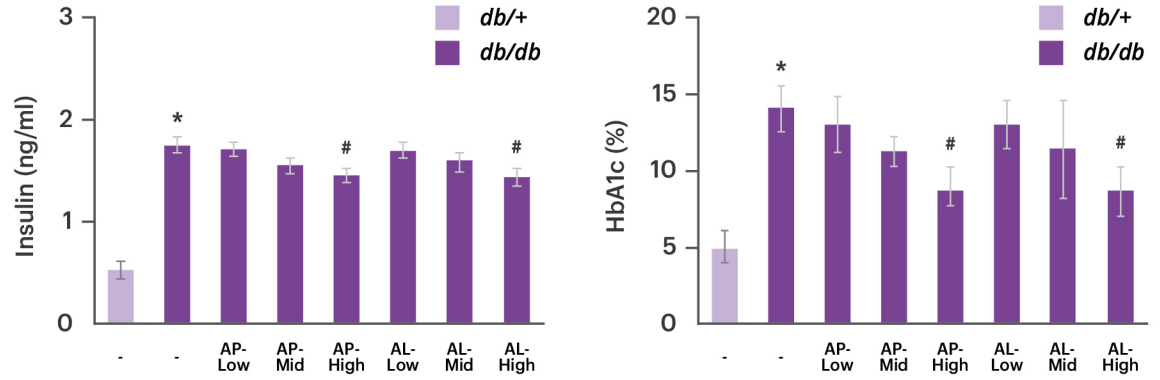
To determine the effect on changes in postprandial blood glucose levels, two types of Nexweet® Allulose samples, liquid (AL) and crystalline powder (AP) type, were orally administered at a daily dose of 1.02 g/kg (low), 3.07 g/kg (mid), and 5.16 g/kg (high) to mice. The oral glucose tolerance test (OGTT) and the insulin tolerance test (ITT) were conducted on diabetic (*db/db*) mice. For the OGTT, 1 g/kg of glucose was orally administered to mice after an overnight fast. Subsequently, blood samples were collected from the tail vein at 0, 15, 30, 45, 60, 90, and 120 minute(s) to measure glucose levels. As a result, there was an improvement in postprandial blood glucose levels in the *db/db* group treated with Nexweet® Allulose, compared to the vehicle-treated group.

▲Figure 5. Effects of Allulose on blood glucose levels (OGTT, ITT)



In a separate experiment, insulin (0.75 IU/kg BW) was administered via intraperitoneal injection after 6 hours of fasting to perform the ITT. As a result, diabetic mice administrated AL or AP exhibited reduced insulin levels and HbA1c scores compared to the vehicle group.

▲ Figure 6. Effects of Allulose on insulin and HbA1c concentrations levels



*$P < 0.05$ versus *db/+*, #$P < 0.05$ versus *db/db*

Lee, H. Y., Lee, G. H., Hoang, T. H., Park, S. A., Lee, J., Lim, J., ... & Chae, H. J. (2022). d-Allulose Ameliorates Hyperglycemia Through IRE1α Sulfonation-RIDD-Sirt1 Decay Axis in the Skeletal Muscle. *Antioxidants & Redox Signaling*, *37*(4-6), 229-245. https://doi.org/10.1089/ars.2021.0207

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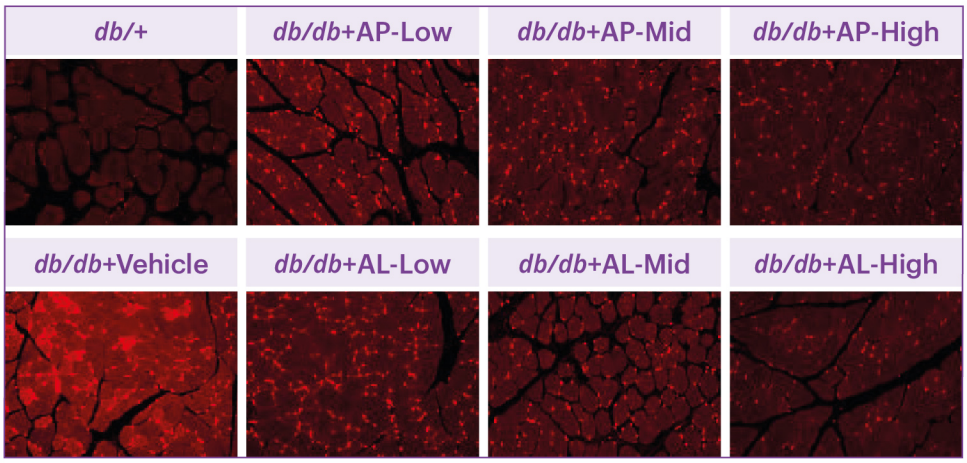
4 Controls oxidation states

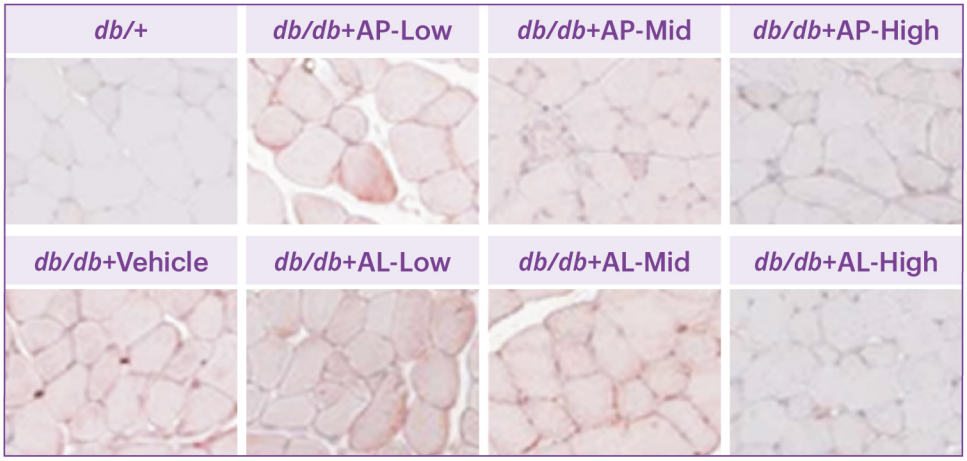
Nexweet® Allulose controls oxidative stress and ER redox balance in skeletal muscle cells under hyperglycemic conditions.

In diabetic patients, high glucose level is associated with increased reactive oxygen species (ROS) production. It causes oxidative stress, eventually leading to several cellular damages, such as the apoptosis of β-cells. The ROS level in the skeletal muscles of diabetic mice (diabetic *db/db* mice) was higher than that in non-diabetic mice. When Nexweet® Allulose (liquid [AL] or crystalline powder [AP]) was administered to diabetic mice, the ROS level is alleviated. ROS generation related to glucose metabolism is influenced by the conversion of NADPH to NADP+. The ratio of NADP+/NADPH decreased upon Nexweet® Allulose administration, leading to reduced NADPH oxidase (Nox) activity and decreased Nox4 expression.

▲Figure 7. Representative DHE-stained images depicting ROS production



▲Figure 8. Representative images of Nox4 staining in tibialis anterior muscle



Volpe, C. M. O., Villar-Delfino, P. H., Dos Anjos, P. M. F., & Nogueira-Machado, J. A. (2018). Cellular death, reactive oxygen species (ROS) and diabetic complications. *Cell death & disease*, *9*(2), 119. https://doi.org/10.1038/s41419-017-0135-z
Lee, H. Y., Lee, G. H., Hoang, T. H., Park, S. A., Lee, J., Lim, J., ... & Chae, H. J. (2022). d-Allulose Ameliorates Hyperglycemia Through IRE1α Sulfonation-RIDD-Sirt1 Decay Axis in the Skeletal Muscle. *Antioxidants & Redox Signaling*, *37*(4-6), 229-245. https://doi.org/10.1089/ars.2021.0207

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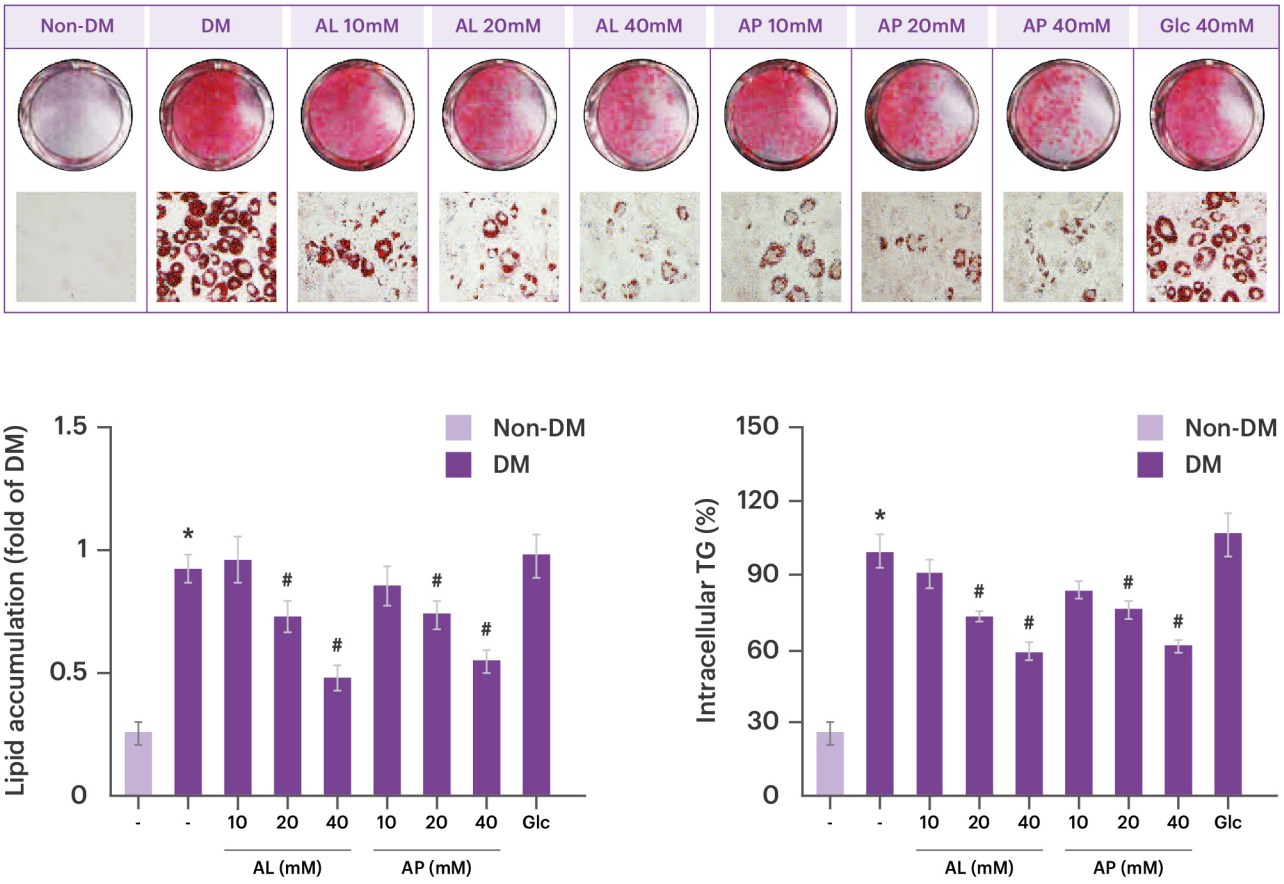
5 Ameliorates adiposity

Nexweet® Allulose modulates the lipid accumulation and intracellular triglyceride levels in 3T3-L1 adipocytes.

To investigate the anti-adipogenic effect, *in vitro* Oil red O (ORO) staining was performed using 3T3-L1 preadipocytes. When Nexweet® Allulose (liquid [AL] or crystalline [AP]) was treated in a test group with the differentiated medium (DM), lipid accumulation was significantly reduced in a dose-dependent manner against the DM-only group. On the other hand, when glucose was treated instead of Nexweet® Allulose, there was no improvement in lipid accumulation. In addition, the high-concentration Nexweet® Allulose treatment group showed a significant reduction in intracellular triglyceride (TG) levels compared to the other groups.

▲Figure 9. Lipid accumulation and intracellular TG content in differentiated 3T3-L1 adipocytes



*$P < 0.05$ versus Non-DM, #$P < 0.05$ versus DM

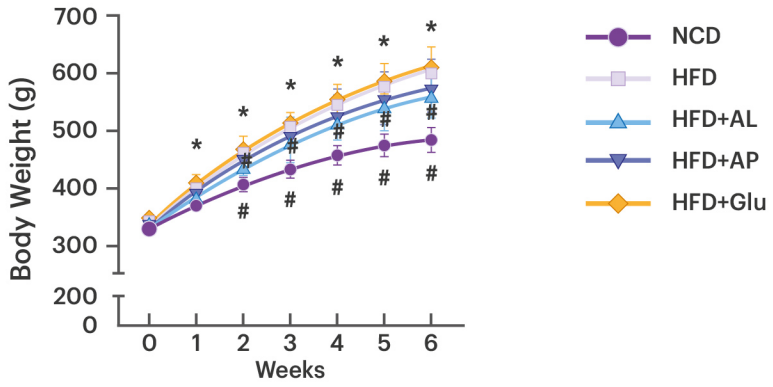
Lee, G. H., Peng, C., Lee, H. Y., Park, S. A., Hoang, T. H., Kim, J. H., ... & Chae, H. J. (2021). D-allulose ameliorates adiposity through the AMPK-SIRT1-PGC-1α pathway in HFD-induced SD rats. *Food & Nutrition Research, 65.* https://doi.org/10.29219/fnr.v65.7803

5 Ameliorates adiposity

Nexweet® Allulose alleviates weight gain.

Nexweet® Allulose was administered to SD rats at a daily dose of 0.4 g/kg fed with a high-fat diet (HFD) to evaluate its efficacy in inhibiting fat accumulation. In the tests, Weight loss was observed in the Nexweet® Allulose-fed group compared to the group that only fed HFD. Since there was no difference in total food intake between each experimental group, it means that Nexweet® Allulose alleviates the rate of weight gain.

▲Figure 10. Effects of Allulose on changes in body weights



When biochemical parameters in serum were analyzed in each test group, Nexweet® Allulose showed a decrease in ALT and AST, which increased when HFD was supplied. In addition, the levels of triglyceride, total cholesterol, and LDL-cholesterol were alleviated. Hormones that secreted by adipocytes were also affected by HFD. Leptin is a hormone related to regulate energy balance, while adiponectin is a hormone that plays a role in improving insulin resistance. In general, leptin is known to help weight control homeostasis through regulating appetite, but in obesity, the level of leptin in plasma is high due to leptin resistance. Therefore, leptin levels are high and adiponectin levels are low in obesity. However, when Nexweet® Allulose was administered with HFD, it was confirmed that the levels of leptin and adiponectin were improved.

▲Table 2. Effects of Allulose on the serum levels of biochemicals parameters in HFD-induced SD rats

Biochemical parameters	NCD	HFD	HFD+AL	HFD+AP
ALT (IU/L)	8.81 ± 0.38	42.24 ± 1.08 *	26.43 ± 0.78 #	22.79 ± 0.94 #
AST (IU/L)	8.78 ± 0.36	45.15 ± 1.43 *	32.1 ± 0.85 #	30.27 ± 1.05 #
Triglyceride (mg/dL)	40.47 ± 2.08	67.47 ± 3.42 *	49.25 ± 3.17 #	54.62 ± 3.91 #
Total-cholesterol (mg/dL)	83.51 ± 1.62	106.07 ± 3.71 *	76.34 ± 2.46 #	79.95 ± 3.05 #
LDL-cholesterol (mg/dL)	30.74 ± 1.39	44.54 ± 1.60 *	31.00 ± 0.97 #	27.47 ± 2.06 #
Leptin (ng/mL)	27.29 ± 0.99	39.27 ± 1.54 *	32.59 ± 1.72 #	31.43 ± 1.47 #
Adiponectin (μg/mL)	7.07 ± 0.27	4.10 ± 0.27 *	6.19 ± 0.28 #	6.42 ± 0.18 #

Results are means ± SEM, $^{*}P < 0.05$ versus NCD-group, $^{\#}P < 0.05$ versus HFD-group. NCD, Normal chow diet; HFD, High fat diet.

Lee, G. H., Peng, C., Lee, H. Y., Park, S. A., Hoang, T. H., Kim, J. H., ... & Chae, H. J. (2021). D-allulose ameliorates adiposity through the AMPK-SIRT1-PGC-1α pathway in HFD-induced SD rats. *Food & Nutrition Research, 65*. https://doi.org/10.29219/fnr.v65.7803

Kim, S. E., Kim, S. J., Kim, H. J., & Sung, M. K. (2017). D-Psicose, a sugar substitute, suppresses body fat deposition by altering networks of inflammatory response and lipid metabolism in C57BL/6J-ob/ob mice. *Journal of Functional Foods, 28*, 265-274. https://doi.org/10.1016/j.jff.2016.11.029

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5 Ameliorates adiposity

Nexweet® Allulose inhibits fat accumulation.

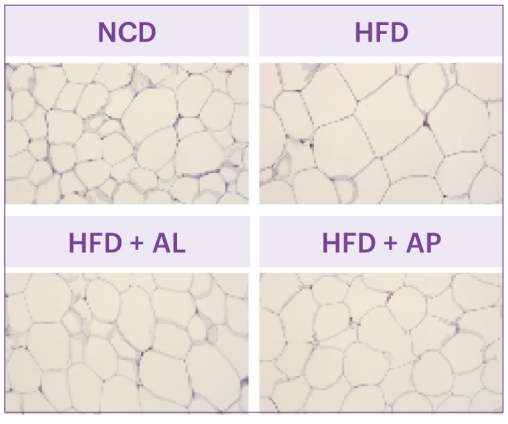
In addition, the amounts of white adipose tissue (WAT) in each adipose tissue were measured. WAT accumulates lipids, and the amount of WAT is associated with visceral adiposity. WAT increased significantly in each adipose tissue (abdominal, epididymal, and perirenal fat). On the other hand, it was shown to be significantly reduced in abdominal and epididymal fat in the group administered with Nexweet® Allulose, and decreased in perirenal fat, but there was no statistical significance. Epididymal fat is a typical visceral fat tissue and is a widely used indicator to analyze the relationship between adipose tissue and obesity. The size of the adipocytes increased in the HFD and the HFD + glucose intake group. On the other hand, it was shown that the size of adipocytes decreased in the group fed AL or AP.

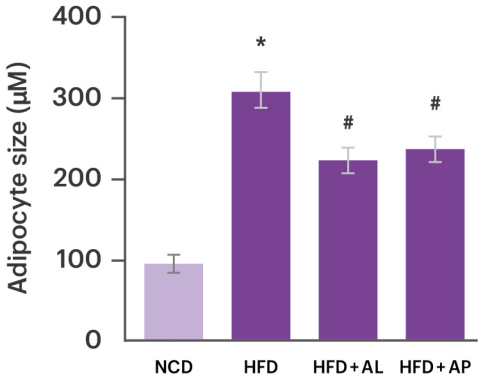
▲Table 3. Effects of Allulose on WAT weight distribution in HFD-induced SD rats

White adipose tissue	NCD	HFD	HFD+AL	HFD+AP
Abdominal fat (g)	11.56 ± 0.84	23.35 ± 0.95 *	17.45 ± 0.67 #	18.41 ± 0.93 #
Epididymal fat (g)	7.62 ± 0.65	17.90 ± 0.82 *	13.40 ± 0.54 #	13.54 ± 0.79 #
Perirenal fat (g)	3.57 ± 0.24	6.33 ± 0.45 *	5.43 ± 0.38	6.17 ± 0.53
Total fat (g)	22.75 ± 1.45	47.57 ± 2.00 *	36.28 ± 1.10 #	38.12 ± 1.89 #

Results are means ± SEM, $^{*}P < 0.05$ versus NCD-group, $^{\#}P < 0.05$ versus HFD-group. NCD, Normal chow diet; HFD, High fat diet.

▲Figrure 11. The morphology of epididymal WAT and the average diameter of adipocytes





$^{*}P<0.05$ versus NCD-group, $^{\#}P<0.05$ versus HFD-group

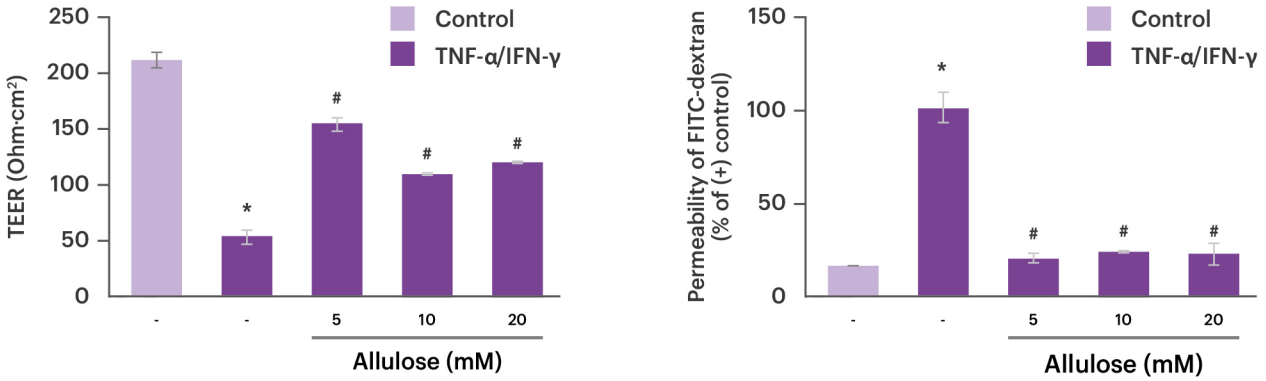
Lee, G. H., Peng, C., Lee, H. Y., Park, S. A., Hoang, T. H., Kim, J. H., ... & Chae, H. J. (2021). D-allulose ameliorates adiposity through the AMPK-SIRT1-PGC-1α pathway in HFD-induced SD rats. *Food & Nutrition Research, 65*. https://doi.org/10.29219/fnr.v65.7803

6 Improves epithelial barrier function

Nexweet® Allulose enhances the tight junctions between intestinal epithelial cells.

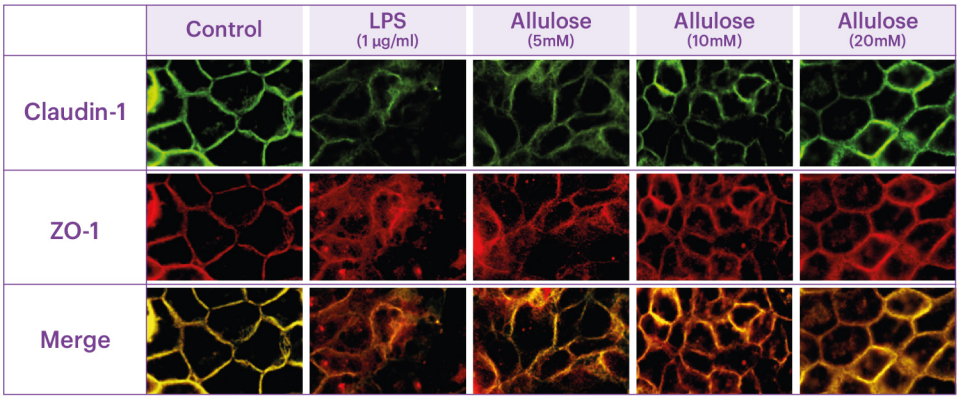
To confirm extracellular permeability, transepithelial electrical resistance (TEER) and fluorescein isothiocyanate (FITC) - dextran permeability assay were conducted. When Caco-2 cells were exposed to TNFα/IFN-γ, TEER decreased, and paracellular dextran flux increased. However, when Nexweet® Allulose was treated simultaneously, it was observed that TEER increased, and the permeability of FITC-dextran decreased. The reinforcement of the intercellular barrier entails the participation of tight junction (TJ) proteins (ZO-1, occludin, claudin-1) that establish connections between cells. Upon treatment of Caco-2 cells with LPS, there was a reduction in the levels of TJ proteins. On the other hand, Nexweet® Allulose treatment resulted in an observed increase in the mRNA expression levels of TJ proteins, which had been reduced by LPS. Consequently, it was confirmed that the intercellular TJ proteins in Caco-2 cells were restored through Nexweet® Allulose treatment, thereby reinforcing the epithelial barrier function.

▲Figure 12. Effects of Allulose on epithelial permeability (TEER and FITC-dextran fluorescence)



*$P < 0.05$ versus Control, #$P < 0.05$ versus TNF-α/IFN-γ-treated group.

▲Figure 13. Effects of Allulose on claudin-1 and ZO-1 identification, and co-localization in Caco-2 cells



Baek, J., Kim, J. H., Nam, Y., Kim, G. E., Ryu, K., Sa, S., ... & Kim, W. (2023). Allulose enhances epithelial barrier function by tight junction regulation via the TLR4/MyD88/NF-κB immune signaling pathway in an intestinal Caco-2 cell model. *Journal of Functional Foods, 108*, 105721. https://doi.org/10.1016/j.jff.2023.105721

7 Cariogenic potential

Allulose has non-cariogenic characteristics.

Three studies of the non-cariogenic effect of allulose are described in the FDA Memorandum.
In the first study, three subjects were tested using 10% allulose and sucrose solutions for plaque that was created 3, 4, 5, and 7 days later. The mouth was rinsed for 2 minutes for each sample, and after resting for 30 minutes, paraffin was chewed to obtain plaque, and the pH was measured. When comparing the pH change of the plaque for the two samples, the allulose group did not drop below pH 5.7, while the 10% sucrose group showed a pH drop below 5.0. The results suggest that allulose maintains the pH of the tooth plaque, showing non-infectiousness, and can help with dental health compared to sucrose.

In another clinical study conducted on seven subjects who had experienced dental caries in the past year, the test was conducted using samples of a 4.7% allulose solution, a sucrose solution, and water (as negative control). After each sample was held in the mouth for 1 minute, pH changes were measured in 8 areas of 6 teeth for 60 minutes. The pH of the allulose test group was 6.43 ± 0.12, which was not significantly different from that of the negative control group, but there was a significant difference of 5.42 ± 0.11 from sucrose.

Last, the pH change and OD value of the medium inoculated with *Streptococcus mutans*, a bacteria known to cause cavities, were measured. 1% allulose, glucose, and sucrose were added to the phenol red broth medium inoculated with *S. mutans* MT8148 strain and compared. A non-treated group was used as a control. The pH of the final medium was measured to be 5.9 for allulose, 3.9 for glucose and sucrose, and 5.9 for control. The OD value was measured as 0.02 for allulose, while 0.26 for glucose, and 0.14 for sucrose. Therefore, allulose was found to have higher pH and lower bacterial growth compared to glucose or sucrose-added media.

Therefore, allulose can be said to have a non-cariogenic effect of inhibiting the growth of cavity-inducing bacteria and suppressing dental caries by maintaining a high level of pH in the oral cavity.

Moura, F. (2019). *FDA Memo to the File_Scientific Review for Allulose Re: The Declaration of Allulose and Calories from Allulose on Nutrition and Supplement Facts Labels: Guidance for Industry Draft Guidance* (FDA-2019-D-0725-0012). Food and Drug Administration. https://www.regulations.gov/document/FDA-2019-D-0725-0012

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