

Anticoagulants, pain relief and cannabis based products

If you are on long term anticoagulation therapy, there may become a time when you need to explore ways to best manage niggles, joint and muscle pains and you may have already discussed pain relief with your clinician when initiating your treatment.

It's pretty straightforward with anticoagulants; NICE has provided some information advising patients to speak to your GP, anticoagulant clinic or pharmacist before taking any other medication, remedy or supplement. This includes prescription medicines, medicines bought over the counter without a prescription (such as aspirin), and any herbal remedies (such as St John's Wort or similar homeopathic products).

Some treatments can stop anticoagulants working or can increase the effect they have and these can include certain

- antibiotics
- antidepressants
- corticosteroids (medications used to reduce inflammation)
- anticonvulsants (medications used to treat epilepsy)
- non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (take paracetamol instead if you need pain relief)

NICE recommends that patients check the patient information leaflet that comes with the drugs for a full list of medicines that you should avoid and, you should always advise any clinician you engage with that you take anticoagulants

The internet has provided us with access to so much information and if you google 'pain relief for arthritis or muscle pain, natural remedies for pain relief' and add anticoagulants, the screen will pop with links to a plethora of pills, potions and lotions which will cure all your ills.

Unfortunately, some of these treatments whilst seeming to be natural alternatives can cause more harm than good. Often, they are not regulated and have not been through stringent licensing protocols as demanded by evidence based medicines bound by rigorous and robust clinical trials.

There has been a huge surge of advertising for Cannabis oil (CBD oil) and some people may be curious and try a cannabis derived product probably in the hope it will not interfere with their prescribed medications.

So, what is Medical cannabis and cannabis oils? According to www.nhs.uk Medical cannabis is a broad term for any sort of cannabis – based medicine to relieve symptoms. Cannabis based products are available to buy online or over the counter, but frequently their quality and content is not known. They may be illegal or potentially dangerous.

Some products that claim to be medical cannabis such as CBD oil or hemp oil are available to buy legally as food supplements from health stores but there is no guarantee these are of good quality or provide health benefits.

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Getting a prescription for medical cannabis in the UK is limited to

- Children and adults with rare, severe forms of epilepsy,
- adults with vomiting or nausea caused by chemotherapy and
- people with muscle stiffness and spasms caused by multiple sclerosis.

Whilst there is some evidence medical cannabis can help certain types of pain, this evidence is not yet strong or developed enough to recommend it for all types of pain relief.

The risk of using cannabis products containing THC (Tetrahydrocannabinol, the chemical that gives the high) is unclear and clinical trials are needed before they can be used.

The main risks of THC cannabis products are psychosis and dependency on the medicine although scientists believe this risk to be small when its used in a controlled manner and monitored by a doctor.

Do we know if CBD products interact with anticoagulants?

We asked Frances Akor, Consultant Pharmacist, Anticoagulation at Imperial NHS Healthcare Trust to shed some light.

Firstly, it is important to recognise that CBD products sold as food supplements without a medicinal license are not subject to good manufacturing practice requirements. Different CBD products and even different batches of the same product may contain varying quantities of CBD, this may affect the likelihood of a potential drug interaction. Further, although CBD products are frequently advertised as free from THC, they could potentially contain traces of THC.¹ Therefore, although the focus is on whether CBD interacts with anticoagulants it is also worth considering the potential for interaction between THC and anticoagulants. Due to the lack of licensed cannabis-based medicinal products there has been limited surveillance of drug interactions in humans, much of the available data is based on laboratory experiments. Therefore, there is still relatively little known about drug interactions with cannabis-based products.²

So, what *do we know*?

We know that laboratory experiments have shown that CBD blocks certain enzymes produced by the liver that break down (metabolise) a range of drugs. Some of the enzymes blocked by CBD are involved in the metabolism of warfarin and the DOACs, rivaroxaban and apixaban.^{3,4} It is anticipated that the use of CBD in a patient taking warfarin could result in a reduction in the metabolism of warfarin, leading to a build-up of warfarin, a high INR and even a serious bleed, if extreme. In a published case report, smoking cannabis significantly raised the INR of a patient taking warfarin to over 10 and was associated with an upper gastrointestinal bleed.⁵ In another case report, a patient taking warfarin received CBD oil for epilepsy seizures that continued despite the use of conventional anti-epilepsy drugs. Warfarin dosage adjustments were made in an effort to maintain an INR within therapeutic

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range. However, with gradual increased doses of CBD oil, an increase in the INR was seen, with the INR getting as high as 6.9.⁶ Some studies have suggested that THC may also block the main enzyme that metabolises warfarin.⁷ In addition, it has been suggested that THC may displace warfarin that is bound to proteins in the blood making more 'free' active warfarin available.⁸

At present there are no published case reports concerning an interaction between CBD and the DOACs. Based on laboratory experiments there is potential for reduced metabolism of apixaban and rivaroxaban when CBD is used⁷, however it is *currently* anticipated that an interaction would be unlikely to be clinically significant.⁹ There is also some data that CBD may potentially affect the pathways involved in the metabolism of edoxaban and dabigatran,¹⁰ therefore an interaction with these DOACs cannot be ruled out.

In short, we know that there is a potential for an interaction between CBD and warfarin / DOACs. However, further human studies are required to fully evaluate CBD interactions and safety profile.¹¹

In terms of NICE guidance, CBD is only recommended for use as a licensed medicinal product within its licensed indications (see above).^{12,13} NICE guidance on use of cannabis-based medicinal products for chronic pain states, 'Do not offer CBD to manage chronic pain in adults unless as part of a clinical trial'.¹⁴

In addition, the Food standards Agency (FSA) is advising people who are pregnant, breastfeeding or taking *any* medication not to consume non-prescription CBD products.¹⁵

Aside from the potential interactions, there are also potential side-effects such as drowsiness which may affect the ability to drive.¹⁶

For these reasons, I would advise against the unsupervised use of non-prescription CBD products. If you are experiencing pain do speak to a relevant clinician for a review of your current medicine and maybe a referral to a specialist pain service for management that takes into account all your other medicines including your anticoagulants and minimises the risk of you experiencing harm from drug-interactions or side-effects. If you are already using a CBD product without supervision, please discuss with your anticoagulation service provider for a review as appropriate. If you are still considering CBD, please discuss with your GP and inform your anticoagulation clinic beforehand for discussion and relevant support.

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