FPP Evidence Series 2

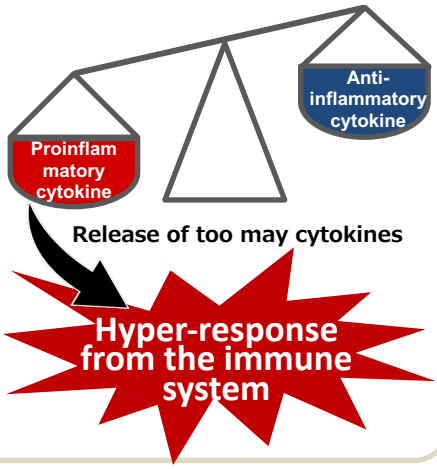
Cytokine storm linked with serious diseases including thrombosis

Covid-19 is still being elucidated. We have received questions about cytokine storm, which seems to be linked with severe symptoms of the Covid-19 including thrombosis.
We reviewed our clinical studies on FPP (Fermented Papaya Preparation) in terms of protecting from causing severe cases due to infection and summarized relevant studies.

What is "Cytokine Storm"?

Cytokines are small secreted proteins released by cells, which have a specific effect on the interactions and communications between cells. There are many types of Cytokines, some of which play important roles in activating or regulating immune cells. After infection, proinflammatory cytokines activate immune cells which attack infected cells, causing symptoms such as high fever, severe fatigue, headache and clotting problem. Once the viruses weaken, normally anti-inflammatory cytokines would work to stop the symptoms. Cytokines protect the body by balancing our immune system like accelerator and brake. However, being out of cytokine balance, proinflammatory cytokines would be released all at once without control and hyper-response from the immune system would attack even normal cells or tissues, which inflicts multi-organ inflammatory damage leading to death in the worst case. This is "cytokine storm".

Out of Cytokine Balance

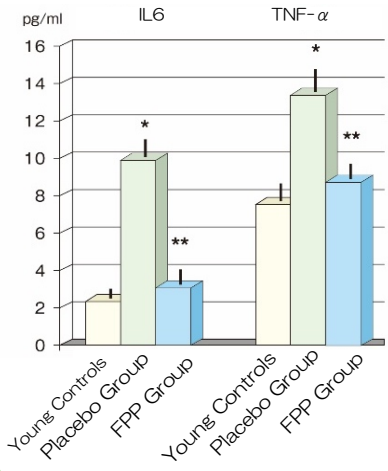


FPP Evidence 2-1

Nutraceutical Strategy in Aging Targeting Heat Shock Protein and Inflammatory Profile through Understanding Interleukin-6-Polymorphyzm:
Ann. N. Y. Acad. Sci. Nov;1119:196-202 (2007)

Effect of FPP on Inflammatory Cytokines !

Downregulating IL6 & TNF-α



The aging process is paralleled by two-to-fourfold increases in plasma/serum levels of inflammatory mediators, such as cytokines and acute-phase proteins. In this study, we assessed the inflammatory profile of 40 healthy elderly subjects and the influence of FPP.

We divided forty elderly into two matched groups, and gave either FPP 9 g/day by mouth or the same amount of placebo. Treatments were carried out in a cross-over manner with a 3-month supplementation period. Ten healthy young subjects served as controls. We measured proinflammatory cytokines, IL-6 and TNF-α.

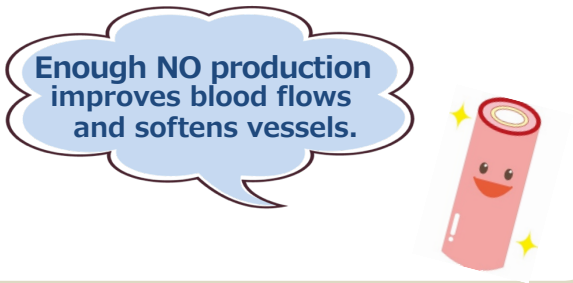
Shown in the left chart, inflammatory profile, such as TNF-α and IL-6, of the elderly subjects were approx. 5 times and twice higher than the young controls. In the FPP supplemented group, TNF-α and IL-6 were downregulated close to the young controls, suggesting that inflammatory reaction were decreased by FPP.

In this study, blood levels for redox status, high sensitivity C-reactive protein, and serum 70 kDa heat shock protein (Hsp70) concentrations were also assessed and IL-6 promoter −174 G/C polymorphism genotype was determined. In the FPP intervention, we observed influence of polymorphism genotype. Prevention or regulation of excessive proinflammatory cytokines could prevent cytokine storm leading to severe symptoms in infectious diseases. On this non-side effect medical food, further clinical studies in this field are expected.

What is “thrombosis” ?

When cytokine storm occurs, the more likely abnormal blood clotting is to be formed to plug up damaged blood vessels. Thrombosis occurs when the blood clots block or obstruct blood flow. It may cause serious complications leading to death if the clot moves to a crucial part of circulatory systems, such as the brain or the lungs. Pneumonia makes the mortality rate higher.
In Covid-19, a negative chain of cytokine storms and thrombosis seems to cause serious symptoms.

To avoid thrombosis, good blood circulation is important. Nitric Oxide (NO) is deemed to improve blood flow. No is produced in endothelial cell of blood vessels, softening and delating blood vessels.



FPP Evidence 2-2

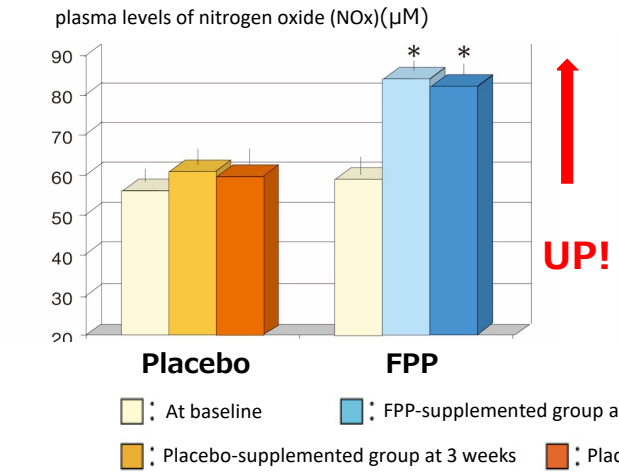
Cardioprotective Effect of a Biofermented Nutraceutical on Endothelial Function in Healthy Middle-aged Subjects:
Rejuvenation Research. 2012 Apr;15(2):178-81.

FPP induces NO production and delates blood vessels !

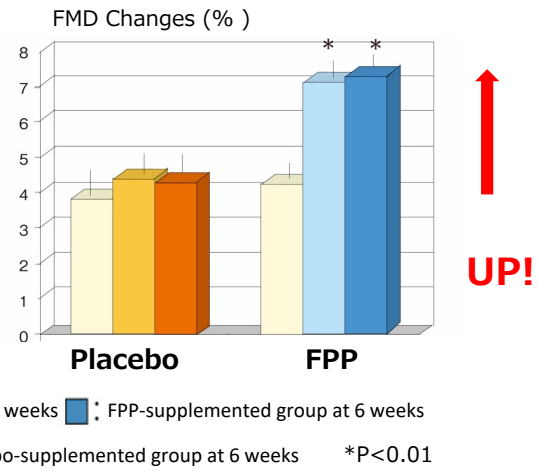
This is a clinical study to evaluate cardioprotective effect of FPP on endothelial function. 42 participants were healthy middle-age subjects (42-57 years old) and not taking any drugs or supplements. The subjects were given 3 grams of FPP three times a day for 6 weeks. Tests were repeated at 3 and 6 weeks. The placebo group was given the same quantity of flavored sugar.

In result, a significant increase of plasma NO level was detected in the FPP supplemented group. FMD (Flow Mediated Dilation) also increased by FPP consumptions, which represents actual dilation of blood vessels with high NO bioavailability. This result shows possible effect of FPP to prevent decrease of NO production due to aging as well as to prevent thrombosis by increasing blood flows with dilation of blood vessels.

Increase of NO production



Increase of FMD



: At baseline : FPP-supplemented group at 3 weeks : FPP-supplemented group at 6 weeks
: Placebo-supplemented group at 3 weeks : Placebo-supplemented group at 6 weeks *P<0.01

Regarding accelerated production of NO by FPP, it is confirmed that FPP improves not only NO production but also iNOS gene expression in other study on wound healing by FPP [1].

【引用文献】 1)Improved function of diabetic wound-site macrophages and accelerated wound closure in response to oral supplementation of a fermented papaya preparation Antioxidants & Redox Signaling September 1, 2010:

FPP is a fermented food in granule form made by fermenting papaya for about a year, which is a blessing from nature. FPP has a lot of evidences with clinical studies with 9g/day supplementation, which proves its **antioxidant, immunostimulant and anti-inflammatory effects**. We recommend to take FPP between meals and let the granule dissolve with saliva before swallowing.

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