

# CRANBERRIES: EVALUATING THE EVIDENCE OF HEALTH BENEFITS

Ocean Spray® cranberries launched in South Africa

## Introduction

Unhealthy diet and lack of exercise are leading global risks to health. In addition to protecting against all forms of malnutrition, a healthy diet helps to protect against noncommunicable diseases, including heart disease and stroke, obesity, diabetes and cancer.<sup>1-4</sup> As an essential component of this diet, the World Health Organisation advises intake of 400 g of vegetables and fruit per day in adults, the equivalent of five servings of 80 g each.<sup>2</sup>

Fruit and vegetables, the classification of which excludes potatoes, sweet potatoes, cassava and other starchy roots, are foods that are low in energy, comparatively rich in micronutrients, phytochemicals and other bioactive compounds, and good sources of dietary fibre. Because they promote satiety, diets high in fruit and vegetables are associated with less weight gain than those with lower intake and WHO recommends that whole grain cereals, vegetables and fruits are the most appropriate sources of dietary carbohydrate.<sup>2,4</sup> Recommendations are that a wide variety of different colours and types of vegetables and fruit should be consumed every day, including fresh raw fruit, or, where it may be more palatable, fruit that is cooked or dried. Tinned or frozen vegetables and fruit (without added sugar, salt or fat) can be nutritious alternatives to fresh varieties. 100% fruit juices contain most of the micronutrients that are present in the fruit, but do not contain the fibre and may be high in extrinsic sugar content, especially where sugar is added.<sup>1</sup>



## Cranberries

### KEY MESSAGES

- South African dietary guidelines recommend that adults and children should “eat plenty of vegetables and fruit every day”.<sup>1</sup>
- Variety is important and consumption of fibre-rich, high-polyphenol fruits, such as the cranberry, is important for the maintenance of good health and quality of life.
- Because of the cranberry’s high nutritional and antioxidant content, it has earned a formidable reputation as a superfruit.
- *In vitro* and animal studies, and clinical studies in humans indicate that cranberry products have potential to help reduce risk factors associated with noncommunicable diseases.

The cranberry is a fruit that is native to North America. It grows on long running vines in sandy bogs and marshes and is widely consumed for its bold, tart and refreshing taste. Because of the unpalatable tartness and astringency of the raw berry, cranberries products are often sweetened and consumed in the form of juice or dried berries, which may be eaten alone or added to baked goods and confectionaries, cereal bars, cheeses, and sauces. Cranberry powders and extracts are used in food products and dietary supplements.

Cranberries are widely known for their beneficial effects on health. They are rich in fibre, vitamins C, E and K and rank

high among fruits in antioxidant quality and quantity. They are a particularly rich source of flavanoids and polyphenols, including procyanidins, quercetin, myricitrin and anthocyanins.<sup>5-7</sup>

In *in vitro* studies, polyphenols have been associated with antibacterial, antiviral, antimutagenic, anticarcinogenic, antitumourigenic, antiangiogenic, anti-inflammatory and antioxidant properties. Clinically, berry extract and cranberry-based products have been shown to confer numerous health benefits, with potential to improve cardiovascular health, prevent urinary tract infections (UTIs) and maintain dental and periodontal health (Table 1).<sup>7-9</sup>

**Table 1. Potential health effects of cranberry extract and cranberry-based products<sup>6-23</sup>**

<i>In vitro</i> studies and <i>in vivo</i> animal models	Human clinical studies
<ul style="list-style-type: none"> <li>• Reduced CRP</li> <li>• Reduced proinflammatory interleukins</li> <li>• Increased NO synthesis</li> <li>• Reduced ACE; angiotensin II and angiotensin type I receptor expression</li> <li>• Suppress <i>Helicobacter pylori</i> infection</li> <li>• Improve pancreatic <math>\beta</math>-cell mass and responsiveness to glucose</li> <li>• Reduce biofilm formation and adhesion of pathogenic bacteria</li> <li>• Reduce biofilm formation and adhesion of <i>Candida</i> sp.</li> <li>• Reduce production and activity of bacterial proteolytic enzymes</li> </ul>	<ul style="list-style-type: none"> <li>• Improvements in cardiovascular parameters and markers of the metabolic syndrome               <ul style="list-style-type: none"> <li>– Reduce LDL cholesterol</li> <li>– Reduce oxidative modification of LDL cholesterol</li> <li>– Increase HDL cholesterol</li> <li>– Reduce triglycerides</li> <li>– Improve endothelial function</li> <li>– Reduce glycaemic response (improve insulin sensitivity)</li> <li>– Reduce fasting plasma glucose</li> <li>– Reduce blood pressure</li> </ul> </li> <li>• Reduce CRP</li> <li>• Elevate plasma antioxidant capacity</li> <li>• Modulate ulcerogenic gastric <i>H. pylori</i> colonization</li> <li>• Decrease cariogenic <i>Streptococcus mutans</i> and total bacterial counts in saliva</li> <li>• Protection against urinary tract infection (UTI)</li> <li>• Reduce biofilm formation and adhesion of pathogenic bacteria</li> <li>• Improvement of lower urinary tract symptoms (LUTS) in men</li> <li>• Modulation of immune response and reduction of symptoms associated with viral upper respiratory tract infection</li> </ul>

CRP: C-reactive protein; NO: nitric oxide; ACE: angiotensin converting enzyme

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## Cranberries and cardiovascular health

The potential for favourable effects of cranberry on cardiovascular health has been demonstrated in a number of *in vitro* studies, animal studies and clinical trials (Table 1). These effects include modulation of risk factors, including dyslipidaemia, diabetes, hypertension, inflammation, oxidative stress, endothelial dysfunction, arterial stiffness and platelet function.

In a recently published double-blind, placebo-controlled, parallel-arm study, 56 men and women were randomised to low-calorie cranberry juice 480 ml daily or placebo in conjunction with a fully controlled diet that included 3-5 servings of fruits or vegetables daily.<sup>19</sup> Study participants were aged between 25 and 65 years (mean age 50 years) with a mean body mass index (BMI) of 28 kg/m<sup>2</sup>. They were nondiabetic, non-smokers in basic good health with triglycerides <3.39 mmol/l.

After 8 weeks, in comparison to

placebo, fasting plasma triglycerides, serum CRP, diastolic blood pressure and fasting plasma glucose were all significantly lower in the group assigned to cranberry juice. Among participants with high baseline values, the juice was also associated with a beneficial effect on homeostasis model assessment of insulin resistance. Similarly, the treatment effect on triglycerides was greater among subjects with higher baseline values.

This study was small and included overweight, but otherwise healthy individuals without other significant risk factors for cardiovascular disease. Nevertheless, these intriguing results, combined with those from observational studies showing that anthocyanins and flavonols are associated with reduced risk of cardiovascular events and cardiovascular death, warrant further well designed prospective studies, which include patients at higher risk for cardiovascular disease.<sup>7</sup>

## Cranberries and prevention of urinary tract infection

A number of clinical studies have shown that cranberry is effective in preventing UTIs in adults and children, including pregnant women, those with frequent recurrent UTI and after surgery.<sup>7,9-13</sup> Cranberry products and extracts have been widely advocated for this purpose. If they are effective, they may provide an attractive alternative to the use of low dose antibiotics, which carries a serious potential risk of development of antibiotic resistance with important consequences to public health.

Various mechanisms have been proposed to account for the efficacy of cranberry observed in clinical studies. The most important of these is the anti-adhesion properties, thought to be imparted by the anthocyanidin/proanthocyanidin moieties. Prevention of adhesion of pathogenic *E. coli* to cells in the urinary tract impairs colonisation and subsequent infection.<sup>7,15-18</sup>

However, whereas the anti-adhesion properties of cranberry can be demonstrated both *in vitro* and in the urine *ex vivo*, evidence in clinical studies for prevention of UTI has been inconsistent. Choice

of study participants, small sample sizes, product used, dose and method of administration, length of exposure, compliance with regimen and choice of comparator agent varies widely, and are likely to account for heterogeneity among results. Two recent large meta-analyses illustrate this, with contradictory results. Both aimed to update the Cochrane meta-analysis published in 2008, which concluded that cranberry products are associated with reduction in the number of symptomatic UTIs, particularly in women with recurrent UTI. Wang and colleagues (2012) analysed 13 studies including 1616 patients and found that cranberry was associated with a protective effect against UTI, despite considerable heterogeneity among studies (Table 2).<sup>9</sup> In contrast, Jepson and colleagues (2012) reviewed 24 studies (n=4473) and included 13 of these in qualitative meta-analyses.<sup>13</sup> They found that, although smaller studies were positive, no statistically significant benefit of cranberry could be demonstrated when the results of a much larger study were added. Interestingly, they found that, although cranberry was not significantly

different from placebo overall, it was also not significantly different to antibiotics (RR 1.31; 95%CI 0.85-2.02 for women; RR 0.69; 95%CI 0.32-1.51 for children). In subgroup analyses, the risk ratios (RR) associated with cranberry use for women with recurrent UTIs (RR 0.74; 95%CI 0.42-1.31), older people (RR 0.75; 95%CI 0.39-1.44) and children with recurrent

UTIs (RR 0.48; 95%CI 0.19-1.22) were all less than 1, but the confidence intervals included 1 (not statistically significant) and were wide. Heterogeneity among study designs and poor quality of individual studies complicate analyses and the interpretation thereof, and may potentially bias aggregate outcome measures towards the null.<sup>24</sup>

**Table 2. Meta-analyses of cranberry for prevention of UTI, based on the results from 10 trials (n = 1494)<sup>9</sup>**

Population group	Risk ratio (RR)	95% Confidence interval
Cranberry user vs. nonuser	0.62	0.49-0.80
Subgroups		
Women with recurrent UTI	0.53	0.33-0.83
Female population	0.49	0.34-0.73
Children	0.33	0.16-0.69
Cranberry juice drinkers	0.47	0.30-0.72
Subjects consuming cranberry-containing products more than twice daily	0.58	0.40-0.84

## Cranberries and drug interactions

Although *in vitro* cranberry is an inhibitor of cytochrome P450 (CYP) 3A4 and CYP 2C9, unlike grapefruit juice, no clinically relevant drug interactions, with perhaps the exception of warfarin, have been demonstrated with normal consumption of cranberry products.<sup>25</sup> Although the majority of the pharmacokinetic and pharmacodynamic studies did not find a significant interaction between cranberry

and warfarin, there are case reports of clinically significant interactions associated with elevated INR.<sup>26</sup> Therefore, although it may not be necessary to avoid cranberry altogether in patients taking warfarin, it seems prudent to approach the combination with caution and to consider cranberry as a potential contributor when INR is at a supratherapeutic level in a patient receiving warfarin.

## Ocean Spray® launches its cranberry range in South Africa

Ocean Spray® is an agricultural cooperative owned by more than 700 cranberry growers in North America, Canada and Chile. Formed in 1930, Ocean Spray® is now the leading producer of cranberry juices, juice drinks and dried cranberries, and is the best-selling brand in the North American bottled juice category. Their products are sold in over 90 countries worldwide. A selection of Ocean Spray® cranberry products, including juices, sauces and dried berries are now available from leading retailers in South Africa.

More information may be found at [www.oceanspray.com](http://www.oceanspray.com).

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