# Interaction between red berries and treatment for blood clotting disorders

Blood clotting disorders occur when there is too much or too little protein in the blood, called platelets. Patients who tend to form blood clots within the body are at risk of stroke, pulmonary embolism, or heart attack. A ubiquotous medication given to patients to prevent this is warfarin. Warfarin has a narrow therapeutic range, meaning that too higher dose may cause excessive bleeding, while too lower dose will be ineffective. Because of the difference in individual responses to warfarin, and interactions of warfarin with other drugs and ingested substances, the time taken for a patient’s blood to clot must be monitored regularly to ensure a safe dose of warfarin is administered. The INR is a measurement of the time taken for blood to clot.

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 abnormally large INR levels. These berries were cranberries (*Vaccinium macrocarpon*) and Gojis (*Lycium barbarum*).

In 2004, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a warning about a suspected interaction between cranberry juice and warfarin, based on twelve reports they received (MHRA, 2004). Since the MHRA report, five clinical trials have been identified investigating the relationship between cranberries and warfarin

MHRA, 2004, <https://webarchive.nationalarchives.gov.uk/20141206134907/http://www.mhra.gov.uk/home/groups/pl-p/documents/websiteresources/con007448.pdf>

Warfarin, a blood thinner, is a common first line treatment for patients whose blood tends to clot within the body. This condition predisposes them to stroke, pulmonary embolism and heart attacks. INR is the biomarker that measures blood clotting time. Warfarin has a narrow therapeutic range. Values of INR between 2.0 and 3.0 are considered in this range, while values above 4.0 increase risk of bleeding (1).

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In 2004, the Medicines and Healthcare products Regulatory Agency (MHRA) issued a warning about a suspected interaction between cranberry juice and warfarin, based on twelve reports they received (MHRA, 2004). They recommonded that patients taking warfarin cease drinking cranberry juice unless a known health benefit outweighs the risk, and that increased INR monitoring should be performed on patients taking both substances.

Case reports are useful to generate hypotheses, but clinical studies 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 (Ansell et al., 2009; Abdul et al., 2008; Li et al., 2006; Lilja et al, 2007, review by Izzo, 2012), of which the abstract by Lilja et al. was accessible. These trials used cross-over or parallel group designs, sometimes blinded, with a power of 80% and type I error of 5% (although Li et al. used a one sided test). Of these four trials only Abdul et al. found a mean significant increase in INR values (2.8) in healthy volunteers drinking cranberry juice compared to the healthly volunteer control group (2.6). It is notable that no clinical trials could be found published after 2009. With a lack of quality clinical trials it has been difficult to establish a cause-effect relationship between the interaction of cranberry juice and warfarin. As such, the recommendation by the MHRA (2004) is still valid.

Case reports have been published whereby patients on warfarin medication experienced raised INR levels or bleeds within a week of ingesting goji berry juice or wine (reviewed by Ge et al., 2014; Zhang et al., 2015). Because of the INR changes in several case reports, an interaction between gojis and warfarin may exist ( Ge et al., 2014). However, no published clinical trials investigating this interaction were found in the literature, nor any recommendation by MHRA about concomitant intake of goji products with warfarin medication. Until futher investigation.

1. MHRA
2. Li et al.
3. Ansell et al.
4. Abdul et al.
5. Izzo
6. Ge
7. Zhang