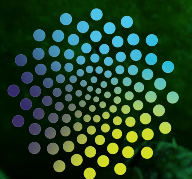




# FEIOLIX<sup>®</sup> SOLUTION

SCIENCE PERFECTED  
IN MARKET<sup>®</sup>

Feioli<sup>®</sup>lix



Anagenix.

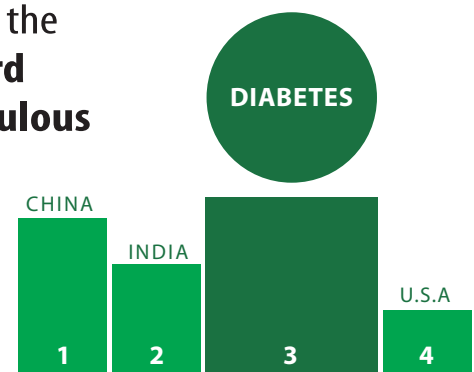
# Diabetes

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Worldwide, the number of adults with **type 2 diabetes** is expected to **rise by more than a fifth** from 406 million in 2018 to 511 million in 2030<sup>1</sup> with **over half living in just three countries:**

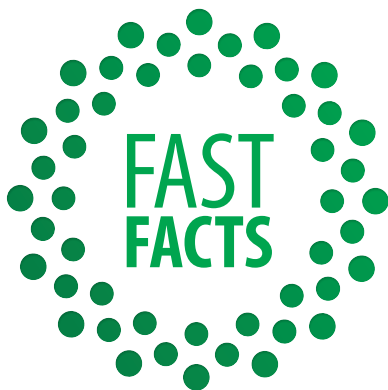
- China (130 million)
- India (98 million)
- USA (32 million)

Diabetes is the **World's 3rd most populous country**



<sup>1</sup> Lancet.2019, 7 (1), 25-33.

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- Diabetes onset **parallels obesity.**
  - Diabetes is an **inflammatory disease.**
  - Type I diabetics don't make **insulin**, the hormone required to control blood sugar.
  - Type II diabetics **lose insulin** production or become **insensitive to insulin.**
  - Blood glucose levels increase
  - Long term complications of uncontrolled blood sugar increases include increased infection susceptibility, limb amputation and blindness.
-



**1 in 11** adults (20-79 years) have diabetes (463 million people)



**1 in 2** adults with diabetes are undiagnosed (232 million people)



**1 in 13** adults (20-79 years) have impaired glucose tolerance (374 million people)



**1 in 5** people with diabetes are above 65 years old (136 million people)



**10%** of global health expenditure is spent on diabetes (USD 760 billion)

Non-GMO super-fruit grown in New Zealand



## FEIOLIX™ concentrate

Reduces  
weight gain

Lowers  
blood  
glucose



The Pre-diabetic Opportunity

Hydrosylable  
tannins

Xyloglucans

Absciscic  
acid



From feijoa fruit

## FeioliX®



To control blood glucose  
+ reduce weight gain



# About Feijoas

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## Feijoa plant

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### Name

Feijoa, Acca sellowiana aka pineapple guava, guavasteen, New Zealand banana.

### Family

Myrtaceae, which includes guava, clove and eucalyptus.

### General description

Evergreen, perennial shrub, red flowers in spring, green on the upper surface of leaves and silvery grey underneath.



## Feijoa fruit

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- Fruit is small, green and egg-shaped, about the size of a chicken egg.
- Juicy flesh divided into a clear gelatinous seed pulp and a firmer, slightly granular, opaque flesh nearer the skin.
- Skin texture is rough, close to that of a pear or guava.

### Aromatics

Distinctive, potent smell and sweet, aromatic flavour - mix of pineapple, banana, mint, strawberry and guava flavours.



# About Feijoas

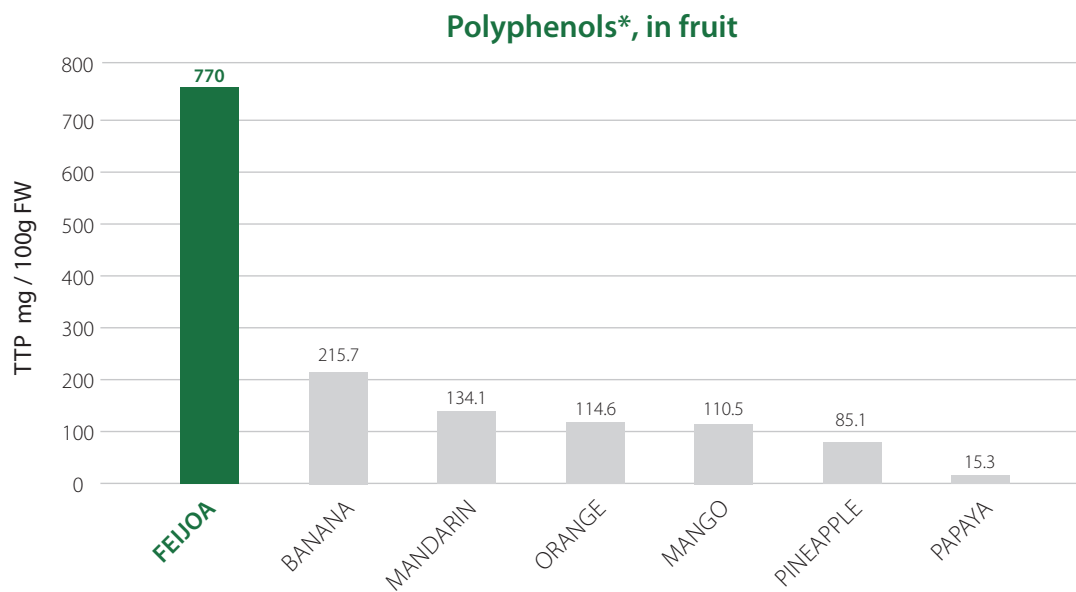
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## Feijoa nutritional information

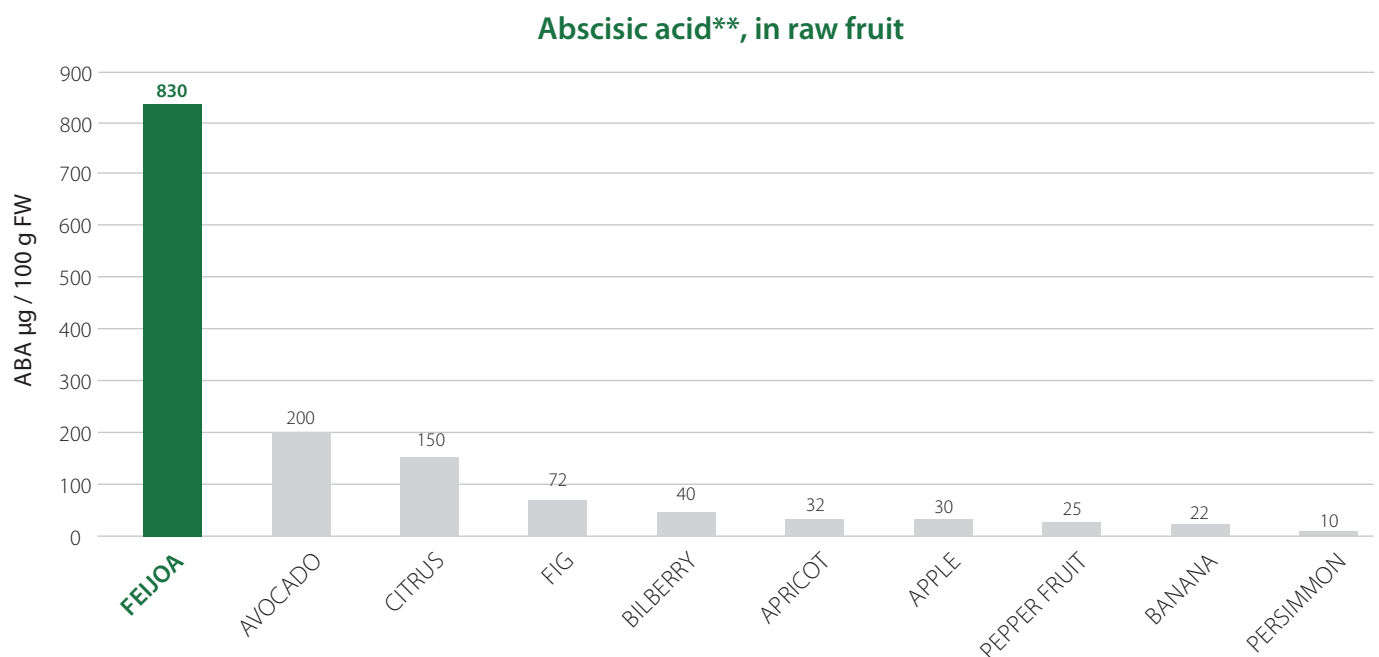
Nutrient	Unit	Value per 100 g <sup>1</sup>
Water	g	85
Energy	kcal	55
Protein	g	1.0
Total lipid (fat)	g	0.60
Carbohydrate, by difference	g	13
Fibre, total dietary	g	6.4
Sugars, total	g	8.2
Calcium, Ca	mg	17
Iron, Fe	mg	0.14
Magnesium, Mg	mg	9.0
Phosphorus, P	mg	19
Potassium, K	mg	170
Sodium, Na	mg	3.0
Zinc, Zn	mg	0.06
Vitamin C, total ascorbic acid	mg	33
Folate, DFE	µg	23
Polyphenols	mg	59

<sup>1</sup> USDA National Nutrient Database - Nutrient data for: 09334, Feijoa, raw

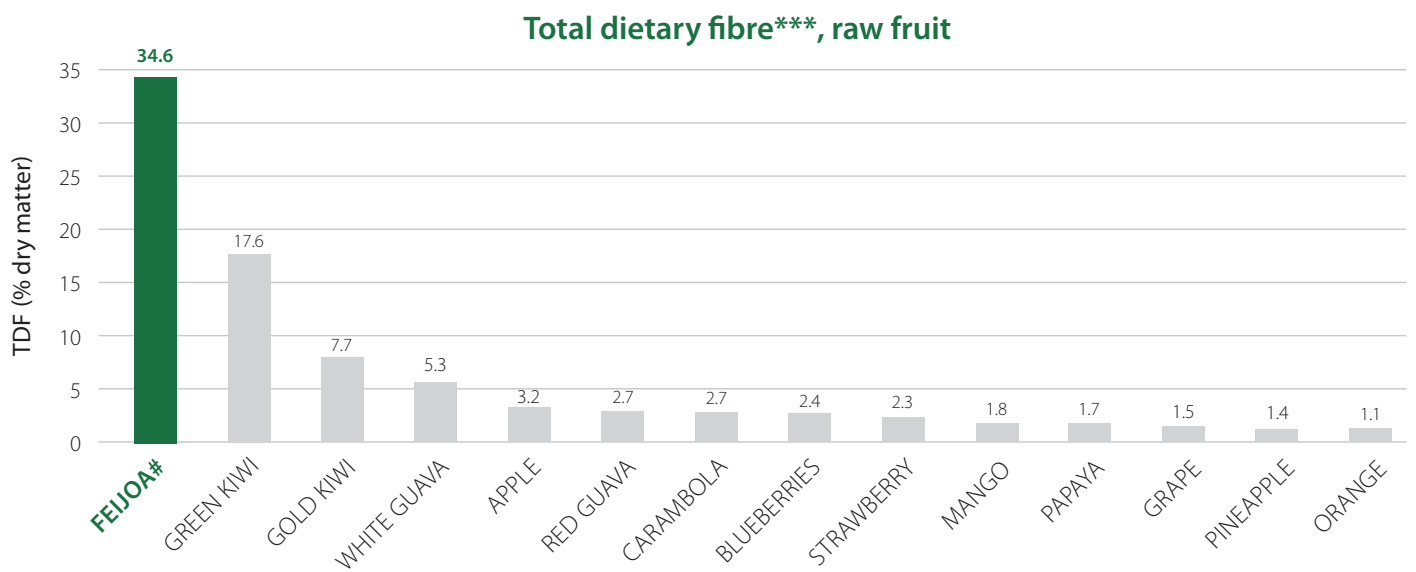
# Feijoas vs other fruit



\* Faller and Fialho 2009



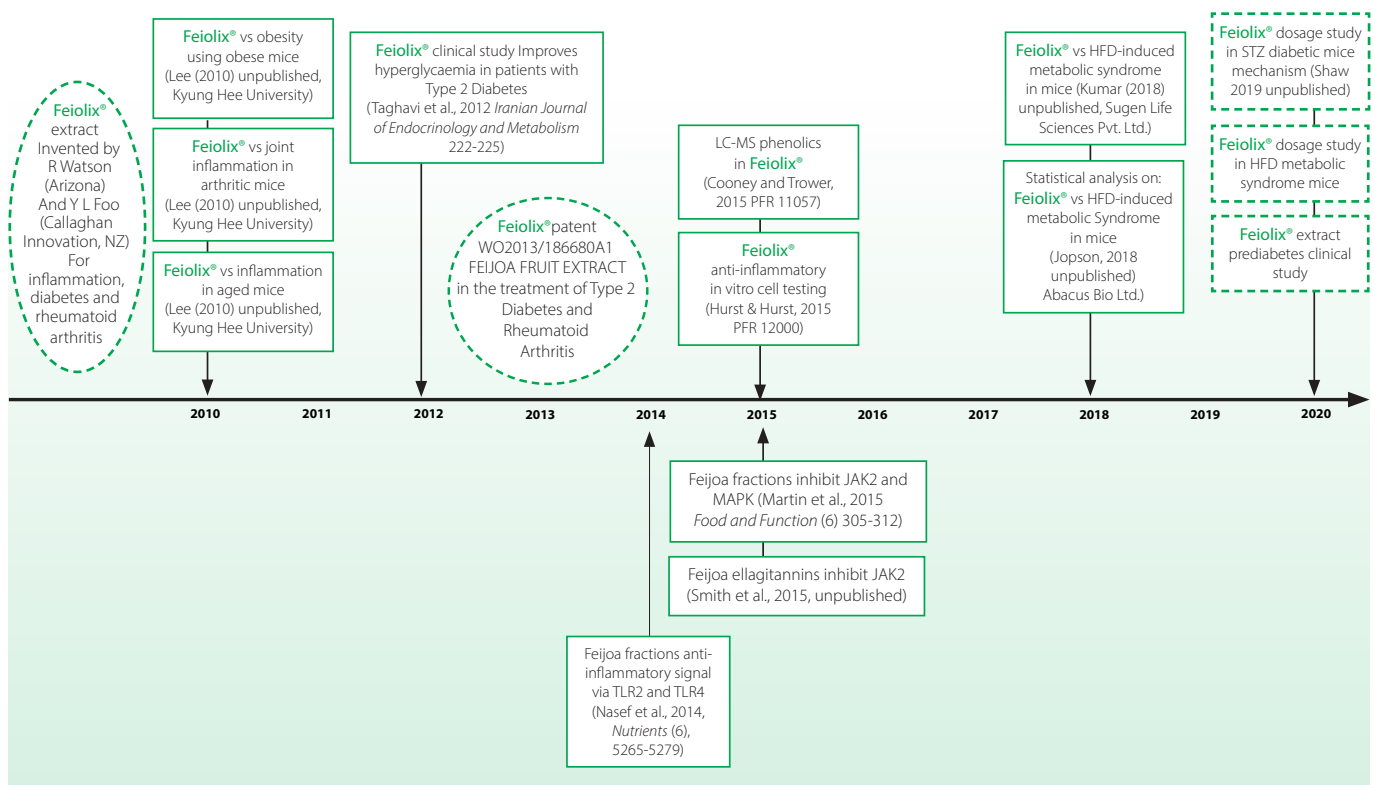
\*\* Zocchi et al 2017



\*\* \*Ayala-Zavala 2014

# Phan et al 2019





## Invention

**Feiolix®** was invented by polyphenol experts, Dr Yeap Foo (Callaghan Innovation, NZ) and Prof. Ron Watson (University of Arizona, USA). They developed an extract of feijoa fruit high in **anti-inflammatory hydrolysable tannins**.

It was designed to **mitigate symptoms of inflammatory conditions**:



diabetes



obesity



rheumatoid arthritis

# Feiolix<sup>®</sup> clinical studies vs Type 2 Diabetes

*Feiolix<sup>®</sup> extract DECREASED BLOOD GLUCOSE and HbA1c in type 2 diabetics.*

## Study design

Randomised, double-blind, placebo-controlled, parallel arm, n = 34

Participants fed either Feiolix extract (150 mg/day) or placebo every day for 12 weeks.

Blood pressure, serum level of fasting blood sugar, total cholesterol, LDL, HDL, triglycerides, glycosylated haemoglobin, were measured and compared at the beginning and after 12 weeks treatment.

The subjects were 40-75 years old with type-2 diabetes. There were no significant differences between the 2 groups regarding age, height, and body weight.

	Placebo	Fejoa extract (Feiolix <sup>®</sup> )
Number of participants	14	20
Male : Female ratio	7 : 7	4 : 16
Age (years)	52.6	55.0
Weight (kg)	77.6	77.2
Height (cm)	164.4	158.6

Mean years of diabetes treatment is the same for both groups. 19 of the 20 subjects supplemented with feijoa extract used additional medication: 95% use a combination of Metformin and Glibenclamide with two participants using insulin. 13 of the 14 subjects in the placebo group used additional medication: 55% use Metformin and Glibenclamide, insulin (1 subject) or Atenolol.

### Key results:

- After 12 weeks, patients in the Feiolix extract group had significant decreases ( $p < 0.05$ ) in fasting blood glucose and haemoglobin A1c (HbA1c).
- The magnitude of change seen with HbA1c (decrease by 0.86) is considered by FDA as clinically significant as pharmaceuticals for diabetes treatment are approved with changes of greater decrease than 0.5.
- Cholesterol and triglycerides also decreased significantly in the Feiolix extract group in comparison to the placebo group ( $p < 0.05$ ), and trending decrease for systolic blood pressure ( $p < 0.08$ )
- Trial participants in the Feiolix extract group showed no significant changes in the standard liver enzyme, serum creatine, albumin, and urea. These data show no toxicity is observed in the feijoa extract.
- This study showed that Feiolix extract extract can improve diabetes control, reduce antihypertensive medicine use, and may favour a reduction in cardiovascular disease risk in individuals with Type-2 diabetes.

Taghavi, M., Farid Hoseyni, R., Rafat Panah, H., Sharifian Razavi, M., Watson, R. Effect of feijoa supplementation in patients with type 2 diabetes. *Iranian Journal of Endocrinology and Metabolism*, 2012, 14 (3).

Variables	Placebo			Feijoa fruit extract		
	Baseline	Post Treatment	Change	Baseline	Post Treatment	Change
Triglyceride (mg/dL)	208.2 ± 23.5	241.9 ± 29.7	+33.6 ± 12.6	197.9 ± 28.1	159.8 ± 20.8*	-38.1 ± 20.9
Blood glucose (mg/dL)	168.4 ± 8.4	181.9 ± 10.3	+13.5 ± 30.7	184.0 ± 8.2	147.7 ± 8.0*†	-36.3 ± 2.7
HbA1c (%)	7.5 ± 0.4	8.1 ± 0.4	+0.49 ± 0.19	8.6 ± 0.3	7.7 ± 0.2*†	-0.86 ± 0.14
Total Cholesterol (mg/dL)	194.8 ± 9.6	209.8 ± 10.1	+15.0 ± 9.8	201.1 ± 9.9	183.6 ± 7.3*	-17.5 ± 6.9
LDL - cholesterol (mg/dL)	109.3 ± 37.2	116.1 ± 40.3	+6.8 ± 7.5	105.2 ± 15.2	87.2 ± 8.7†	-18.1 ± 14.4
Systolic BP (mmHg)	144.2 ± 0.2	142.9 ± 0.5	+0.36 ± 1.5	144.3 ± 1	137.6 ± 3.3	-6.7 ± 2.7

Analysed by Student's t-test, \* $P < 0.05$  compared with the placebo group, † $P < 0.05$  compared with the baseline. Measurements are performed on serum samples after 8-hours of fasting at the baseline and after 12 weeks of treatment. Values are means ± SEM ( $n = 20$  subjects in feijoa fruit extract group and 14 in placebo except for LDL-cholesterol when both groups are 6).

# Feiolix® studies vs obesity

## Feiolix® extract **REDUCED WEIGHT GAIN** and **FAT** tissue accumulation in obese mice

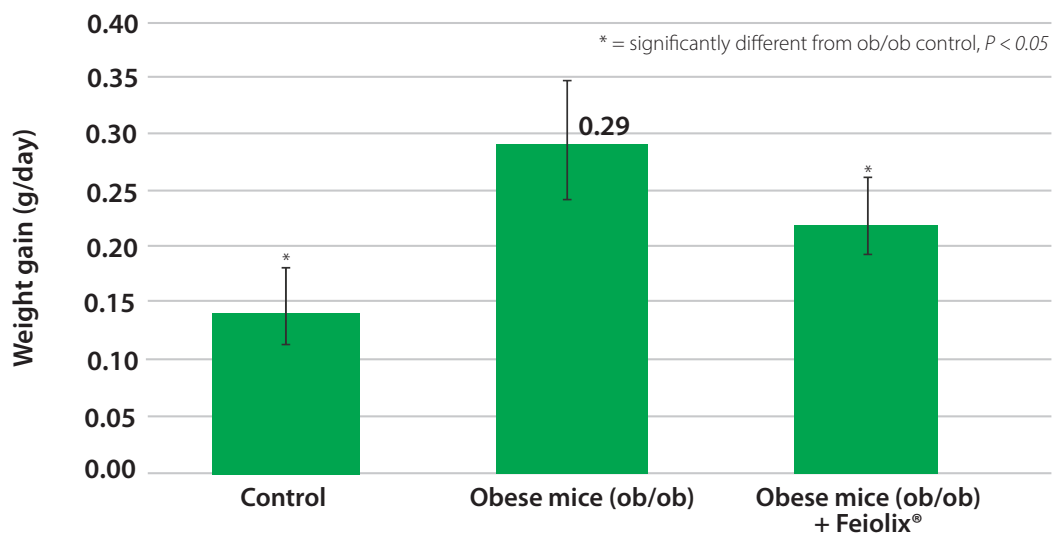
- Study used mice deficient in the hormone leptin (which decreases hunger and inhibits fat storage) that become very obese.
- Leptin-deficient mice were fed Feiolix® extract every day over 16 weeks and compared to non-Feiolix® extract-fed obese mice and normal control mice.
- There was a significant ( $P < 0.05$ ) **decrease** in the **food efficiency ratio** (conversion of food to body weight) compared to obese non-Feiolix® extract-fed control mice.
- There was a significant **reduction** in epididymal **adipose tissue** compared to obese non-Feiolix® extract-fed control mice.
- There was a significant **reduction** in liver total **cholesterol** compared to obese non-feiolix extract-fed control mice
- There were **reductions** in spleen weight, retroperitoneal adipose tissue, serum triglycerides and liver triglycerides compared to obese non-Feiolix® extract-fed control mice.

### Key results:

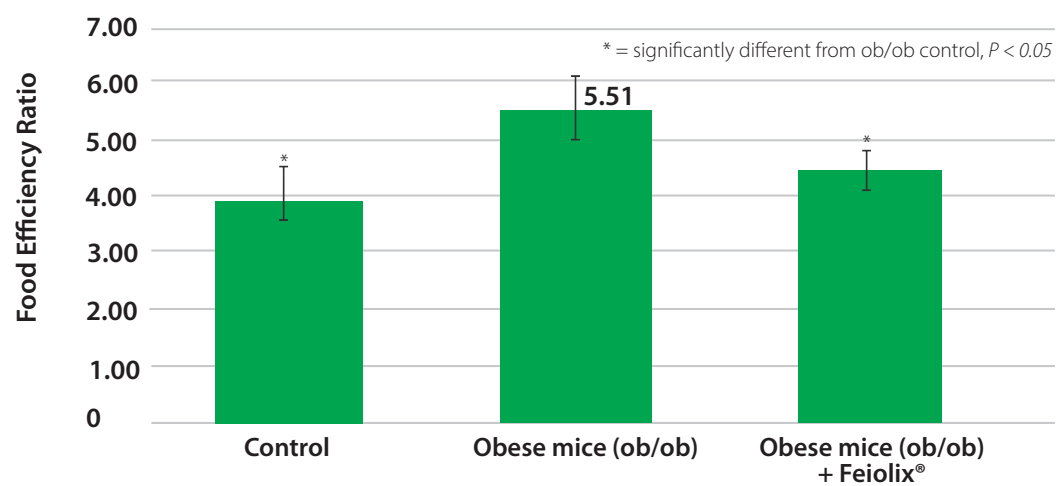
- There was a significant ( $P < 0.05$ ) **decrease** in the amount of **weight gain** (24% less than non-Feiolix® extract-fed obese mice)

	Baseline	Post Treatment	Change
<b>Change in body weight and food consumption</b>			
Initial body weight (g)	21.79 ± 1.09*	32.45 ± 2.15	34.40 ± 1.96
<b>Final body weight (g)</b>	37.29 ± 3.11*	65.23 ± 3.97	<b>59.05 ± 2.72*</b>
<b>Weight gain (g/day)</b>	0.14 ± 0.03*	0.29 ± 0.05	<b>0.22 ± 0.04*</b>
<b>Food efficiency ratio</b>	3.90 ± 0.49*	5.51 ± 0.57	<b>4.49 ± 0.37*</b>
<b>Weight of organs and adipose tissues</b>			
Kidney weight (g)	0.22 ± 0.02*	0.27 ± 0.02	0.25 ± 0.02
<b>Liver weight (g)</b>	1.89 ± 0.17*	4.44 ± 0.39	<b>3.97 ± 0.31*</b>
Spleen weight (g)	0.07 ± 0.01	0.07 ± 0.01	0.06 ± 0.01
Retroperitoneal adipose tissue weight (g)	0.53 ± 0.19*	3.15 ± 0.46	2.63 ± 0.36
<b>Epididymal adipose tissue weight (g)</b>	1.58 ± 0.26*	4.23 ± 0.36	<b>3.63 ± 0.43*</b>
<b>Serum lipid profile</b>			
Total Cholesterol (mg/dl)	154.67 ± 37.39*	415.36 ± 29.79	386.04 ± 41.42
Triglyceride (mg/dl)	77.57 ± 15.07*	142.53 ± 17.16	121.28 ± 22.17
<b>Hepatic lipid profile</b>			
<b>Total Cholesterol (mg/dl)</b>	179.15 ± 9.85*	453.64 ± 26.44	<b>413.59 ± 18.76*</b>
Triglyceride (mg/dl)	116.03 ± 11.87*	266.73 ± 31.91	229.76 ± 32.02

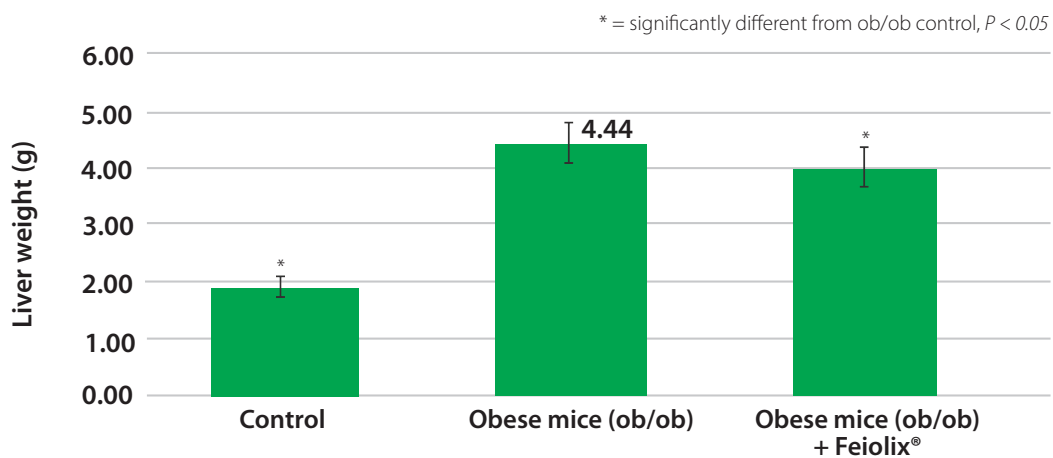
Values are means ± SD from 6 mice/ group. Mean with \* indicates a significant difference at  $p < 0.05$ , compared to obese control.



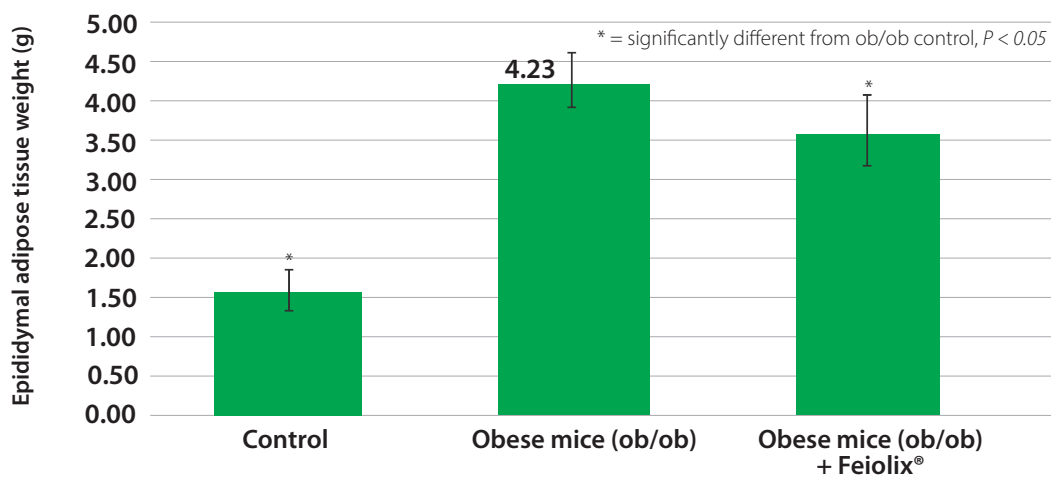
Feiolix® extract consumption for 16 weeks significantly decreases weight gain in obese mice.



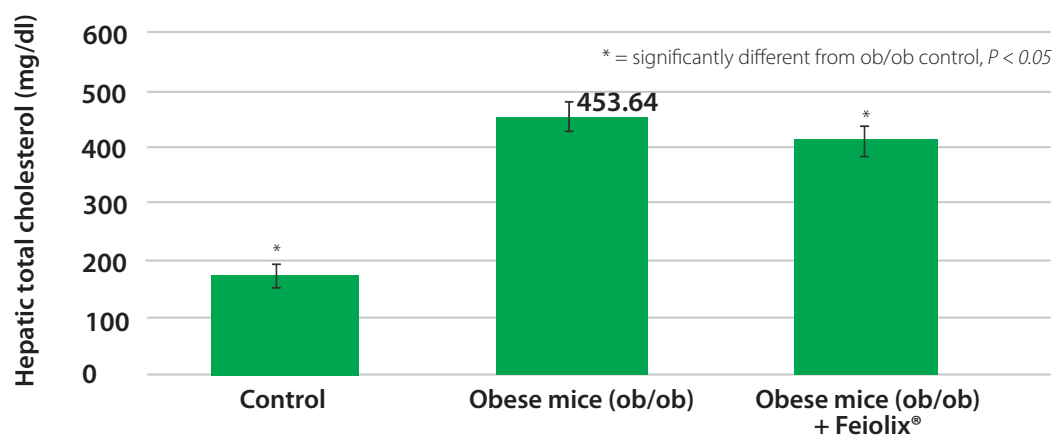
Feiolix® extract consumption for 16 weeks significantly reduces conversion of food to body weight (food efficiency ratio) in obese mice.



Feiolix® extract consumption for 16 weeks significantly reduces liver weight in obese mice.



Feiolix® extract consumption for 16 weeks significantly reduces epididymal adipose tissue weight of obese mice.



Feiolix® extract consumption for 16 weeks significantly lowers hepatic total cholesterol in obese mice.



# Feiolix® studies vs high fat-induced diabetes

## *Feiolix® extract improved symptoms in high fat diet-induced diabetic mice*

- Normal healthy mice were fed with standard (low fat) diet or HFD (high fat diet) for 8 weeks.
- Fasting blood glucose levels were measured to confirm a diabetic condition following the weight gain in HFD mice.
- Mice then fed **Feiolix®** extract for 12 more weeks.

Group	Treatment Details	Diet & Dose (mg/kg body weight per day)	Mice per group
1	Control	Standard diet, 10 Kcal 4% fat	10
2	Disease control	High fat diet, 60 Kcal, 35% fat	15
3	HFD + Feiolix®	High fat diet, 60 Kcal, 35% fat + Feiolix® 0.7 mg/20 g mouse (equiv. to 150 mg human dose of the extract)	15

Measurement	Effect of Feiolix®
Body weight	<ul style="list-style-type: none"> <li>• Mice fed with HFD had significant weight gain compared to control.</li> <li>• Feiolix® treatment showed significant decrease compared to HFD group by the end of the experiment at Week 20 (after 12 weeks treatment).</li> </ul>
Liver Index	<ul style="list-style-type: none"> <li>• Liver index (liver weight/body weight x 100) was high in mice fed with HFD.</li> <li>• Feiolix® treatment showed significant decrease compared to HFD group.</li> </ul>
Non-esterified Fatty Acids (free fatty acid)	<ul style="list-style-type: none"> <li>• Mice fed with HFD showed significantly elevated levels of free fatty acids.</li> <li>• Feiolix® treatment showed significant decrease compared to HFD group.</li> </ul>
Total cholesterol	<ul style="list-style-type: none"> <li>• Mice fed with HFD showed significantly elevated levels of cholesterol.</li> <li>• Feiolix® treatment showed significant decrease compared to HFD group.</li> </ul>
Triglyceride	<ul style="list-style-type: none"> <li>• Mice fed with HFD showed significantly elevated levels of triglycerides.</li> <li>• Feiolix® treatment showed significant decrease compared to HFD group.</li> </ul>
Fasting glucose	<ul style="list-style-type: none"> <li>• Mice fed with HFD had significantly higher fasting glucose levels than the control group.</li> <li>• Feiolix® treatment significantly reduced fasting glucose.</li> </ul>
Insulin resistance: HOMA-IR	<ul style="list-style-type: none"> <li>• Insulin resistance was increased in mice fed with HFD.</li> <li>• Feiolix® treatment showed significant decrease in HOMA-IR.</li> </ul>
Oral Glucose Tolerance Test (OGTT)	<ul style="list-style-type: none"> <li>• Glucose administration to the HFD fed animals resulted in increased blood glucose levels compared to control.</li> <li>• Feiolix® treatment significantly reduced blood glucose level after glucose challenge compared to mice fed with HFD only.</li> </ul>
Insulin Tolerance Test (ITT)	<ul style="list-style-type: none"> <li>• The Insulin Tolerance Test was designed to determine the sensitivity of insulin receptors in tissue by measuring blood glucose levels before and after insulin administration through the intra-peritoneal route.</li> <li>• Insulin administration resulted in higher blood glucose levels in HFD mice than control.</li> <li>• Feiolix® treatment significantly decreased blood glucose levels, this effect was seen at Week 16 and Week 20 (8th week and 12th weeks after Feiolix® treatment respectively).</li> </ul>

## Body weight

Treatment Group	Bodyweight (g) at Week 20		Change in body weight of individuals (gain as slope in g per week from W 8 to W 20)	
	Mean	SEM	Mean	SEM
Control	37.60 <sup>c</sup>	0.50	0.60 <sup>g</sup>	0.090
HFD	51.84 <sup>d</sup>	0.45	1.26 <sup>h</sup>	0.090
HFD + Feiolix®	44.61 <sup>f</sup>	0.41	0.63 <sup>g</sup>	0.090

## Liver Index

Liver tissues were collected at the end of the experiment and fixed in 10% neutral buffered formalin solution, processed and embedded in paraffin wax. The Liver Index is expressed as = 100(Liver weight/Body weight).

Treatment Group	Mean	SEM
Control	3.20 <sup>a</sup>	0.091
HFD	4.06 <sup>b</sup>	0.082
HFD + Feiolix®	2.96 <sup>d</sup>	0.075

## Fasting glucose

Treatment Group	Fasting glucose at Week 20 (mg/dl)	
	Mean	SEM
Control	115.3 <sup>c</sup>	5.46
HFD	156.0 <sup>d</sup>	4.88
HFD + Feiolix®	125.8 <sup>c</sup>	4.46

## Insulin Resistance Index (HOMA-IR) at Week 20

Insulin Resistance Index: The homeostatic model assessment (HOMA) is a measure of insulin resistance observed in metabolic syndrome. It was calculated by using the following formula: fasting insulin  $\mu\text{M/L}$  x fasting glucose  $\text{mmol/L}/22.5$ .

Treatment Group	Insulin ( $\mu\text{U/ml}$ )		Insulin Resistance Index (HOMA-IR)	
	Mean	SEM	Mean	SEM
Control	11.0 <sup>a</sup>	1.08	3.0 <sup>e</sup>	0.45
HFD	29.4 <sup>bc</sup>	0.96	11.0 <sup>f</sup>	0.40
HFD + Feiolix®	19.5 <sup>d</sup>	0.88	5.0 <sup>h</sup>	0.37

## Oral glucose tolerance test (OGTT) (at Week 20)

Treatment Group	0 hour		15 min		60 min		120 min	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Control	115.2 <sup>d</sup>	22.1	180.7 <sup>d</sup>	13.6	124.8 <sup>j</sup>	4.2	117.6 <sup>l</sup>	5.2
HFD	156.0 <sup>b</sup>	15.2	322.3 <sup>e</sup>	12.6	246.5 <sup>j</sup>	8.2	213.5 <sup>m</sup>	14.2
HFD + Feiolix®	125.8 <sup>c</sup>	9.2	297.9 <sup>f</sup>	11.1	220.6 <sup>k</sup>	12.2	192.3 <sup>n</sup>	7.4

## Insulin tolerance test (ITT) (at Week 20)

Treatment Group	0 hour		15 min		60 min		120 min	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Control	115.2 <sup>d</sup>	22.1	180.7 <sup>d</sup>	13.6	124.8 <sup>i</sup>	4.2	117.6 <sup>l</sup>	5.2
HFD	156.0 <sup>b</sup>	15.2	322.3 <sup>e</sup>	12.6	246.5 <sup>j</sup>	8.2	213.5 <sup>m</sup>	14.2
HFD + Feiolix®	125.8 <sup>c</sup>	9.2	297.9 <sup>f</sup>	11.1	220.6 <sup>k</sup>	12.2	192.3 <sup>n</sup>	7.4

## Non-esterified Free Fatty Acid

Treatment Group	Baseline NEFA at Week 20		Change in baseline NEFA of individuals (change as slope per week (μM/ml) from W 8 to W 20)	
	Mean	SEM	Slope (μM/ml/week)	SE of the slope
Control	487 <sup>a</sup>	28.0	7.6 <sup>a</sup>	2.1
HFD	866 <sup>b</sup>	25.1	9.4 <sup>a</sup>	2.8
HFD + Feiolix®	669 <sup>d</sup>	22.9	-6.1 <sup>b</sup>	2.7

## Cholesterol

Treatment Group	Baseline Total Cholesterol at Week 20		Change in baseline Total Cholesterol of individuals (change as slope in per week (mg/dl) from W 8 to W 20)	
	Mean	SEM	Slope (mg/dl/week)	SE of the slope
Control	146.0 <sup>a</sup>	7.92	3.58 <sup>a</sup>	0.81
HFD	217.4 <sup>bc</sup>	7.09	3.15 <sup>a</sup>	0.82
HFD + Feiolix®	165.9 <sup>a</sup>	6.47	-1.24 <sup>b</sup>	0.80

## Triglycerides

Treatment Group	Baseline Tri-glycerides at Week 20		Change in baseline Tri-glycerides of individuals (change as slope per week (mg/dl) from W 8 to W 20)	
	Mean	SEM	Slope (μM/ml/week)	SE of the slope
Control	79.8 <sup>a</sup>	4.93	1.50 <sup>ac</sup>	0.53
HFD	156.9 <sup>b</sup>	4.41	3.00 <sup>b</sup>	0.54
HFD + Feiolix®	106.3 <sup>d</sup>	4.02	-1.14 <sup>d</sup>	0.53

# Feiolix<sup>®</sup> studies vs Rheumatoid Arthritis

*Feiolix<sup>®</sup> extract improved the joint condition of arthritic mice*

## Study design

In this study, mice were injected with collagen to stimulate rheumatoid arthritis.



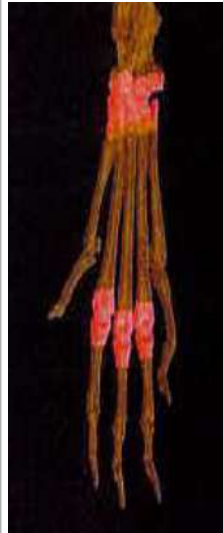

The arthritic mice were fed Feiolix extract every day over 12 weeks and compared to non-Feiolix<sup>®</sup> extract-fed arthritic mice and normal control mice.

Performance (foot pressure, running speed and footprint) were assessed on a treadmill

Microcomputerized tomographic (microCT) imaging of mouse paw bones were collected.

### Key results:

- Significant ( $P < 0.05$ ) **increase** in **running speed**.
- “**Relatively normal**” joint structures and **little soft tissue swelling**
- Significant ( $P < 0.05$ ) **decrease in inflammatory cytokines**
  - TNF- $\alpha$ , IL-2 and interferon-gamma (IFN- $\gamma$ )
- The effects of **Feiolix<sup>®</sup>** were **as good as the rheumatoid arthritis drug** methotrexate (MTX)

	Normal mice control	Negative control (arthritic)	Arthritic + Feijoa extract	Arthritic + MTX
<b>Change in body weight and food consumption</b>				
Final body weight (g)	22.27 ± 0.95	21.25 ± 0.49	23.33 ± 1.74	24.23 ± 1.95
Weight gain (g/day)	9.80 ± 0.36	8.60 ± 0.06	10.27 ± 0.78	7.67 ± 0.09
Food efficiency rate (body weight gain/food intake (kcal))	0.012 ± 0.002	0.013 ± 0.005	0.017 ± 0.019	0.011 ± 0.032
<b>Treadmill performance</b>				
Running speed (mm/s)	133.05 ± 3.40 <sup>a</sup>	91.24 ± 2.24 <sup>b</sup>	120.54 ± 5.01 <sup>a</sup>	121.36 ± 2.34 <sup>a</sup>
Foot pressure	148.54 ± 3.89	136.89 ± 0.93	143.97 ± 5.28	141.33 ± 5.28
<b>MicroCT parameters</b>				
Bone volume/total tissue volume (%)	39.65	24.03	33.81	33.96
Bone surface/volume ratio (mm <sup>-1</sup> )	8.09	10.46	8.49	8.49
Trabecular number (mm <sup>-1</sup> )	23	17	26	21
MicroCT				

Superscripted letters that are different are significantly different ( $P < 0.05$ )

# Feiolix<sup>®</sup> studies vs Inflammation in aged mice

*Feiolix<sup>®</sup> extract **decreased** levels of **pro-inflammatory** cytokines in aged mice.*

*Aging leads to the deterioration of the immune system which is thought to be a **contributing factor** to the **development** of **type-2 diabetes**.*

## Study design

In this study, aged mice were divided into groups according to diet: a control group and a feijoa extract supplemented group.

Aged mice were fed Feiolix extract every day over 32 weeks

Various immune parameters and organs were measured

### Key results:

- Significant ( $P < 0.01$ ) **decrease in pro-inflammatory cytokines** interleukin-4 (IL-4) and **tumour necrosis factors** a and b (TNF-a and TNF-b)
- **77% increase in hepatic vitamin E levels**

- Aged mice supplemented with feijoa extract significantly decreased splenic T-cell production of proinflammatory cytokines IL-4, TNF- $\alpha$  and TNF- $\beta$ . Anti-inflammatory cytokines IL-2 and IFN- $\gamma$  production was not significantly affected in either groups.
- Aged mice supplemented with **Feiolix<sup>®</sup>** extract had a significant (44%) decrease in IL-4 production versus the non-**Feiolix<sup>®</sup>** extract-fed aged mice.
- Aged mice supplemented with **Feiolix<sup>®</sup>** extract had a significant (20%) decrease in Concanavalin
- A-stimulated splenic T-cell mitogenesis vs. the non-**Feiolix<sup>®</sup>** extract-fed aged mice.
- Aged mice supplemented with feijoa fruit extract had a significant (14%) decrease in lipopolysaccharide-stimulated splenic B-cell mitogenesis.

Aged animals often have spontaneously stimulated B-cells, which do not function as well as those in younger animals and also inhibit T-cells. Therefore, lowering mitogenesis or cell division by B-cells should be beneficial to host defences.

Immunosenescence (deterioration of the immune system by age advancement) is a major contributing factor in survival to old age or premature death in humans and animals. Some of the adverse effects include dysregulated cell division of T- and B-lymphocytes upon stimulation by mitogens in vitro, or pathogens in vivo with altered cytokine production.

In the present studies, B- and T-lymphocytes from aged mice divide less than those of young mice, and those from aged mice fed Feiolix extract.

The key observations on regulatory cytokines include stimulation of INF- $\gamma$ , TNF- $\alpha$ , - $\beta$  and - $\gamma$ , and IL-4 by consequences of immunosenescence in aging.

*The lowering of these cytokines due to consumption of **Feiolix<sup>®</sup>** extract suggests **better overall immune regulation**, which can provide **improved disease resistance***

## Physical measures

Mice group		Body weight (g)	Spleen (mg)	Liver (g)	Heart (mg)
Mouse age	Treatment				
Young	Chow diet	26.36 ± 3.20	89.71 ± 16.25	1.46 ± 0.23	153.48 ± 14.12
Aged	Chow diet	43.08 ± 2.30	174.95 ± 15.15	1.76 ± 0.15	163.88 ± 16.81
Aged	Chow diet + <b>Feiolix</b> <sup>®</sup>	44.2 ± 3.1	133.5 ± 19.2	1.7 ± 0.2	160.2 ± 12.9

Mice supplemented with **Feiolix**<sup>®</sup> extract consume 6 g food/day, which equates to 1.8 mg of extract/day.

The **Feiolix**<sup>®</sup> extract was added to the diet at a dose of 300mg/kg. Data indicates mean ± SD from 6 mice per group.

## Immune measures

Measure	Young Unsupplemented	Aged Unsupplemented	Aged Supplemented (Feijoa)
<b>T-cell proliferation (%)</b> (aged unsupplemented =100)	130 ± 15*	100 ± 9	<b>78 ± 9*</b>
<b>B-cell proliferation (%)</b> (aged unsupplemented =100)	130 ± 8*	100 ± 4	<b>85 ± 4*</b>
<b>IL-2 level by splenocytes</b> (pg/mL)	278 ± 26	264 ± 38	216 ± 47
<b>IFN-γ level by splenocytes</b> (pg/mL)	1555 ± 12	750 ± 37	907 ± 12
<b>TNF-α level by splenocytes</b> (pg/mL)	290 ± 30*	650 ± 53	<b>450 ± 35*</b>
<b>TNF-β level by splenocytes</b> (pg/mL)	95 ± 20*	142 ± 18	<b>70 ± 10*</b>
<b>IL-4 level by splenocytes</b> (pg/mL)	135 ± 40	165 ± 45	<b>90 ± 30*</b>
<b>MDA levels in liver tissue</b> (mol/mg protein)	0.12 ± 0.02*	0.325 ± 0.07	<b>0.19 ± 0.03*</b>
<b>Hepatic vitamin E level (%)</b> (aged unsupplemented =100)	200 ± 26*	100 ± 9	<b>177 ± 3*</b>

Data indicates mean ± SD from 6 mice per group.

\* Shows the statistical significance compared to aged control determined by unpaired Students t-test.

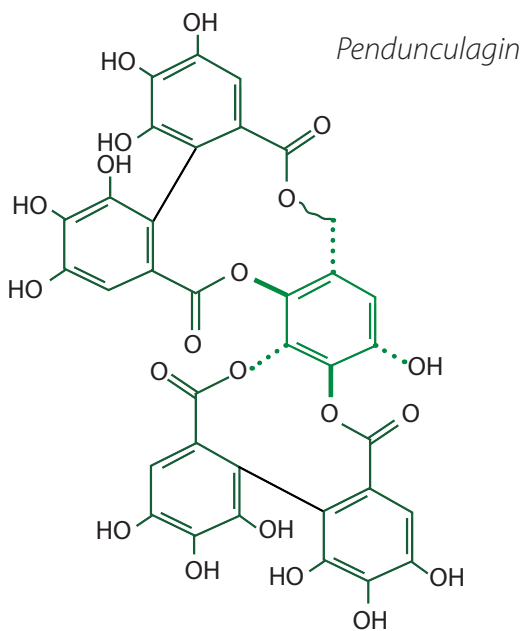


# Polyphenols

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*Feiolix® contains anti-inflammatory polyphenols*

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- Hydrolysable tannins (ellagitannins)
  - » **a** and **b-pedunculagin** (comprises **60% of the total polyphenols** in **Feiolix®** extract)
- Flavans
- Proanthocyanidins (condensed tannins)
  - » Catechin
  - » Gallocatechin
  - » Catechin B2
  - » Epicatechin
  - » Same polyphenols as contained in **green tea**

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*These polyphenols explain the anti-inflammatory effects of Feiolix®*

*The underlying causes of obesity, arthritis and diabetes are **all based on inflammation***

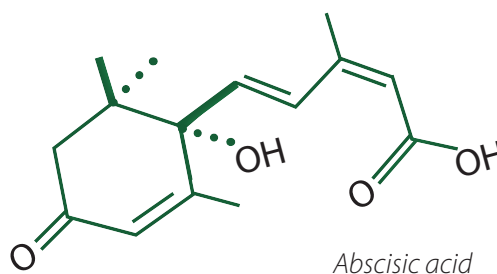
# Absciscic Acid

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## Feiolix® contains **Absciscic Acid (ABA)**

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- Natural plant hormone, very high in ripe feijoa
- Also **co-secreted with insulin by humans** at very low levels
- Like insulin, also **decreased in type 2 diabetics**
- Binds to dedicated ABA receptor (LANCL2) to **control blood sugar**<sup>1-3</sup>
- **Key bioactive** explaining Feiolix ability to **control blood glucose**



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1. Zocchi et al., (2017) Absciscic acid: a novel nutraceutical for glycemic control. *Front Nutr.* 4:24.
  2. Bassaganya-Riera et al., (2010) Mechanisms of action and medicinal applications of absciscic acid. *Curr Med Chem.* 17 (5), 467-478.
  3. Bassaganya-Riera et al., (2011) Absciscic acid regulates inflammation via ligand-binding domain-independent activation of peroxisome proliferator-activated receptor gamma. *J Biol Chem*, 286 (4), 2504-2516.

# Feiolix® Patented

## WO2013/186680A1 FEIJOA FRUIT EXTRACT in the treatment of Type 2 Diabetes and Rheumatoid Arthritis

### Claims summary:

1. A method of **lowering serum lipids** in a patient...
2. A method of **lowering serum glucose** in a patient...
3. A method according to claim 2 wherein **HbA1c is reduced**...
4. A method of **lowering blood pressure**...
5. A method of ameliorating the symptoms of metabolic syndrome...
6. A method of preventing or **reducing obesity**...
7. A method of **regulating immune function**...
8. A method of treating a disease or disorder associated with **immunosenscence**...
9. A method according to any one of the preceding claims wherein the patient has **type 2 diabetes**...
10. A method of ameliorating the **symptoms of diabetes**...
11. A method of treating or preventing the symptoms of **rheumatoid arthritis**...

### REDEVELOPMENT

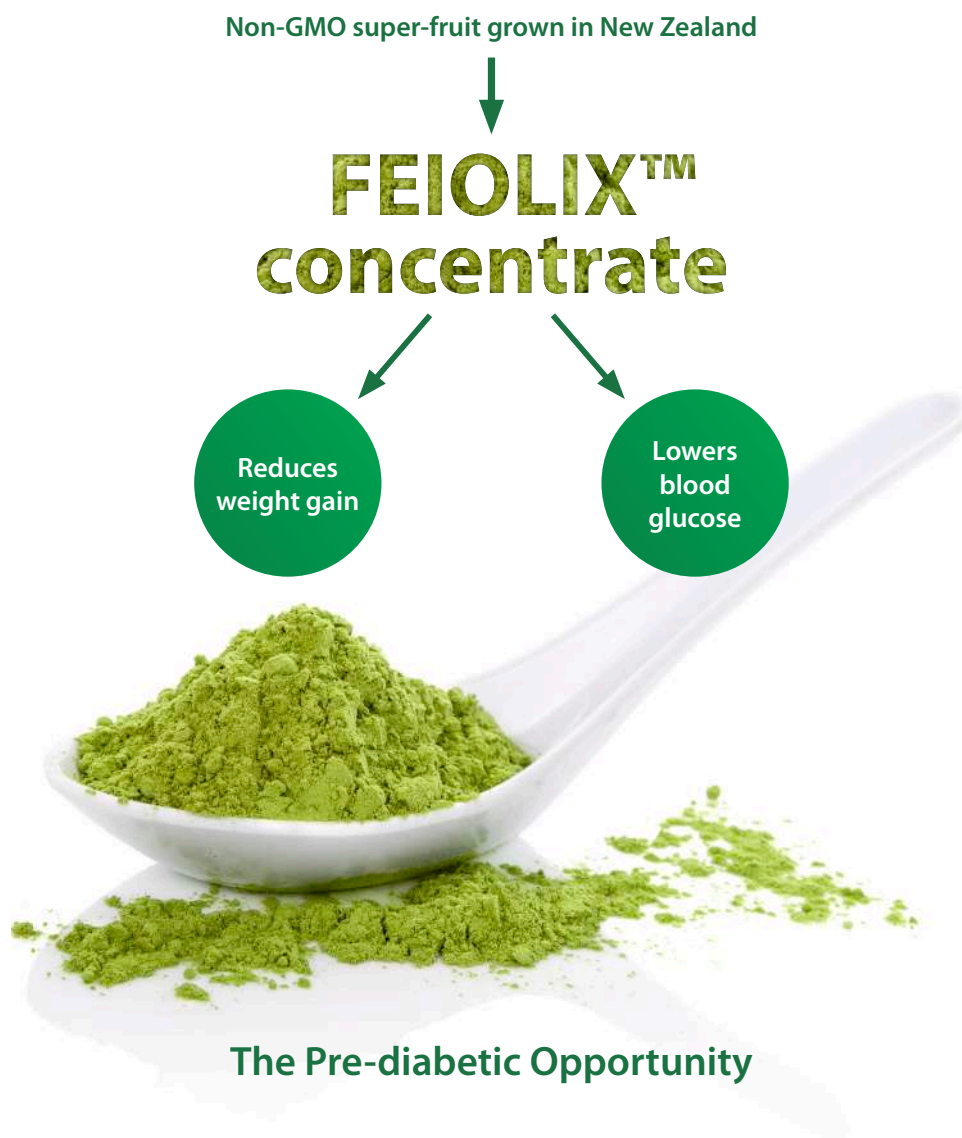
Feiolix® has been re-designed for better pricing and functionality

- Minimally processed whole fruit powder better pricing and more natural than fruit extract.
- Retains all of the bioactive polyphenols and ABA
- Also contains feijoa cell wall polysaccharides
  - » Dietary fibre has known benefits on **satiety** and **weight gain**
  - » High feijoa xyloglucan component is a **precision prebiotic**
  - » Xyloglucan targets propionate-producing gut bacteria
  - » Propionate is a **postbiotic** that **increases satiety** and **decreases** liver gene expression for **fat synthesis**
- **Performs as well as or better than original extract in preclinical comparison study**



# Take-home messages

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- NEW ZEALAND origins.
- Sourced from a natural “SUPER-FRUIT”.
- High level of anti-inflammatory polyphenols and blood glucose-lowering ABA.
- Clinically significant reduction of weight gain and blood glucose.

# Regulatory and science

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- ✓ Known mechanisms of action
- ✓ Validated by preclinical and clinical evidence
- ✓ Self-Determined GRAS
- ✓ 100% non-GMO feijoa fruit
- ✓ Dairy free, gluten free, preservative free
- ✓ Comprehensive specifications including microbes and heavy metals
- ✓ Quarterly quality assurance programme including pesticides screen (300+)