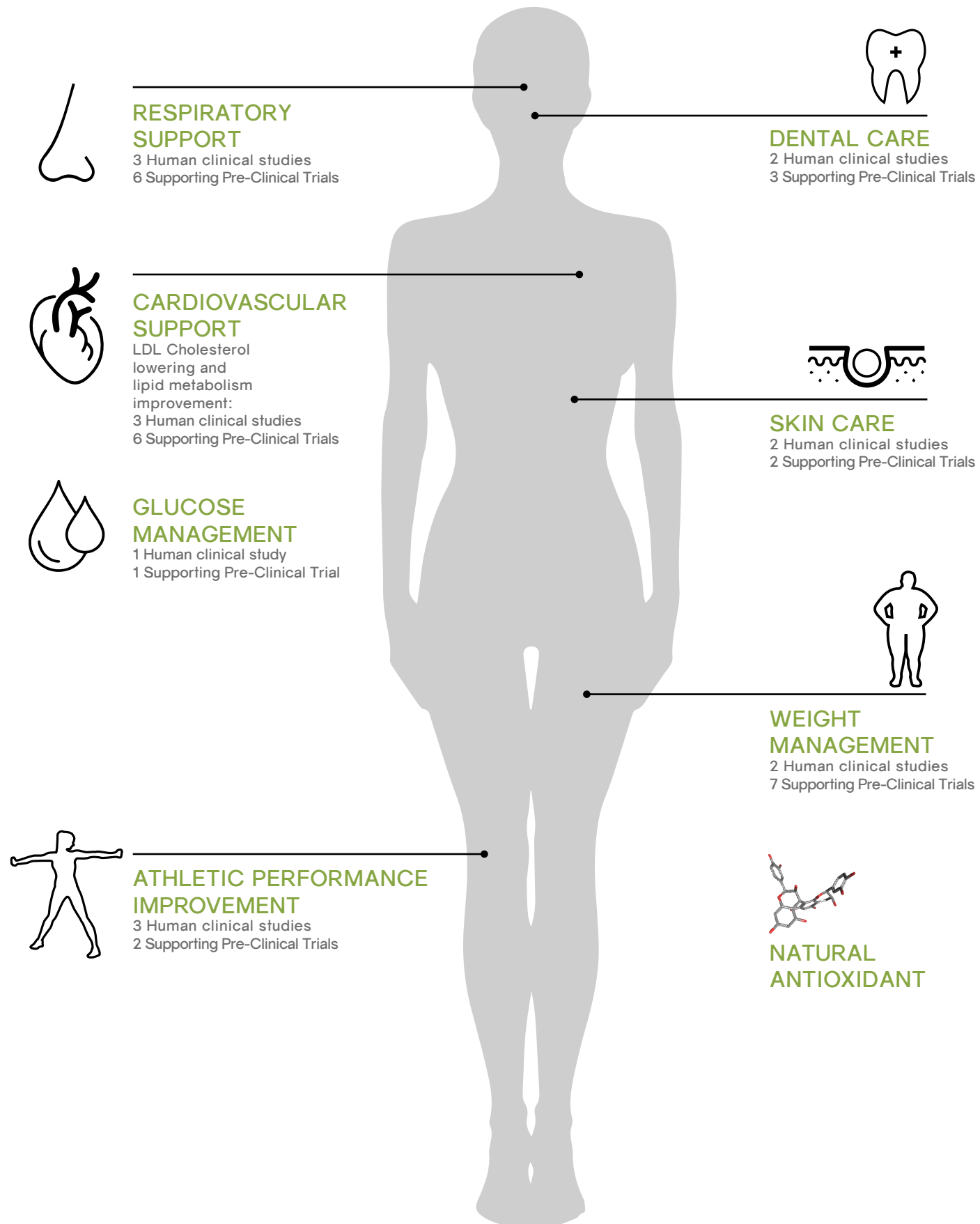




# APPLEPHENON® POLYPHENOLS

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# FROM THE LAND OF THE ORIGINAL APPLE

ApplePhenon® is carefully extracted from specially selected wildcrafted immature green apples from Central Asia, the "Land of the Original Apple." Using a proprietary gentle extraction process, ApplePhenon® from BGG preserves the highest concentration of apple polyphenols, strong antioxidant activity and an optimized profile of proanthocyanidins. Clinical studies have shown that ApplePhenon® plays an effective role in antioxidant, weight, glucose management, dental care, cardiovascular protection, athletic enhancement and allergy support. ApplePhenon® has been GRAS self-affirmed in USA and can be used in all food, beverage and dietary supplement applications.

- **Patented:** Protected by 5 international product, process and use patents
- **Trademarked:** Worldwide trademark registration
- **Researched:** Supported by more than 50 publications
- **Tested:** Clinically validated for 7 different health benefits
- **Safe:** Self-affirmed GRAS in USA
- **Wildcrafted:** Extracted from hand-picked apples from the "Land of the Original Apple"
- **Water Soluble:** Suitable for beverages, cosmetics and dental products
- **Exclusive:** BGG is the worldwide exclusive supplier Ex-Japan
- **Highly Stable:** 36 month shelf life

# ADVANCED PROPRIETARY PROCESS

ApplePhenon® by BGG is a patented, proprietary polyphenol extract produced from wild, unripe apples from the Central Asia region where the species originated. Using a proprietary mild extraction process and advanced purification technology, ApplePhenon® is produced to preserve high concentrations of apple polyphenols, strong antioxidant properties and optimized profile of proanthocyanidins. The starting raw material for producing ApplePhenon® are unripe apples containing at least ten times the level of polyphenols found in ripe apples.

# WHAT IS APPLEPHENON® POLYPHENOLS EXTRACTED FROM WILD UNRIPE APPLES

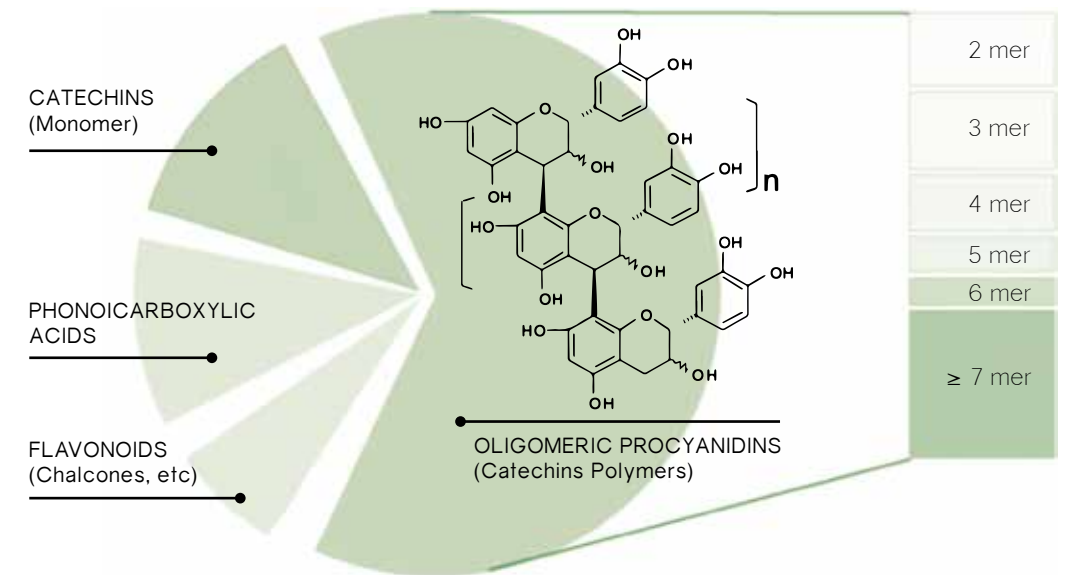


Fig 1. Major flavonoids in ApplePhenon®

# UNIQUE PHYTOCHEMICAL BOUQUET

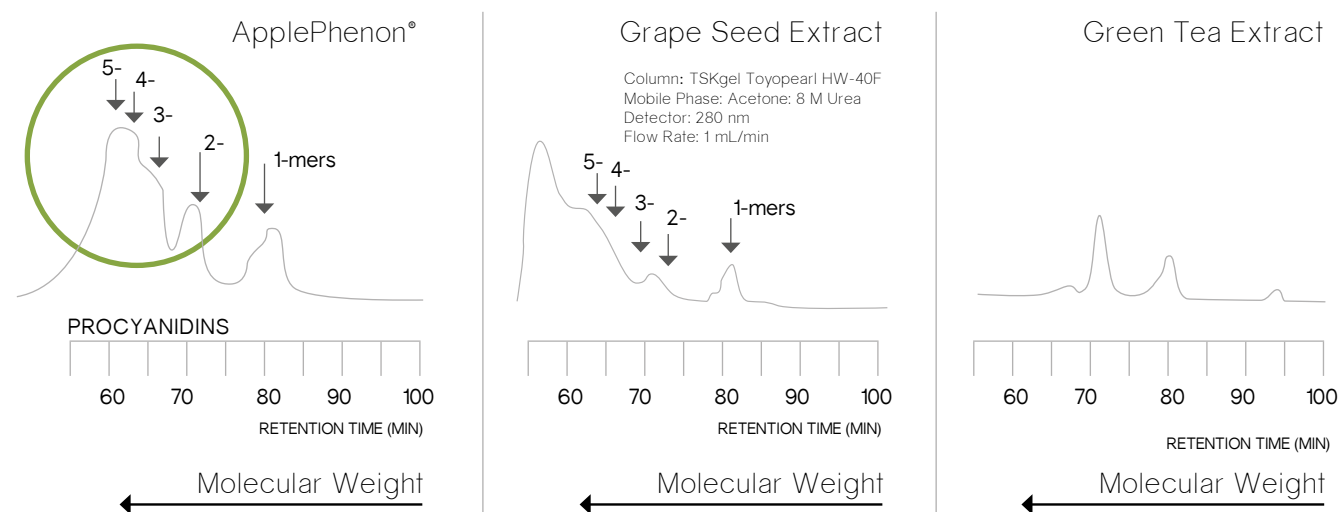
ApplePhenon's active constituents are listed in the table below. ApplePhenon® possesses a unique phytochemical profile, with about 12% of flavanol monomers (catechin and epicatechin) and a high content of oligomeric proanthocyanidins.

Formulation: Components, Residuals, Contaminations	Mean (%)	SD (%)	Test Method	Formulation: Components, Residuals, Contaminations	Mean (%)	SD (%)	Test Method
<b>Principal Components</b>				<b>Flavonoid</b>			
Total Procyanidins	63,8	1,14	Porter method	<b>Flavon-3-ols</b>			
Procyanidin B1 (Dimer)	1,7	0,31	RH-HPLC	Epicatechin	10,5	0,82	RH-HPLC
Procyanidin B2 (Dimer)	9,4	2,14	RH-HPLC	Catechin	2	0,3	RH-HPLC
PB1 + PB2	11,1	2,4	RH-HPLC	SUM	12,4	0,66	
Procyanidin C1 (Trimer)	5	0,68	RH-HPLC	<b>Chalcones</b>			
Procyanidin Dimer	13	2,31	RH-HPLC	Phloridzin	1,9	0,54	RH-HPLC
Procyanidin Trimer	12,3	0,69	RH-HPLC	Phloretin-2'-xyloglucoside	4,6	0,48	RH-HPLC
Procyanidin Tetramer	8,7	0,59	RH-HPLC	SUM	6,5	0,99	
Procyanidin Pentamer	5,9	0,44	RH-HPLC	<b>Phenolcarboxylic acids</b>			
Procyanidin Hexamer	4,9	1,28	RH-HPLC	Chlorogenic acid	8,2	0,91	RH-HPLC
Heptamer + other	20,9	3,12	RH-HPLC	p-Coumaroyl quinic acid	2,6	0,29	RH-HPLC
<b>Other Related Substances</b>				SUM	10,8	0,87	
<b>Total Polyphenols</b>					93,5	2,48	

Table 1. Composition of Polyphenols in ApplePhenon®.

ApplePhenon® has a much higher content of oligomeric proanthocyanidins compared to grape seed extracts. Green tea extracts contain monomer and dimers almost exclusively while grape seed extracts are rich in polymeric proanthocyanadins. This is of paramount import; in a pre-clinical trial, the polymeric procyanidins in ApplePhenon® positively and synergistically promoted the absorption of procyanidin oligomers (which are the only procyanidins that are absorbed by the human body).

## ApplePhenon® – Oligomeric Procyanidins



More than 60% of polyphenols are proanthocyanidins, 70% of which are oligomers between 2-mer to 6-mer

More than 60% of polyphenols are proanthocyanidins, 70% of which are oligomers bigger than 6-mer

About 90% of polyphenols are monomers like catechin and EGCG

Fig 2. Size-exclusion chromatography of ApplePhenon® and other polyphenol products. Yanagida, A.; Shoji, T.; Kanda, et al. *Biotechnol. Biochem.* 2002, Sep; 66(9):1972-5.

# HIGH BIOAVAILABILITY OF APPLEPHENON®

Oligomeric procyanidins in ApplePhenon® are more easily absorbed in blood than other polyphenol products.

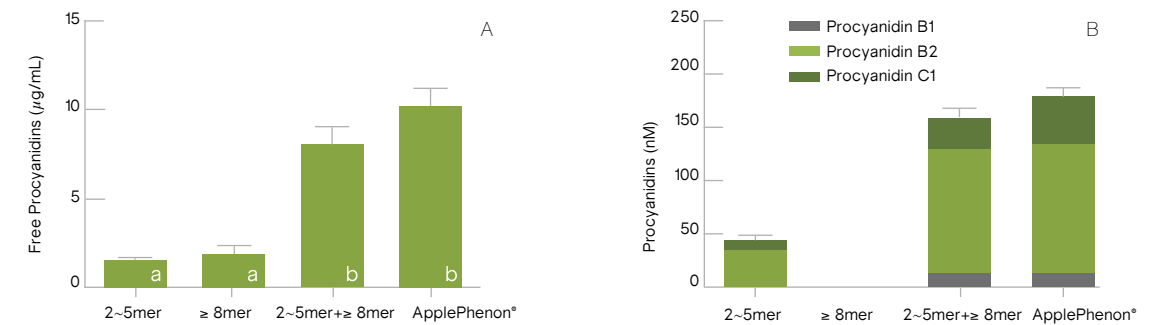
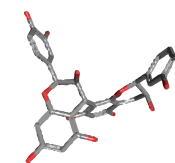


Fig 3. Free non-conjugated procyanidins in rat plasma 2 hours after administration. A\_ Free proanthocyanidins analyzed by Porter method (expressed as procyanidin B2) B\_ Total amounts of procyanidins B1, B2 and C1 by HPLC/MS.

Shoji, T.; Masumoto, S.; Moriichi, N.; et al. *Agric. Food Chem.* 2006, 54, 884-892.



# NATURAL ANTIOXIDANT

The ORAC (Oxygen Radical Absorbance Capacity) value of ApplePhenon® is extremely high in comparison to other polyphenol products.

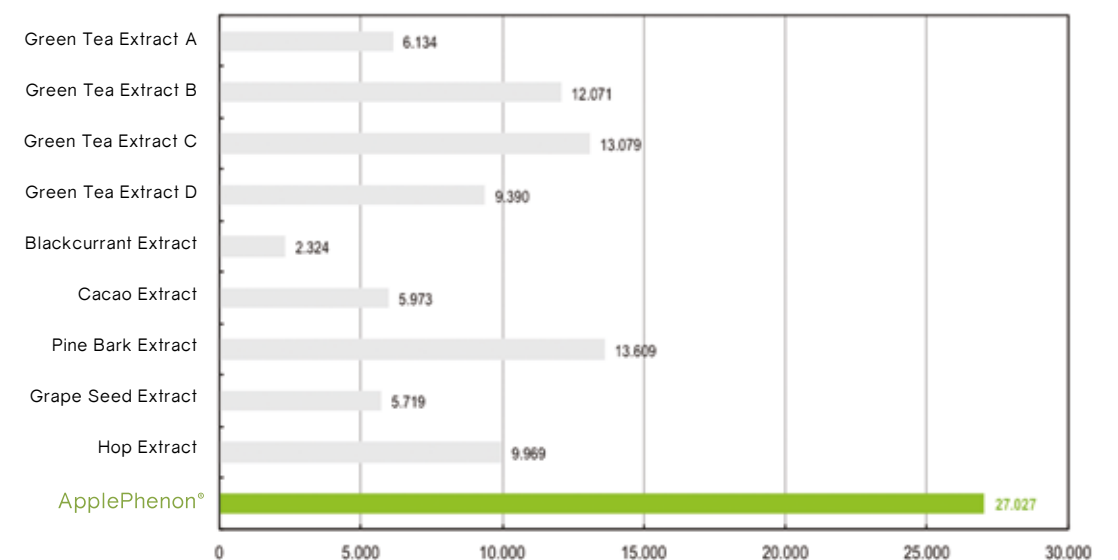
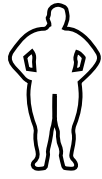


Fig 4. ORAC values of polyphenols (µmolTE/g)





# WEIGHT MANAGEMENT

Pre-clinical studies demonstrated that ApplePhenon® decreases the transcription of genes involved in fatty acid synthesis<sup>1</sup> similarly to a restricted food diet<sup>2</sup>. It may also contribute to suppression of visceral adipose tissue accumulation.

Furthermore, it has been shown that administering apple polyphenols markedly decreases the Firmicutes/Bacteroidetes ratio and increases the proportion of Akkermansia by a factor of eight. This influences the gut microbiota and the intestinal metabolome (which has beneficial effects on metabolic homeostasis)<sup>3</sup>.

Clinically, ApplePhenon® at 600 mg per day has proven effective in decreasing visceral fat within an 8 to 12 week time frame in a randomized, double-blind and placebo controlled study in 94 subjects with BMI 25-30. In addition, in a smaller group of 30 subjects (BMI 18-30) an excessive dose of ApplePhenon® for 4 weeks has been shown to have no deleterious effects<sup>4</sup>.

Similarly, the visceral fat area and the level of adiponectin in the Applephenon® group improved as compared to the control group in a 20 week (4 weeks observation, 12 weeks treatment, 4 weeks follow up) randomized, double-blind, placebo-controlled comparative study<sup>5</sup>.

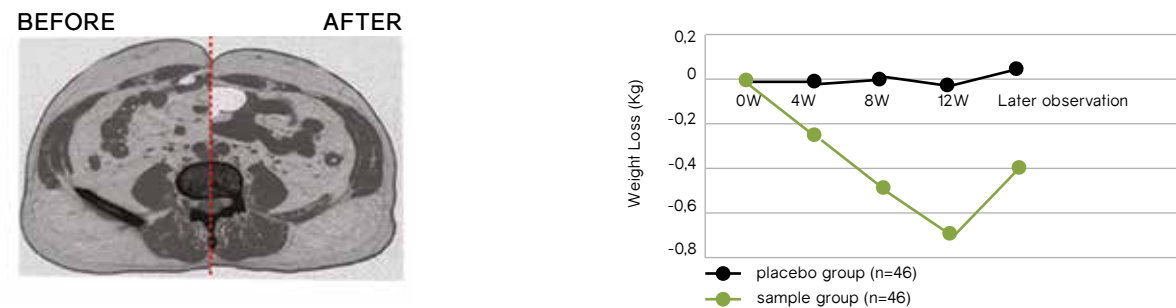


Fig 5. CT images of visceral fat areas (left) and body weight change (right)

- Ohta Y, Sami M, Kanda T, Saito K1, Osada K, Kato H. *Gene Expression Analysis of the Anti-obesity Effect by Apple Polyphenols in Rats Fed a High Fat Diet or a Normal Diet.* *Journal of Oleo Science* Vol. 55 (2006) No. 6 P 305-314
- Saito K, Ohta Y, Sami M, Kanda T, Kato H. *Effect of mild restriction of food intake on gene expression profile in the liver of young rats: reference data for in vivo nutrigenomics study.* *Br J Nutr.* 2010 Oct; 104(7):941-50.
- Masumoto S, Terao A, Yamamoto Y, Mukai T, Miura T, Shoji T. *Non-absorbable apple procyanidins prevent obesity associated with gut microbial and metabolomic changes.* *Sci Rep.* 2016 Aug 10; 6:31208.
- Akazome Y, Kametani N, Kanda T, Shimasaki H, Kobayashi S. *Evaluation of safety of excessive intake and efficacy of long-term intake of beverages containing apple polyphenols.* *J Oleo Sci.* 2010; 59(6):321-38.
- Nagasako-Akazome Y1, Kanda T, Ohtake Y, Shimasaki H, Kobayashi T. *Apple polyphenols influence cholesterol metabolism in healthy subjects with relatively high body mass index.* *J Oleo Sci.* 2007; 56(8):417-28.



# CARDIOVASCULAR SUPPORT

Several clinical studies support the cardiovascular health activity of Applephenon®. In a 4-week pilot study with 48 healthy volunteers with cholesterol levels between 200 and 260 mg/dL, a dose-dependent decrease in total cholesterol and LDL cholesterol and an increase in HDL cholesterol were found at dosages of 300mg, 600mg and 1500mg per day<sup>1</sup>. These results were corroborated in a longer duration study with 71 moderately-overweight subjects (BMI 23 - 30 and total cholesterol averaging 220 mg/dL)<sup>2</sup>. Finally, in a small crossover study on 6 volunteers, ApplePhenon® at 600mg per day was shown to inhibit the absorption of triglycerides from a high-fat diet<sup>3</sup>.

- Nagasako-Akazome Y, Kanda T, Ikeda M, Shimasaki H. *Serum Cholesterol-Lowering Effect of Apple Polyphenols in Healthy Subjects.* *J Oleo Sci.* 2005; 54(3): 143-151.
- Nagasako-Akazome Y, Kanda T, Ohtake Y, Shimasaki H, Kobayashi T. *Apple polyphenols influence cholesterol metabolism in healthy subjects with relatively high body mass index.* *J Oleo Sci.* 2007; 56(8):417-28.
- Sugiyama H, Akazome Y, Shoji T, Yamaguchi A, Yasue M, Kanda T, Ohtake Y. *Oligomeric procyanidins in apple polyphenol are main active components for inhibition of pancreatic lipase and triglyceride absorption.* *J Agric Food Chem.* 2007 May; 30:55(11):4604-9.



# GLUCOSE MANAGEMENT

Recent preclinical studies suggest that chronic administration of ApplePhenon® help maintaining healthy blood sugar metabolism in obese diabetic ob/ob mice.

Furthermore, cohort studies associate fruit consumption with a lower risk of type 2 diabetes mellitus. A double-blind study was done recently on 65 subjects with fasting plasma glucose levels of 100-125mg/dL over 12 weeks. The subjects randomly received 600mg per day of ApplePhenon® tablets or placebo. The treatment group receiving ApplePhenon® experienced a significant reduction in glucose increases at 30-min post 75gm oral glucose tolerance test compared to placebo, suggesting that ApplePhenon® may help maintain to maintain normal range healthy blood sugar levels<sup>1</sup>.

1. Shoji T, Yamada M, Miura T, Nagashima K, Ogura K, Inagaki N, Maeda-Yamamoto M. *Chronic administration of apple polyphenols ameliorates hyperglycaemia in high-normal and borderline subjects: A randomised, placebo-controlled trial.* *Diabetes Res Clin Pract.* 2017 Jul; 129:43-51.



# DENTAL CARE

ApplePhenon® can inhibit glucosyltransferase (GTE) of dental bacteria *Streptococci mutans* and *Porphyromonas gingivalis*, therefore preventing dental plaque formation. A clinical study on twenty 19 - 20 year old women who rinsed their mouths with 10 mL of ApplePhenon® solution (0.5 mg/mL) three to five times a day for three days showed a significant decrease of dental plaque formation. Chewing gum with a low dose of 0.024% ApplePhenon® for five minutes can inhibit the production of methanethiol (MeSH), the main cause of bad breath.



# SKIN CARE

Applephenon® has been evaluated in two clinical studies targeting the skin. In a first pilot study on 24 subjects it has been shown that oral administration of Applephenon® at 10mg/kg may be effective as a complimentary support for skin disorders. A second 3-armed study on 65 female subjects at dosages of 300mg and 600mg per day over 10 weeks showed an obvious skin-whitening effect versus placebo.

Kojima, T., Akiyama, H., Sasai, M. et al. *Allergol Int.* 2000 49(1):69-73.



# RESPIRATORY SUPPORT



Studies have shown that ApplePhenon® can be supportive during allergic rhinitis challenges, as shown in a randomized, double-blind clinical trial on 33 patients with persistent allergic rhinitis. These patients were of various ages from 15 to 65 and had persistent moderate to severe symptoms for a period of at least three years. Patients in the treatment group were given a drink containing ApplePhenon at either a low-dose or high-dose level versus placebo. Results indicated that both the low-dose and high-dose treatment groups experienced significant improvements in sneezing attacks. In addition to improved sneezing attacks, the high-dose group also experienced reduced nasal discharge; and the percentage of people who showed improvement in the swelling of the nasal turbinate was higher in the treatment groups.



# ATHLETIC PERFORMANCE IMPROVEMENT

In a clinical trial study on college athletes, 20 subjects (male and female) randomly took ApplePhenon® (1,200 mg/day), CoQ10 (300 mg/day) and placebo for 8 days (crossover). On day 9, performance was tested through a bicycle ergonomic exercise load measuring pedal speed differences between the first 30 minutes and the last 30 minutes. Compared with the CoQ10 group and the placebo group, the ApplePhenon® group experienced a significant improvement in performance levels.

## Applications

				
DIETARY SUPPLEMENTS	CHEWING GUM	BEVERAGES	COSMETICS	MOUTH WASH, TOOTH PASTE

## Recommended Dosage by Application

USE	DOSAGE (ADULTS)
LDL Cholesterol Decreasing	600 mg/day
Lipid Metabolism Improvement	600 mg/day
Weight Control	600 mg/day
Respiratory support	50 – 200 mg/day
Dental Care	5 mg/3-5 times/day
Skin Care	300 – 600 mg/day
Athletic Performance Improvement	1200 mg/day

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