Summary of interactions between red berries and treatment for blood clotting disorders

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Warfarin, a blood thinner, is a common first line treatment for patients whose blood abnormally clots within the body. This medication predisposes patients to stroke, pulmonary embolism and heart attacks. International Normalised Ratio (INR) is a biomarker that measures blood clotting time. Values of INR above 4.0 increase risk of bleeding [Li et al., 2006].

A search of the literature found incidences of people concomitantly taking warfarin and ingesting products of two types of red berries, who subsequently suffered bleeding episodes or were recorded with large INR levels. These berries were cranberries, *Vaccinium macrocarpon*, and goji berries, *Lycium barbarum*.

In 2004, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a warning about possible bleeding enhancement effect of cranberry juice on warfarin, based on twelve reports they received [MHRA, 2004]. Other reports of people taking warfarin included the death of a man drinking 300-400ml cranberry juice for six weeks, and another man experiencing major bleeding shortly after beginning drinking 710 ml cranberry juice daily[reviewed by Ge et al., 2014].

Case reports are useful to generate hypotheses, but clinical trials are required to determine cause-effect relationships. Four randomised controlled clinical trials investigating the effect of cranberry juice on INR levels of people taking warfarin were found [reviewed by Izzo, 2012]. Most of these trials used cross-over or parallel group designs, sometimes blinded, with a power of 80% and type I error of 5%. Of these four trials only one found a mean significant increase in INR values of those intaking cranberry matter (57g per day) compared to control groups. It is notable that no clinical trials could be found published after 2009. In the abscence of high quality and large scale clinical trials, it has been difficult to establish the enhancement effect of cranberry juice on warfarin anticoagulation.

Case reports have been published whereby patients on warfarin medication experienced raised INR levels or bleeds within a week of ingesting goji berry juice [reviewed by Ge et al., 2014]. One such patient consumed 30ml goji juice morning and evening for four days before experiencing bruising and rectal bleeding. Because of the INR changes in several case reports, an enhancement effect of goji derivative products on warfarin anticoagulation may exist. However, no published clinical trials investigating this interaction, nor any recommendation by MHRA about this association could be found. Therefore this interaction effect appears speculative at present.

Words:498

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