

## Nobiletin + Tangeretin Specifications

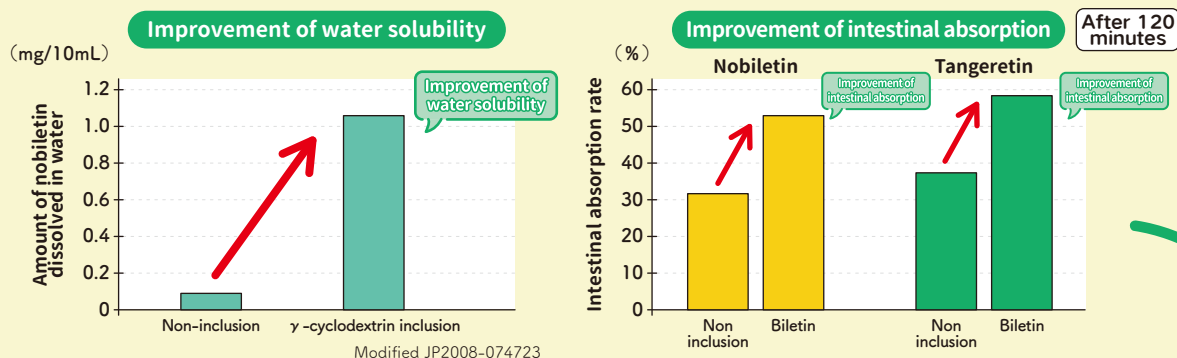
# Biletin



## What is Biletin?

Biletin is a functional material containing standardized amounts of highly concentrated polymethoxyflavonoids (nobiletin and tangeretin), which is extracted from the pericarps of Okinawan shiikuwasha (*Citrus depressa*) that are discarded after being juiced.

**Cyclic oligosaccharide inclusion makes it more soluble in water and improves its absorption in the intestine.**

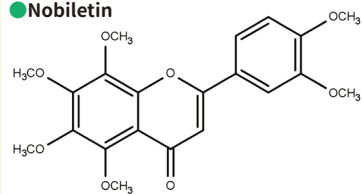


Due to their lipophilicity, nobiletin and tangeretin have the disadvantage that they are not easily absorbed into the body. As such, we have contained the nobiletin and tangeretin within cyclic oligosaccharides (cyclodextrin) inclusion compounds. Thanks to this inclusion, the material has been made easier to dissolve in water, which improves its absorption within the body compared to that of products without this same inclusion.

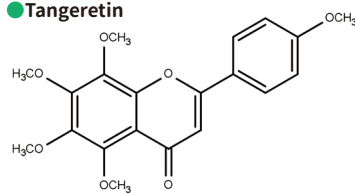


## What are Nobiletin and Tangeretin?

### ● Nobiletin



### ● Tangeretin



Numerous studies on polymethoxyflavonoid (PMF) functionality have shown that, in addition to functions such as increasing adiponectin, improving lipid metabolism, being an anti-inflammatory, an anti-arteriosclerotic, and protecting the skin against ultraviolet rays, PMF also works with the clock gene *Per2* to normalize body rhythms disturbed by age and lifestyle habits and to regulate the body's circadian rhythm, leading to improvements in sleep quality.

## For beverages and jellies



The inclusion with cyclic oligosaccharides improves its solubility, so it can be used for beverages and jellies. This inclusion process also suppresses the unique bitterness of shiikuwasha.

## Effects and Indications

Normalization of the body clock, improvement of liver function, increased adiponectin, inhibitory effect on melanin synthesis (skin-lightening effect), amelioration of allergies, anti-inflammatory effects, anti-metabolic effects, improvement of memory impairment (e.g. dementia)

## Patent and Trademark

- Patent No. 5473191  
Peroxisome proliferator activated receptor (PPAR) activating agent and drugs, supplements, functional foods and food additives that utilize the aforementioned agent.
- Biletin™ is a registered brand by ARKRAY, Inc.

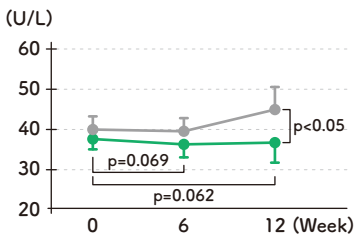


# Liver function

## γ-GTP\*1

### Subgroup

A group of healthy subjects ( $\gamma$ -GTP  $\leq$  80 U/L), with the exclusion of nine subjects classified as "C: Requires re-examination and life improvement" or higher as per the criteria category of the Japanese Society of Ningen Dock



### [Ingesting 20 mg/day as Biletin]

- Placebo group (n = 18)
- Biletin group (n = 16)

mean +/- SEM

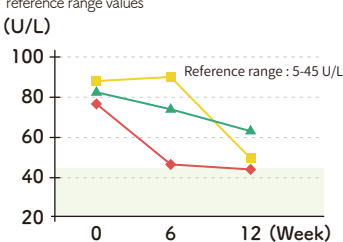
Intragroup: Wilcoxon signed-rank test  
Between groups: Mann-Whitney U test

Compared to the placebo group, the liver function item  $\gamma$ -GTP, AST and ALT improved before and after ingestion.

## ALT\*2

### Subgroup

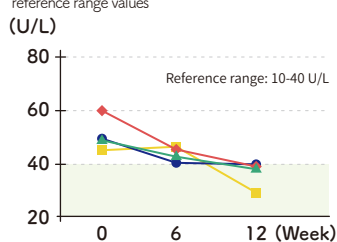
Of the group ingesting 100 mg of the product, three subjects had ALT values that deviated from the reference range values



## AST\*2

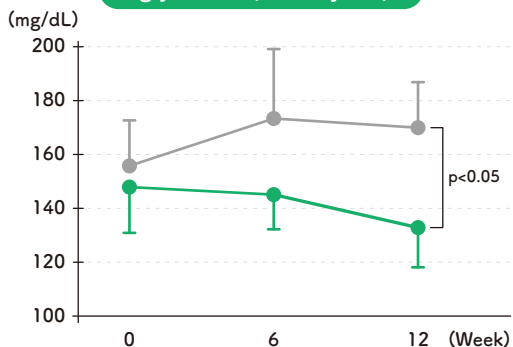
### Subgroup

Of the group ingesting 100 mg of the product, four subjects had AST values that deviated from the reference range values



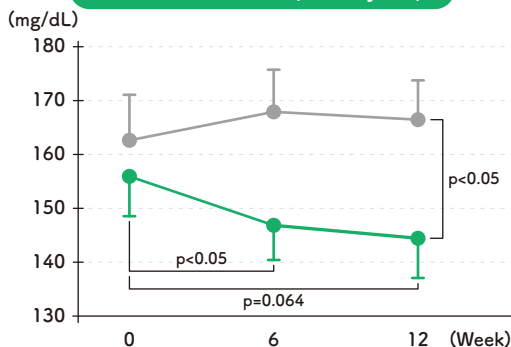
# Lipid Metabolism

## Triglycerides (All Subjects)\*1



Triglycerides significantly decreased in the Biletin group compared to in the placebo group.

## Non-HDL Cholesterol (All Subjects)\*1



Non-HDL cholesterol significantly decreased in the Biletin group compared to in the placebo group.

### [Ingesting 20 mg/day as Biletin]

- Placebo group (n = 22)
- Biletin group (n = 21)

mean +/- SEM

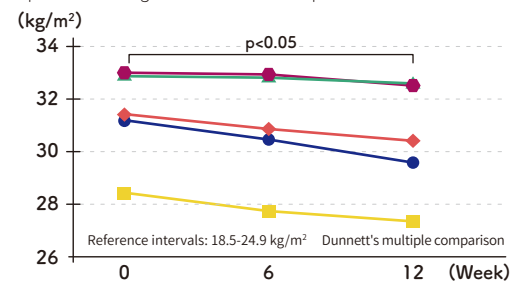
Intragroup: Wilcoxon signed-rank test  
Between groups: Mann-Whitney U test

Double-blind, parallel group, comparative study

## BMI\*2

### Subgroup

Of the group ingesting 20 mg of the product, five subjects were suspected of having nonalcoholic steatohepatitis

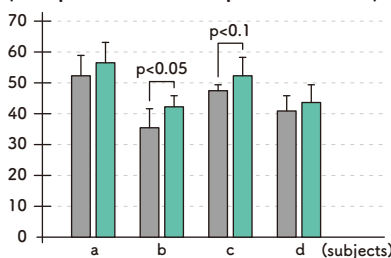


There was a significant reduction in BMI before and after ingestion.

# Quality of Sleep

## Factor II

(Sleep Onset and Sleep Maintenance)



### [Ingesting 20 mg/day as Biletin]

- Placebo foods
- Foods containing Biletin

Subjects: Four male subjects aged 28-41  
Questionnaire: OSA Sleep Inventory (MA version)

Double-blind, crossover, comparative study

Based on the results of the survey, improved quality of sleep can be expected.

## Product Specifications

Properties	Powder, pale-brown to brown in color, with a distinctive smell
Loss on drying	8% or less
PMF (Polymethoxyflavonoids)	10% or higher
*PMF = Sum of nobiletin and tangeretin	
*Content as anhydrides	
Arsenic	2 ppm or less
Heavy metals	20 ppm or less
Total viable count	1,000 cfu/g or less
Fungal count	300 cfu/g or less
Coliforms	Negative

## Storage conditions

Sealed and stored at room temperature

## Product Appearance



## Packing

100 g, 1 kg (GL FILM pack)

## Recommended daily intake

10-45 mg/day (1.0-4.5 mg/day as PMF)

## Ingredients

Extract of shiikuwasha fruit (*Citrus depressa* HAYATA) via hydrous ethanol (this product contains cyclic oligosaccharides).

## Example of Use

Supplement, health foods, etc.

## Example of Labeling

Shiikuwasha extract / cyclic oligosaccharides

## References

\* 1 Hiroshige Kawai, et al. Japanese Pharmacology & Therapeutics, 2021, 49(7), 1123-31.

\* 2 Yoshio Sumida, et al. Associate Journal of Japanese Society for Medical Use of Functional Foods. 2017, 10(6), 345-8.

