Cannabis extract shrinks brain tumours

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Cannabis extracts may shrink brain tumours and other cancers by blocking the growth of the blood vessels which feed them, suggests a new study.

An active component of the street drug has previously been shown to improve brain tumours in rats. But now Manuel Guzmán at Complutense University, Spain, and colleagues have demonstrated how the cannabis extracts block a key chemical needed for tumours to sprout blood vessels – a process called angiogenesis.

And for the first time, the team has shown the cannabinoids impede this chemical in people with the most aggressive form of brain cancer - glioblastoma multiforme.

Cristina Blázquez at Complutense University, and one of the team, stresses the results are preliminary. “But it’s a good point to start and continue,” she told New Scientist.

“The cannabinoid inhibits the angiogenesis response - if a tumour doesn’t do angiogenesis, it doesn’t grow,” she explains. “So if you can improve angiogenesis on one side and kill the tumour cells on the other side, you can try for a therapy for cancer.”

"This research provides an important new lead compound for anti-cancer drugs targeting cancer's blood supply,” says Richard Sullivan, head of clinical programmes, at Cancer Research UK.

Fat molecule

The team tested the effects of delta-9-tetrahydrocannabinol in 30 mice. They found the marijuana extract inhibited the expression of several genes related to the production of a chemical called vascular endothelial growth factor (VEGF).

VEGF is critical for angiogenesis, which allows tumours to grow a network of blood vessels to supply their growth. The cannabinoid significantly lowered the activity of VEGF in the mice and two human brain cancer patients, the study showed.

The drug did this by increasing the activity of a fat molecule called ceramide, suggests the study, as adding a ceramide inhibitor stifled the ability of the cannabinoid to block VEGF.

Small and pallid

“We saw that the tumours [in mice] were smaller and a bit pallid,” adds Blázquez. The paleness of the cancer reflected its lack of blood supply as a result of the treatment. In the human patients, she says: "It seems that it works, but it's very early."

Sullivan points out: “Although this work is at an early stage of development other research has already demonstrated that VEGF is an important drug target for a range of cancers.”

He emphasises the need for further work on cannabinoid combinations. “Cannabinoids would need to generate very strong data in the future as there are already a number of VEGF inhibitors in clinical development,” he says.

The two patients in the ongoing study are among 14 in a clinical

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Cannabis may help combat cancer-causing herpes viruses

The compound in marijuana that produces a high, delta-9 tetrahydrocannbinol or THC, may block the spread of several forms of cancer causing herpes viruses, University of South Florida College of Medicine scientists report.

The findings, published Sept. 15 in the online journal BMC Medicine, could lead to the creation of antiviral drugs based on nonpsychoactive derivatives of THC.

The gamma herpes viruses include Kaposi's Sarcoma Associated Herpes virus, which is associated with an increased risk of cancer that is particularly prevalent in AIDS sufferers. Another is Epstein-Barr virus, which

predisposes infected individuals to cancers such as Burkitt's lymphoma and Hodgkin's disease.

Once a person is infected, these viruses can remain dormant for long periods within white blood cells before they burst out and begin replicating. This reactivation of the virus boosts the number of cells infected thereby increasing the chances that the cells will become cancerous.

The USF team, led by virologist Peter Medveczky, MD, found that this sudden reactivation was prevented if infected cells were grown in the presence of THC. While cells infected with a mouse gamma herpes virus normally died when the virus was reactivated, these same cells survived when cultured in the laboratory along with the cannabinoid compound – further evidence that THC prevents viral reactivation.

Furthermore, the researchers showed that THC acts specifically on gamma herpes viruses. The chemical had no effect on another related virus, herpes simplex-1, which causes cold sores and genital herpes.

Small concentrations of THC were more potent and selective against gamma herpes viruses than the commonly used antiviral drugs acyclovir, gancicyclovir and foscamet, said Dr. Medveczky, a professor in the Department of Medical Microbiology and Immunology.

The USF researchers suggest that THC selectively inhibits the spread of gamma herpes viruses by targeting a gene these viruses all share called ORF50.

Dr. Medveczky emphasized that more studies are needed. "We have not evaluated the effect of THC in an animal model yet so we do not recommend people start using pot to prevent or treat cancers."

In fact, Dr. Meveczky said, THC has also been shown to suppress the immune system so smoking marijuana could "do more harm than good" to patients whose immune systems are often already weakened.

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Marijuana may block Alzheimer's

The active ingredient in marijuana may stall decline from Alzheimer's disease, research suggests.

Scientists showed a synthetic version of the compound may reduce inflammation associated with Alzheimer's and thus help to prevent mental decline.

They hope the cannanbinoid may be used to developed new drug therapies.

The research, by Madrid's Complutense University and the Cajal Institute, is published in the Journal of Neuroscience.

"*We would warn the public against taking marijuana as a way of preventing Alzheimer's*"
Dr Susanne Sorensen

The scientists first compared the brain tissue of patients who died from Alzheimer's disease with that of healthy people who had died at a similar age.

They looked closely at brain cell receptors to which cannabinoids bind, allowing their effects to be felt.

They also studied structures called microglia, which activate the brain's immune response.

Microglia collect near the plaque deposits associated with

Alzheimer's disease and, when active, cause inflammation.

The researchers found a dramatically reduced functioning of cannabinoid receptors in diseased brain tissue.

This was an indication that patients had lost the capacity to experience cannabinoids' protective effects.

The next step was to test the effect of cannabinoids on rats injected with the amyloid protein that forms Alzheimer's plaques.

Those animals who were also given a dose of a cannabinoid performed much better in tests of their mental functioning.

The researchers found that the presence of amyloid protein in the rats' brains activated immune cells.

However, rats that also received the cannabinoid showed no sign of microglia activation.

Using cell cultures, the researchers confirmed that cannabinoids counteracted the activation of microglia and thus reduced inflammation.

Drug target

Researcher Dr Maria de Ceballos said: "These findings that cannabinoids work both to prevent inflammation and to protect the brain may set the stage for their use as a therapeutic approach for Alzheimer's disease."

Dr Susanne Sorensen, head of research at the Alzheimer's Society, said: "This is important research because it provides another piece of the jigsaw puzzle on the workings of the brain.

"There is no cure for Alzheimer's disease, so the identification of another target for drug development is extremely welcome.

"The Alzheimer's Society looks forward to seeing further research being carried out on cannabinoid receptors as drug targets for Alzheimer's disease but would warn the public against taking marijuana as a way of preventing Alzheimer's.

"It is now generally recognised that as well as providing a 'high', long-term use of marijuana can also lead to depression in many individuals."

Different receptors

Harriet Millward, of the Alzheimer's Research Trust, said there were two main types of cannabinoid receptor, CR1 and CR2.

"It is CR1 that produces most of the effects of marijuana,

including the harmful ones.

"If it is possible to make drugs that act only on CR2, as suggested by the authors of this study, they might mimic the positive effects of cannabinoids without the damaging ones of marijuana.

"However, this is a fairly new field of research and producing such selective drugs is not an easy task.

"There is also no evidence yet that cannabinoid-based drugs can slow the decline in human Alzheimer's patients."

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Cannabis compound benefits blood vessels

Roxanne Khamsi

Low dose helps combat formation of arterial blockages.

This computer rendition shows how fatty deposits can narrow blood vessels.
© *SPL*

A compound derived from the cannabis plant protects blood vessels from dangerous clogging, a study of mice has shown. The discovery could lead to new drugs to ward off heart disease and stroke.

The compound, called delta-9-tetrahydrocannabinol (THC), combats the blood-vessel disease atherosclerosis in mice. This disease occurs when damage to blood vessels, by nicotine from cigarettes, for example, causes an immune response that leads to the formation of fatty deposits in arteries.

These deposits form because the immune cells can linger too long, recruiting others and leading to an inflamed blockage that snares fatty molecules. The disease is the leading cause of heart disease and stroke in the developed world.

THC seems to tone down this immune response, report François Mach of the University Hospital Geneva, Switzerland and his colleagues. The compound binds to a protein called CB2 that is present on the surfaces of certain immune cells.

Block buster

Mach's team administered tiny amounts of pure THC to mice. The treatment reduced the progression of blood-vessel blockage formation by more than one-third, the researchers report in this week's *Nature*[1].

Furthermore, feeding the mice a compound that interferes with binding to CB2 abolished the therapeutic effect of THC. This proves that the process involves the CB2 protein rather than a similar protein called CB1, which is found on cells in the brain and nervous system and is responsible for cannabis's psychological effects.

The benefits for atherosclerosis occurred only at a certain dosage, Mach adds. At higher and lower doses, THC has no therapeutic effect on blood vessels, he says. He notes the similarly moderated effects of alcohol on heart disease, adding that a single glass of Bordeaux may reduce risk while overindulgence can increase it.

This paper has nothing to do with smoking marijuana.

François Mach
University Hospital Geneva, Switzerland

The team also emphasises that the THC dose required to protect blood vessels is lower, relative to body weight, than that which would produce the mind-altering altering effects of cannabis in humans. "This paper has nothing to do with smoking marijuana," Mach stresses.

"It does not mean that smoking cannabis is beneficial to the cardiovascular system, as cannabis smoke contains many toxins which may actually lead to cardiovascular diseases," says Michael Randall of the University of Nottingham Medical School, UK, who has studied cardiovascular disease and cannabinoids.

"The body also produces its own cannabis-like chemicals and whether they may play a role in the above beneficial effects is unclear," he adds.

Future drugs

THC could be deployed alongside currently used cholesterol-controlling drugs called statins to fight atherosclerosis, Mach suggests. "I don't think this will replace statins. But we may add another compound that will fight against inflammation," he explains.

Because THC might suppress the immune system in a general way, there is a danger that it may harm the body's ability to fight infection. To avoid this, Mach says, it may be necessary to identify similar compounds that specifically target the CB2 protein.

Still, the discovery adds to the range of potential medicinal benefits of cannabis compounds. Besides its well-publicized use for pain relief, the drug is also given to anorexics to stimulate appetite, and cancer patients to combat the nauseating side-effects of chemotherapy.

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References

1. *Steffens S., et al*. *Nature*, **434**. 782 - 786 (2005). | Article |