Cranberry Extract

Zhejiang Jianfeng Health Technology Co., Ltd.
- to be the pioneer of innovative health products
What’s cranberry

- Name: Cranberry
- Species: Vaccinium macrocarpon
- Cranberry has been marketed as a "superfruit" due to its nutrient content and antioxidant qualities
Where it grows

- Strict conditions: soil, climate and altitude
- Mainly grows on cold wetland of North American, such as Massachusetts state, Wisconsin state, Maine state of USA, Quebec province, British Columbia province of Canada
Composition

- High water content
- Low calorie
- Plenty of vitamins & minerals

- Water
- Carbohydrates
- Protein
- Fat
### Active Substances

<table>
<thead>
<tr>
<th>OPCs</th>
<th>Anthocyanins</th>
<th>Flavonols</th>
<th>Phenolic acids</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Oligomeric proanthocyanidins (OPCs)</td>
<td>• cyanidin 3-galactoside, Cyanidin 3-arabinoside, peonidin 3-galactoside ...</td>
<td>• Hyperoside, Quercetin, myricetin, Quercitrin...</td>
<td>• Benzoic acid, Cinnamic acid ...</td>
<td>• Pectin, Gallogen, Resveratrol, Lignans, Ursolic acid, Tocotrienols, ω-3 fatty acid, Vitamin C, Minerals</td>
</tr>
<tr>
<td>normally refer to short-chain procyanidin from dimers to pentamers</td>
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<tr>
<td>• A-type proanthocyanidins exist in cranberry.</td>
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</table>

Cranberry

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**Unique Structure**

Proanthocyanidins (PACs), also known as condensed tannins, which are widely founded in many kind of plants, such as apples, grapes, Cocoa beans, are not a single chemical, but are phenolic polymers of condensed flavan-3-ols. Oligomeric Proanthocyanidins(OPCs) normally refer to polymers from dimers to pentamers of Proanthocyanidins.

Recent research indicate that A-type OPCs in cranberry are anti-bacterial function substances, while B-type OPCs in apples, grapes don’t have such function.

![Typical structure of A-type OPCs](image-url)
### Functions

<table>
<thead>
<tr>
<th>Anti-bacterial</th>
<th>Anti-oxidant</th>
<th>Other functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Preventing urinary tract infection</td>
<td>• Proanthocyanidins is the most strong anti-oxidant, its antioxidant activity is 20 times of Vitamin C and 50 times of Vitamin E</td>
<td>• Benefit to type 2 diabetic</td>
</tr>
<tr>
<td>• Cleaning Helicobacter pylori</td>
<td></td>
<td>• Anti-tumor</td>
</tr>
<tr>
<td>• Inhibiting oral bacteria</td>
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</table>

- Anti-bacterial: Preventing urinary tract infection, Cleaning Helicobacter pylori, Inhibiting oral bacteria
- Anti-oxidant: Proanthocyanidins is the most strong anti-oxidant, its antioxidant activity is 20 times of Vitamin C and 50 times of Vitamin E
- Other functions: Benefit to type 2 diabetic, Anti-tumor
Bacterial adherence to mucosal surfaces, a prerequisite for the development of urinary tract infections, is facilitated by fimbriae, which are proteinaceous fibers on the bacterial cell wall. Fimbriae produce adhesins that attach to specific oligosaccharide receptors on uroepithelial cells.

Cranberries contain an inhibitor of P-fimbriated E. coli that have been identified as the A-Type Proanthocyanidin (PAC) a compound found only in the American cranberry. These PACs contain alpha-Gal(1->4)beta-Gal receptor sequences similar to those on epithelial cells in the urinary tract. They are responsible for preventing uropathogenic phenotypes of P-fimbriated E. coli from adhering to the urinary tract.
Urinary Tract Infection

Pathogenic bacterias causing Urinary Tract Infection (UTI) are usually Gram-negative bacilus, such as Escherichia coli, Paracolonbacilli, Proteus and etc., in which Escherichia coli accounts 80 to 90 percent.

UTI occurs in all ages including babies and old ages, incidence rate of women is about 2 percent which is more commonly than the rate of men, nearly 40 to 50 percent of women have one infection in their lives. Women of childbearing age have the highest incidence about 5.0%, while pregnant women have 10.2%.
Current Status of UTI

High incidence rate, high recurrence rate

- The first public investigate of urinary tract health in China indicated that in patients, the incidence rate of youth group (18 to 34 ages) accounted 32.4%, initial patient blow 35 ages accounted 31.9%, female patient to male patient is 25 to 75.

High cost of diagnosis & treatment

- In world, around 15 billion people suffer from UTI every year, and costs 600 billion U.S. dollars for diagnosis and treatment. In USA, over 6 million people seek doctors because of acute UTI.

Antibiotics resistance

- The problem of antibiotics resistance is serious at present, “super bacteria” was reported in the world, which could resist more than three or even seven antibiotics. The situation is even more serious in China.
# Anti-bacterial experiments

Through anti-bacterial experiments of cranberry juice, cranberry powder, researchers found that cranberry had effects on gram-negative and gram-positive bacteria.

<table>
<thead>
<tr>
<th>Material</th>
<th>Object</th>
<th>Test result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranberry juice</td>
<td>Escherichia coli</td>
<td>The inclusion of cranberry juice in bacterial growth media was found to significantly impact the doubling time of E. coli.</td>
<td>Iron Chelation by cranberry juice and its impact on Escherichia coli growth[J]. Biofactors, 2011, 37(2):121-130</td>
</tr>
<tr>
<td>European cranberry extracts</td>
<td>Several gram-negative and gram-positive bacteria</td>
<td>European cranberry extracts inhibited the growth of wide range of human pathogenic bacteria, both</td>
<td>Phenolics and anthocyanins in berries of European cranberry and their antimicrobial activity[J]. Medicina(Kaunas),2009, 45(12):992-999</td>
</tr>
<tr>
<td>Cranberry powder</td>
<td>E. coli IA2</td>
<td>Cranberry products can inhibit E. coli adherence to biologically relevant model systems of primary cultured bladder and vaginal epithelial cells.</td>
<td>Cranberry products inhibit adherence of P-fimbriated Escherichia coli to primary cultured bladder and vaginal epithelial cells[J]. Urol, 2007, 177:2357-2360</td>
</tr>
<tr>
<td>Diluted cranberry</td>
<td>Several gram-positive or gram-negative bacterial s</td>
<td>inhibited all 12 bacteria and C. albicans at dilutions of 1:5.</td>
<td>Antibacterial activity of berry fruits used for culinary purposes[J]. Med Food, 2003, 6:57-61</td>
</tr>
</tbody>
</table>
Clinic trials indicated that cranberry juice and cranberry extract had effects to UTI diseases, they could obviously reduce rate of UTI relapse.

<table>
<thead>
<tr>
<th>Clinic trial</th>
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<td>A randomized, placebo-controlled, double-blind study was conducted from October 2007 to September 2009 in Japan, outpatients aged 20 to 79 years who were randomly divided into two groups, examined the rate of relapse.</td>
<td>relapse of UTI was observed in 16 of 55 (29.1 %) patients in group A and 31 of 63 (49.2 %) in group P, cranberry juice prevented the recurrence of UTI in a limited female population with 24-week intake of the beverage.</td>
<td>A randomized clinical trial to evaluate the preventive effect of cranberry juice (UR65) for patients with recurrent urinary tract infection J Infect Chemother 19(1):112-7</td>
</tr>
<tr>
<td>performed a retrospective analysis of 82 transplant recipients with recurrent UTIs, who underwent prophylaxis with cranberry or L-methionine or both modalities. 30 patients without prophylaxis served as controls. Analyzed symptoms, pyuria/nitrituria, and incidence of UTI events during 1 year before versus after initiation of prophylaxis.</td>
<td>Cranberry reduced the annual number of UTI episodes by 63.9% from 3.6 ± 1.4 to 1.3 ± 1.3/year (P &lt; .001) and L-methionine by 48.7% from 3.9 ± 1.8 to 2.0 ± 1.3/year (P &lt; .001). Cranberry juice and L-methionine successfully reduced the incidence of UTI after renal transplantation.</td>
<td>Prophylaxis of recurrent urinary tract infection after renal transplantation by cranberry juice and L-methionine Transplant Proc 44(10):3017-21</td>
</tr>
<tr>
<td>370 patients received intensity-modulated radiotherapy for prostate cancer; 184 patients were also treated with enteric-coated tablets containing highly standardized cranberry while 186 served as controls. During external beam radiotherapy (over 6–7 weeks), all patients underwent weekly examination for urinary tract symptoms.</td>
<td>In the cranberry cohort (n = 184), 16 LUTIs (8.7%) were observed, while in the control group (n = 186) 45 LUTIs (24.2%) were recorded. This difference was statistically significant. It suggested a generally protective effect of cranberry extract on the bladder mucosa.</td>
<td>Enteric-coated, highly standardized cranberry extract reduces risk of UTIs and urinary symptoms during radiotherapy for prostate carcinoma Cancer Manag Res</td>
</tr>
</tbody>
</table>
Clinical effects for UTI

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<td>The study population included 20 (F/M: 13/7) patients with neurogenic bladder with the mean age of 7.25 ± 3.49 (4, 18) years. Six months of treatment with placebo; after a week of wash-out period treatment of cranberry extract tablets (1 capsule/day) for an additional 6 months. Randomization was performed sequentially. Patients and care givers were blinded to drug assignment.</td>
<td>The median UTI rate was 0.5/year during placebo usage whereas 0/year during cranberry capsule usage. Decrease in infection rate was significant with cranberry capsule usage ($P = 0.012$). Decrease in the percentage of the pyuria was also recorded as significant ($P = 0.000$). It concluded that cranberry capsules could be an encouraging option for the prevention of recurrent UTI in children with neurogenic bladder caused by myelomeningocele.</td>
<td>Urinary Tract Infection Prophylaxis in Children with Neurogenic Bladder with Cranberry Capsules: Randomized Controlled Trial. ISRN Pediatr doi: 10.5402/2012/317280</td>
</tr>
<tr>
<td>This open label pilot study 12 Women between the ages of 25 and 70 years old were included with a history of a minimum of 6 UTIs in the proceeding year. The women took one capsule twice daily for 12 weeks containing 200 mg of a concentrated cranberry extract standardized to 30% phenolics.</td>
<td>All 12 subjects participated in the 12-week study and were available for follow up 2 years later. During the study none of the women had a UTI. No adverse events were reported. Two years later, eight of the women who continue to take cranberry, continue to be free from UTIs. Indicated that A cranberry preparation with a high phenolic content may completely prevent UTIs in women who are subject to recurrent infections.</td>
<td>Can a concentrated cranberry extract prevent recurrent urinary tract infections in women? A pilot study. Phytomedicine 14(4):237-41</td>
</tr>
</tbody>
</table>
Helicobacter pylori infection (HPI) is a major cause of peptic ulcer disease and gastric cancer, lot of researches indicated that over 90% of duodenal ulcer and 80% gastric ulcer are caused by HPI. On 1994, HPI was classified as Type I carcinogen by WHO/IARC.

HPI has strong infectivity, a wide investigation covering 19 provinces, 10 cities, 39 centers was held by HPI group Chinese Society Of Gastroenterology on 2001-2004, it suggested that infection rate was high and significant difference (from 40% to 90%) in difference area, average rate was 59%.
## Anti-adhesion activity on HPI

Adherence stage is necessary for HPI to grow on gastric mucosa epithelial cell, it’s hard for HPI to adhere on parietal cell when cranberry is there, then HPI couldn’t reproduce on gastric wall and be flushed out. This mechanism which effects by diet is a good alternative option to medicines.

<table>
<thead>
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<th>Trial</th>
<th>Result</th>
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<tbody>
<tr>
<td>A prospective, randomized, double-blind, placebo-controlled trial was conducted in Linqu County of Shandong Province, China, where 189 adults aged 48.9 ± 11.2 years (mean ± SD) with H. pylori infection were randomly divided into two groups, cranberry juice (n = 97) and placebo (n = 92). Participants were assigned to orally receive two 250-ml juice boxes of cranberry juice or matching placebo beverage daily for 90 days.</td>
<td>At day 35 of intervention, 14 of the 97 (14.43%) from the cranberry juice treatment group and 5 of the 92 (5.44%) of the placebo recipients had negative $^{13}$C-urea breath test results. It suggested that regular consumption of cranberry juice can suppress H. pylori infection in endemically afflicted populations.</td>
<td>Efficacy of cranberry juice on Helicobacter pylori infection: a double-blind, randomized placebo-controlled trial. Helicobacter. 2005 Apr;10(2):139-45</td>
</tr>
<tr>
<td>A double-blind randomized clinical study was carried out. 177 patients with H. pylori infection treated with OAC for 1 week were randomly allocated to receive 250 mL of either cranberry juice (cranberry-OAC, n = 89) or placebo beverage (placebo-OAC, n = 88) twice daily and only cranberry juice or placebo beverage for the next 2 weeks.</td>
<td>For female subjects, the eradication rate was higher in the cranberry-OAC arm (n = 42, 95.2%) than in the placebo-OAC arm (n = 53, 86.8%) and significantly higher than in the non-placebo-OAC group (n = 425, 80%; p = 0.03). These results suggest that the addition of cranberry to triple therapy improves the rate of H. pylori eradication in females.</td>
<td>Effect of cranberry juice on eradication of Helicobacter pylori in patients treated with antibiotics and a proton pump inhibitor. Mol Nutr Food Res 51(6):746-51</td>
</tr>
</tbody>
</table>
Anti-Porphyromonas gingivalis

Porphyromonas gingivalis is the major cause of periodontitis, recent research indicated that A-type procyanidines of cranberry couldn’t reduce bacterial reproduction, but it’s a strong inhibitor to prevent biofilm formation on gingiva. A-type procyanidines reduced the planting ability of Porphyromonas gingivalis, and took good effect on periodontitis.

Advantages of Cranberry

Safe for long term usage

- Cranberry has been consumed for more than 500 years, now in north America, it’s still a food ingredient be applied as jam, juice and pie, no side-effects were found.

No antibiotics resistance

- cranberry has the anti-bacterial effect by inhibiting adherence of bacteria Special, this mechanism is difference as the antibiotic.

Better health effects

- There is plenty of healthy active substances and microelements in cranberry.
Anti-oxidant

Oligomeric Proanthocyanidins (OPC) is the most effective anti-oxidant and the strongest scavenger on free radicals discovered by human beings till now. The capability of anti-oxidation of OPC is 50 times higher than vitamin E and 20 times higher than vitamin C, it provides the most efficient and simplest means of anti-oxidation and anti-aging for people all over the world.

China researcher used different doses of cranberry in natural aging mice model and irradiated mice model, respectively, for 30 days. The activity of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) and the content of malondialdehyde (MDA) were measured in blood and liver samples, respectively. They found cranberry could significantly enhance the activity of SOD and GSH-Px in blood and liver (P<0.05), decrease the level of MDA in blood and liver (P<0.05). It demonstrates cranberry can improve the antioxidant ability in both natural aging and irradiated mice.

Recently a study was conducted to investigate the effects of cranberry power on antioxidant defense system in rats fed an atherogenic diet and injected with lipopolysaccharide (LPS). Total antioxidant status measured by ferric reducing ability of plasma (FRAP) was significantly reduced by LPS injection (24%) and was restored by the cranberry powder treatment (P<0.05). In addition, the mean level of plasma total phenolics was significantly decreased by LPS injection (P<0.05) and tended to be increased when cranberry powder was incorporated into the diet. Activity of serum superoxide dismutase (SOD) tended to be lowered by LPS injection and declined further in cranberry powder fortified groups.

1. 蔓越莓对衰老小鼠和幅照小鼠抗氧化功能的影响 《浙江预防医学》2007年第05期
Other functions

**Type II diabetes**
- It demonstrates that supplementation of a whole cranberry powder at 2% in the diet can attenuate an age-related decline in basal level of insulin and insulin release in response to oral glucose challenge.
- 1 cup Cl for 12 weeks is effective in reducing serum glucose and apoB and increasing apoA-1 and PON-1 activity, so may have favorable effects on reducing CVD risk factors in type 2 diabetic male patients.
- ...

**Anti-cancer / Anti-tumor**
- Phytochemical extracts from the American cranberry (Vaccinium macrocarpon) can affect the behavior of human prostate cancer cells in vitro and further support the potential health benefits associated with cranberries.
- PAC-1A has demonstrated chemotherapeutic potential to treat a broad spectrum of NBs including highly malignant tumors that show resistance to standard chemotherapeutics and apoptotic stimuli.
- Cranberry extract at doses of 0, 5, 10, 20, and 40 mg/mL significantly inhibited proliferation of SGC-7901 cells, and this suppression was partly attributed to decreased PCNA expression and apoptosis induction.
- ...

2. The effects of cranberry juice on serum glucose, apoB, apoA-I, Lp (a), and Paraoxonase-1 activity in type 2 diabetic male patients J Res Med Sci 17(6):Epub
About JF Health

Zhejiang Jianfeng Health Technology Co., Ltd. is wholly-owned subsidiary of JF Group (SSE stock code 600668) for development strategy on health industry. JF-Health has registered capital 30 million RMB and possesses two wholly-owned subsidiaries, Zhejiang Renshoutang & Ybhealth.
About JF Health

Three product series stand like a tripod, complement each other and help JF-Health to become more strong.

Health food, function food

JF Health has GMP certificated soft capsule, hard capsule production lines, solid drinks and jelly sweets production lines.

Herbal Extract

Based on the successful operating experience of JF-Natural, JF Health has big advantage on active substance extraction from TCM herbs and Zhejiang geo-authentic TCM herbs.

Qualified TCM herbs & herbal slices

Using the hundred years brand "RENSHOUTANG", JF-Health also concentrates on the development and promotion of Zhejiang geo-authentic TCM herbs & prepared slices.
About JF Health

Over 20 years experiences on natural herbal extract industrial

Our philosophy: Green, Natural, Health, Safety

To be the pioneer of innovative health product

- Member of China Health Care Association
- Director unit of Zhejiang Health Products Association
- Alliance member of China Medical Pharmaceutical Material Association
About JF Health

- JF Group (SSE Stock code: 600668), Zhejiang well-known firm
- JF Pharmaceutical, top 100 enterprise in China medicine, Key high-tech enterprise of national Torch Plan, top 10 enterprise in Zhejiang medicine.
- Owns academician workstation, provincial new drug research center and two national postdoctoral postdoctoral programmes.
- Jianfeng Graduate School of Business
- Strategic partner of NAPI
Our Advantages

Safety
- Raw material is imported from Canada, where pesticide residue is strictly controlled.
- Only use Ethanol and water for extraction.

Effectiveness
- Keep more active substances by good extraction procedure
- OPCs and Anthocyanins are main controlled items of finish product
- Fingerprint of cranberry

Stability
- Stability research indicates our product is stable within shelf life (according to suggested conditions)
Cranberry Extract of JF Health is all imported from ATOKA Canada, ATOKA was founded in 1984, has over 30 years experience on planting and developing of cranberry, now ATOKA owns the biggest cranberry farm in world.

ATOKA is the biggest manufacturer and distributor of cranberry in Canada.
Raw Material Source

Certificate of Origin
Cranberry Extract

Production Flow Chart

Cranberry Fruit

Extracted by Ethanol

Concentration

Purification

Concentration

Spay Drying

Spay Drying

Packing

Packing

Cranberry Extract (OPC 25%)

Cranberry Extract (OPC 95%)
Quality Control

Cranberry Extract of JF Health
Quality Control

Fingerprint of Cranberry Extract
Quality Control

Certificate of Analysis

Assay
- OPCs, Anthocyanins

Normal items
- Particle size, Bulk density, Ash, Loss on drying

Heavy metals
- Total heavy metals, Pb, Hg, Cr

Solvent residue
- Ethanol

Pesticide residue
- DDT, Benzene hexachloride

Microbiology
- Total plate count, Mold & yeast, E. Coli, Staphylococcus aureus
Quality Control

- 3rd-party Laboratory
- eurofins
  the world leader in food and biopharma product testing
  113 pesticides residue by GC/MS
  112 Pesticides residue by LS-MS/MS
## Our specifications

<table>
<thead>
<tr>
<th>Cranberry Extract OPC 95%</th>
<th>Cranberry Extract OPC 25%</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High purity, no additive</td>
<td>• Dextrin be used only</td>
</tr>
<tr>
<td>• Suitable for soft capsules</td>
<td>• Suitable for simple prescription</td>
</tr>
<tr>
<td>• Suitable for complex prescription or small size capsule</td>
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</tbody>
</table>

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Toxicity testing of grape seed extract proved that the LD50 of OPCs to rats was 4000mg/kg, and LD50 of cranberry juice was more than 5000mg/kg.

Based on the reports, we suggest our cranberry extract OPC 95% dosage is 36 to 108mg per day.
**Application**

- **Cranberry Solid Drink Powder**
  - Cranberry Extract
  - Other Active substance
  - Dextrin
  - ......

- **Cranberry Capsule**
  - Cranberry Extract
  - Vitamin C
  - ......

- **Cranberry Soft Capsule**
  - Cranberry Extract
  - Vitamin C
  - Vitamin E
  - ......
Thanks

---------------- By Zhejiang Jianfeng Health Technology Co., Ltd. 
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