AMICOGEN
HEALTHCARE & NUTRITION

Section
03

SAFETY & STABILITY

DCI

D-chiro-inositol

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✓ DCI Specification

Test item	Specification	Method for determination
Appearance	Whitish powder	Sensory test
Content (purity)	Maximum 95%	HPLC
Other sugars	Maximum 5.0%	HPLC
Loss on drying	Maximum 5.0%	Drying (105°C, 4hr)
Residue on ignition	Maximum 5.0%	Electric furnace (550°C, Over night)
Particle size	40 mesh Minimum 100%	mesh
	60 mesh Minimum 100%	Mesh
	80 mesh Minimum 90%	Mesh
Bulk density	Minimum 0.50 g/ml	Bulk density volumeter method
Tapped density	Minimum 0.85 g/ml	Tap density volumeter method

Arsenic	**Maximum 3.0 ppm**	**ICP**
Lead	Maximum 3.0 ppm	ICP
Cadmium	Maximum 1.0 ppm	ICP
Mercury	Maximum 0.1 ppm	Mercury Analyzer
Coli-form bacteria	Negative	BGLB meyhod
Salmonella	Negative	RV, TT Broth method
E.Coli	Negative	EC method
Yeasts & Molds	Maximum 100 CFU/g	SPC method (PDA)
Total microbial count	Maximum 1,000 CFU/g	SPC method (PDA)

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✓ DCI Safety

Acute oral toxicity test

JFRL

No. 16100620001-0301
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Acute Oral Toxicity Test in Rats

Abstract
The test sample, D-chiro-inositol, was tested for acute oral toxicity in male and female rats. The test sample was orally administered to animals at a single dose of 2000 mg/kg b.w. (body weight), and they were observed for 14 days. As a result, the test sample caused neither abnormalities nor death in any of the rats during the observation period. Consequently, the LD50 value (single dose, oral administration) of the test sample is considered to be more than 2000 mg/kg b.w. in male and female rats.

Bacterial reverse mutation test

JFRL

No. 16100620001-0401
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Bacterial Reverse Mutation Test

Abstract
The test sample, D-chiro-inositol, was examined for its mutagenic activity in bacterial reverse mutation test using four strains of *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, and *Escherichia coli* WP2*uvrA* according to *Iyakushin* No. 1604 (Ministry of Health, Labour and Welfare, November 1, 1999) and *Yakushokushinsahatsu* No. 0920-2 (Ministry of Health, Labour and Welfare, September 20, 2012). The test sample was assayed at the doses ranging from 313 to 5000 μg/plate. As a result, no significant increase in the number of revertant colonies was observed. Consequently, the test sample is considered to be non-mutagenic under the experimental conditions of this study.

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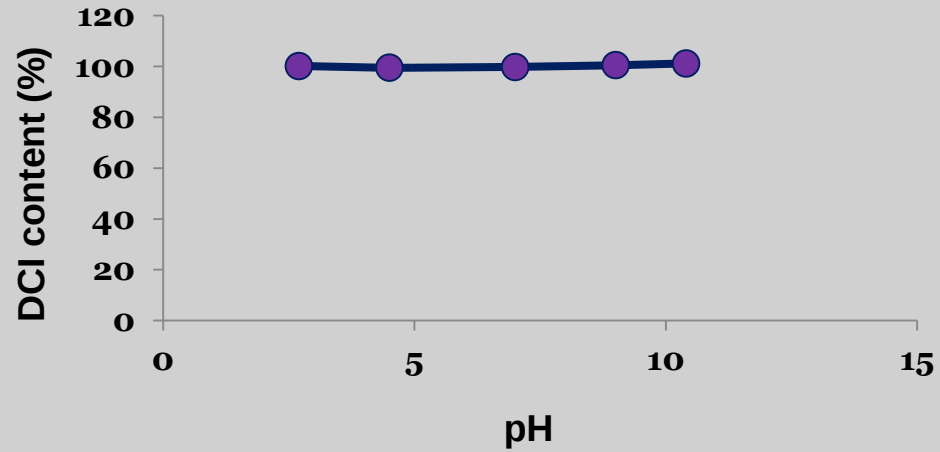
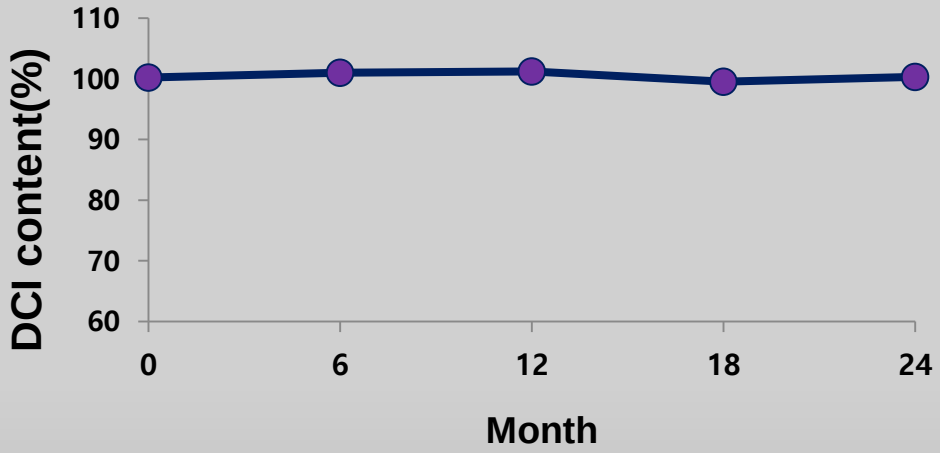
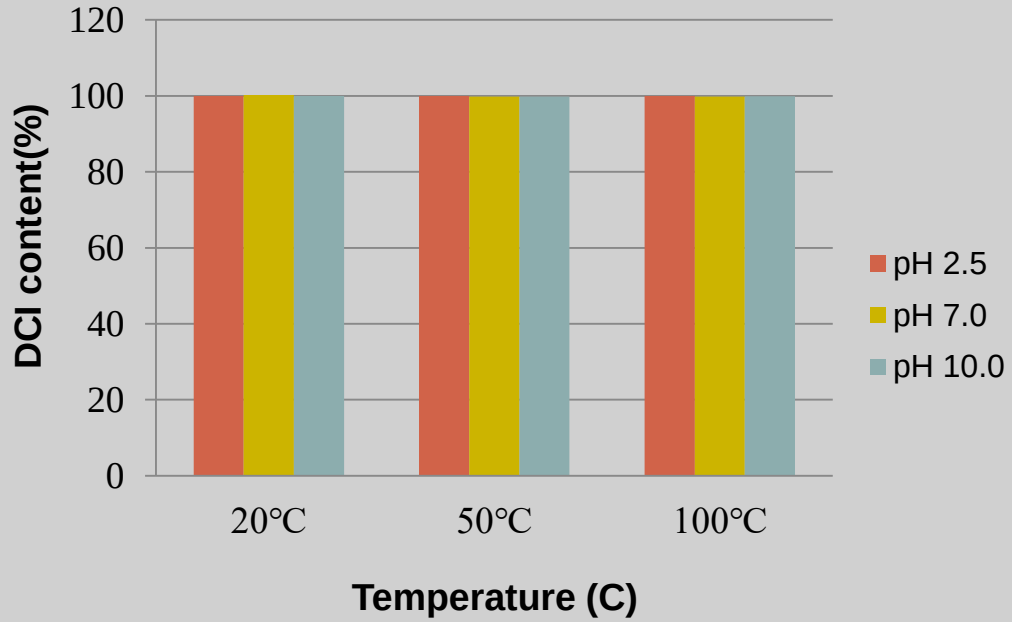
✓ DCI Stability







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✓ DCI Reference Daily Intake (RDI) based on the clinical references

1. RDI for PCOS patients

- DCI 500 ~ 1,500mg/day

2. RDI for gestational diabetes

- DCI 1,000 mg/day

3. RDI for infertile patients

- DCI 27.6 ~ 300 mg/day

4. RDI for type 2 diabetes patients

- DCI 27.6 ~ 1,200 mg/day

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✓ DCI Reference Daily Intake (RDI) based on the clinical references

No.	Category	Intake (mg/day)	References
1	PCOS	500 mg	1. Artini PG et al., Effect of d-chiro-inositol and alpha-lipoic acid combination on COH outcomes in overweight/obese PCOS women, Gynecol Endocrinol. 2020, 36(9):755-759 2. Genazzani AD et al., Modulatory role of D-chiro-inositol (DCI) on LH and insulin secretion in obese PCOS patients, Gynecol Endocrinol., 2014, 30(6):438-43. 3. Piomboni P et al., Protein modification as oxidative stress marker in follicular fluid from women with polycystic ovary syndrome: the effect of inostiol and metformin, J Assist Reprod Genet. 2014, 31(10):1269-76.
2		1,000 mg	1. Laganà AS et al., Evaluation of ovarian function and metabolic factors in women affected by polycystic ovary syndrome after treatment with D-Chiro-Inositol, Arch Gynecol Obstet., 2015, 291(5):1181-6. 2. Cianci A et al., D-chiro-Inositol and alpha lipoic acid treatment of metabolic and menses disorders in women with PCOS, Gynecol Endocrinol., 2015, 31(6):483-6.
3		1,000 ~ 1,500 mg	1. Marca A La et al., he menstrual cycle regularization following D-chiro-inositol treatment in PCOS women: a retrospective study, Gynecol Endocrinol., 2015, 31(1):52-6.

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✓ DCI Reference Daily Intake (RDI) based on the clinical references

No.	Category	Intake	References
4	Gestational diabetes	250 mg	1. Dell'Edera D et al., The influence of D- chiro-inositol and D- myo-inositol in pregnant women with glucose intolerance, Biomed Rep., 2017, 7(2):169-172.
5		500 mg	1. Celentano C et al., The influence of different inositol stereoisomers supplementation in pregnancy on maternal gestational diabetes mellitus and fetal outcomes in high-risk patients: a randomized controlled trial, J Matern Fetal Neonatal Med. 2020, 33(5):743-751.
6		1,000 mg	1. Biase ND et al., The effectiveness of d-chiro inositol treatment in gestational diabetes, Diabetes Case Rep., 2017, 2:3.
7	Type 2 diabetes	27.6 mg	1. Pintaudi B et al., The Effectiveness of Myo-Inositol and D-Chiro Inositol Treatment in Type 2 Diabetes, Int J Endocrino. 2016;9132052.
8		1,200 mg	1. Ku BJ et al., The clinical study to evaluate the safety and efficacy of D-chiro-inositol in patients with type 2 diabetes, Korean J Med., 2007, 72(1), 29-36.

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✓ DCI Reference Daily Intake (RDI) based on the clinical references

No.	Category	Intake (mg/day)	References
1	1:3.6	DCI 150mg + MI 550mg	1. Mendoza N et al., Comparison of the effect of two combinations of myo-inositol and D-chiro-inositol in women with polycystic ovary syndrome undergoing ICSI: a randomized controlled trial, Gynecol Endocrinol., 2019, 35, 8, 695-700.
2		DCI 300 mg + MI 1,100mg	1. Mendoza N et al., High dose of D-chiro-inositol improves oocyte quality in women with polycystic ovary syndrome undergoing ICSI: a randomized controlled trial, Gynecol Endocrinol., 2020, 36(5):398-401.
3	1:40	DCI 27.6mg + MI 1100mg	1. E Benelli et al., A combined therapy with myo-inositol and d-chiro-inositol improves endocrine parameters and insulin resistance in PCOS young overweight women, Int J Endocrinol., 2016, 3204083. 2. S Colazingari et al., The combined therapy myo-inositol plus D-chiro-inositol, rather than D-chiro-inositol, is able to improve IVF outcomes: results from a randomized controlled trial, Arch Gynecol Obstet., 2013, 288, 6, 1405-11.