



Dr Wai Liu, of St George's, University of London, discusses new research which demonstrates that cannabinoids used in sequence with chemotherapy are a more effective treatment for cancer

Cannabis meets chemotherapy

In early July, Greece became one of six EU member states and several countries around the world to legalise the use of cannabis for medical purposes. The controversial decision, which saw cannabis downgraded to a Table B drug alongside the likes of methadone and opium, comes after extensive research which has already shown the efficacy of cannabis and its derivatives against a range of conditions, among them chronic and neuropathic pain, MS-related muscle spasms and stiffness, depression and anxiety, nausea and vomiting, and sleep disorders.

Now, new research from St George's, University of London, UK, has confirmed that cannabinoids – the active chemicals in cannabis – are effective at killing leukaemia cells, particularly when used in combination with chemotherapy treatments.

The study, which was led by senior research fellow Dr Wai Liu and originally published in the *International Journal of Oncology*, is the first to show that the order in which cannabinoids and chemotherapy are used is a key determinant in the overall effectiveness of the treatment.

Most promising of all, it suggests that a lower dose of chemotherapy could be used, in concert with cannabinoids, to produce the same therapeutic result – with fewer of the often unpleasant and sometimes debilitating side effects of chemotherapy.

More research is needed to understand both the full potential of treating patients with cancer with cannabinoids and any possible adverse effects,



Dr Wai Liu

but Liu's study is nonetheless an exciting addition to the growing body of evidence which supports the use of cannabis as a medical substance.

Speaking to PEN, Liu provides an insight into the research and reflects on what more is needed to realise cannabinoids as a cancer therapeutic.

How and why does the order in which cannabinoids and chemotherapy are used impact on the effectiveness of this therapy against cancer cells?

It still is a little unclear what the exact mechanism is that underpins this effect. Our results showed that using chemotherapy before cannabinoids resulted in more apoptosis compared to the reverse order. It is possible that the chemotherapy used up-front alters the apoptotic threshold in the cell, resulting in their responding to subsequent chemical assaults more easily. Similarly, the chemotherapy used may simply prime the cell to the cytotoxic effects of cannabinoids.

We have data from other studies where this sequential administration is important. In these other cases, we have shown that the first drug can increase the expression of proteins that promote apoptosis. This means that a subsequent hit to the cell with another cytotoxic agent is more likely to result in apoptosis as the cell is already primed/prepared. This is something we are currently exploring.

Using lower doses of chemotherapy would mean that its harmful side effects could be lessened, but are there potential adverse effects of using cannabinoids instead, alone or in combination?

The possibility that side effects could be minimised by reducing doses but still achieve

Liu's study demonstrates for the first time that the order in which cannabinoids and chemotherapy are used is crucial to determining the overall effectiveness of the treatment





sufficient anticancer activity is precisely what we see as beneficial. The cannabinoids that have been studied most in cancer are THC (tetrahydrocannabinol) and CBD (cannabidiol) – THC is psychoactive, which intrinsically limits the dosage that can be used. As this dose would be low, the anticancer effect may not be optimal. The adverse effects of THC tend to tiredness, dryness of mouth and of course the well-known psychoactivity. CBD on the other hand is not psychoactive; however, side effects that have been reported to me have been minimal, such as tiredness, and in one case a red rash developing over the torso.

Could the same anticancer effect be achieved by smoking cannabis?

This is difficult to answer, but the answer may be no, as the doses of cannabinoids that we use tend to be higher than that from smoking. We also use CBD at much higher concentrations than typically seen in smoking. Smoking marijuana means exposure to many more cannabinoids, meaning the profile of active ingredients differs.

A growing body of evidence supports the use of cannabis as a medicine

I do not know if this makes smoking more or less effective than using 'pure' CBD and THC, but this would need to be assessed.

I can only say that the people with whom I speak that self-prescribe do not administer by smoking cannabis.

This research adds to a growing body of evidence of the anticancer properties of the cannabis plant – what more is needed to 'prove' its effectiveness as a cancer treatment?

Clinical trials are an absolute requirement – we need these well-controlled studies to confirm a benefit. The set-up in the UK is such that these studies need to be performed before other clinicians are permitted to use them more widely. One could argue that the anecdotal evidence should be enough to justify their inclusion into the pharmacopoeia; however, clinical trials are the key to opening up cannabinoids as a medicine.

What's next for your own research into cannabinoids as potential anticancer drugs?

We're currently expanding our work into other cancer types as well as developing the best/optimum treatment schedules for these drugs. We think it is important to understand the biochemistry of these drugs in a number of cancers, as this allows us to identify those diseases most likely to benefit from its use. Developing this body of work will help our intention to initiate clinical trials using these drugs as treatments for certain forms of cancer.

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Using a lower dose of chemotherapy by supplementing it with cannabinoids could lessen its side effects

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