**Chondroitin ─ what are its drug interactions?**

Prepared by UK Medicines Information ([UKMi](http://www.ukmi.nhs.uk/ukmi/about/default.asp?pageRef=1)) pharmacists for NHS healthcare professionals

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## Background

Chondroitin is a naturally occurring mixture of glycosaminoglycans (GAG) and disaccharide polymers (1). The disaccharide units repeated in chondroitin are made of D-glucuronic acid, D-acetylgalactosamine and sulphates (1). Chondroitin is found in the body in joint cartilage and connective tissue including vessel walls (1). A 2013 summary of the available evidence describing the mechanism of action of chondroitin reports a beneficial effect on the metabolism of different cell lines involved in osteoarthritis. Synthesis of type II collagen and proteoglycan in human articular chondrocytes is increased and production of some pro-inflammatory factors and proteases reduced, thereby reducing cellular death and improving the anabolic/catabolic balance of the extracellular cartilage matrix (2).

Chondroitin is most commonly used orally to reduce pain and facilitate movement in patients with osteoarthritis. It is often combined with glucosamine when used for this indication (3). However the National Institute for Health and Care Excellence (NICE) recommends that neither chondroitin nor glucosamine should be used for the management of osteoarthritis due to limited and uncertain evidence of effectiveness (4). There is no established dose of chondroitin for osteoarthritis, but manufacturers tend to recommend 400-1200mg daily (1). Commercial chondroitin is often of bovine origin but may be from other sources (5). The quality of chondroitin sulphate in several nutraceuticals has been found to be poor therefore it has been recommended that pharmaceutical-grade chondroitin is used (2).

## Answer

There are two published case reports of increased International Normalised Ratio (INR) in patients receiving warfarin who self-medicated with glucosamine-chondroitin supplements (6,7). In one, a 69-year-old man with chronic atrial fibrillation was receiving oral warfarin 47.5mg/week when he started to take glucosamine hydrochloride 3000mg and chondroitin sulphate 2400mg daily. Other medications the patient was taking included fexofenadine (during the allergy season), paracetamol combination product as required for headaches and sumatriptan occasionally for migraines. Four weeks after he started taking the glucosamine-chondroitin supplement, the patient’s INR was found to have risen from 2.58 to 4.52. When the patient’s weekly warfarin dose was reduced to 40mg, his INR fell to 2.15. Three months later, he maintained his target INR despite continuing on the
supplement (6).

The other case report describes a 71-year-old man who had received warfarin 7.5mg/day for atrial fibrillation for five years. The patient’s other medications were ezetimibe, simvastatin, amlodipine, lisinopril, hydrochlorothiazide, aspirin, vitamin C, vitamin E and fish oil. The doses of these medications had remained unchanged for two years. Throughout the time that he had taken warfarin, the patient had also taken glucosamine hydrochloride 1000mg and chondroitin sulphate 800mg daily. Three weeks after increasing his daily supplement dose to glucosamine 3000mg and chondroitin 2400mg, the patient’s INR was found to have increased from 2.3 to 3.9. His INR fell to 2.6 only after the supplement had been stopped and his warfarin dose reduced by 3.75mg on alternate days (7).

The authors of this 2008 case report found further cases in the Food and Drug Administration (FDA) MedWatch Adverse Events Reporting System (AERS) database (n=20), and in a World Health Organisation adverse drug reaction database (n=21), in which warfarin interaction with glucosamine, chondroitin or glucosamine plus chondroitin may have occurred. In three cases (1 FDA, 2 WHO), concomitant use of warfarin and chondroitin alone was reported, but the absence of glucosamine from the chondroitin product used could not be verified. INR was increased with the addition of chondroitin to warfarin in each of these cases. The FDA case reported that INR was increased from 2.9 to 6.6 in a 67 year old male patient who had received warfarin for 2 years on the addition of chondroitin sulphate 1500 mg/day. Two days after the chondroitin was stopped, the INR fell to 2.1 (7).

The possibility of chondroitin (alone) increasing the risk of bleeding in patients receiving anticoagulants or antiplatelet agents cannot be ruled out (8). As it is a component of danaparoid, an anticoagulant that works by inhibiting activated factor X (factor Xa), there is a theoretical risk of chondroitin having an anticoagulant effect in patients who take it for osteoarthritis (8). *In vitro* and animal studies have suggested that chondroitin prolongs bleeding time (9), but significant haematological changes were not seen in patients who received oral or parenteral chondroitin for six months in a non-randomised open-label study (n=200). However patients with cardiovascular or cerebral disease were excluded from this study and no details were given of patients’ drug histories (10).

A search of the literature for this Q&A found no evidence that was supportive of drug interactions between chondroitin and conventional medicines other than warfarin.

Caution should be exercised if chondroitin is used with warfarin or other anticoagulants (such as acenocoumarol and phenindione), direct oral anticoagulants (DOACs) (such as apixaban, dabigatran, edoxaban and rivaroxaban), or antiplatelet agents (such as aspirin, clopidogrel and dipyridamole) or other medicines that may increase the risk of bleeding. It is recommended that patients are monitored for bleeding episodes/changes in coagulation parameters if chondroitin is added to these types of medicines, or if the dose of chondroitin is changed.

Chondroitin is often given in combination with glucosamine. It should be noted that the Medicines and Healthcare products Regulatory Agency (MHRA) recommends patients on warfarin do not take glucosamine. Further information is provided in the ['UKMi Q&A ‘Glucosamine – what are its drug interactions?'](https://www.sps.nhs.uk/articles/glucosamine-what-are-its-drug-interactions/) (11).

## Summary

* There are two published case reports of increased INR in patients receiving warfarin who self-medicated with glucosamine-chondroitin supplements. INR was increased in a further three cases where chondroitin was reportedly used alone.
* Since chondroitin is a component of danaparoid, an anticoagulant that works by inhibiting activated factor X, it might have an anticoagulant effect and could increase the risk of bleeding in patients who are already receiving anticoagulants.
* Caution should be exercised if chondroitin is used with warfarin or other anticoagulants (such as acenocoumarol and phenindione), direct oral anticoagulants (DOACs) (such as apixaban, dabigatran, edoxaban and rivaroxaban), or antiplatelet agents (such as aspirin, clopidogrel and dipyridamole) or other medicines that may increase the risk of bleeding.
* Monitoring for bleeding episodes/changes in coagulation parameters when adding chondroitin to an anticoagulant or antiplatelet, or changing the dose of chondroitin is recommended.
* Chondroitin is often given in combination with glucosamine; readers are therefore advised to refer also to the [UKMi Q&A on glucosamine and drug interactions](https://www.sps.nhs.uk/articles/glucosamine-what-are-its-drug-interactions/).

LimitationsThere is limited published information on chondroitin. The available information relates to chondroitin/glucosamine combinations which makes it difficult to attribute the effect of an interaction to one particular constituent.

### References

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## Quality Assurance

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###  Search strategy

1. Embase (chondroitin sulfate AND exp drug interaction) OR (chondroitin sulfate/it [Drug Interaction]
2. Medline (exp chondroitin sulfates AND exp drug interactions)
3. IDIS ([DR] chondroitin 92520008 AND [DE] drug interaction 50 [until 2014])
4. In-house database (chondroitin AND interact\* (text); chondroitin AND drug interactions (keyword))
5. Micromedex (chondroitin)
6. Stockley’s Drug Interactions (via Medicines Complete) (chondroitin)
7. Dietary Supplements (via Medicines Complete) (chondroitin)
8. Natural Medicines Comprehensive Database (chondroitin)
9. NHS Evidence (“drug interactions” AND chondroitin)
10. Memorial Sloan Kettering Cancer Center site (chondroitin)
11. MHRA website (chondroitin)
12. Cochrane (chondroitin AND interaction)