MedicalXpress

Parkinson's disease drug shows anticancer effects

September 28 2017

Research shows the Parkinson's disease drug carbidopa displays significant anticancer effects in both human cell lines and mice when given at normal patient dosage levels.

This discovery, which is published in the *Biochemical Journal*, may explain the low incidence of many cancers (with the exception of melanoma) in patients with Parkinson's disease and could lead the way to carbidopa being repurposed as an anticancer medication.

"Carbidopa is an FDA-approved drug for treating Parkinson's disease. Hence, clinical trials can be conducted right away to evaluate its efficacy in humans as an anticancer drug," explained lead study author Dr Yangzom Bhutia from Texas Tech University Health Sciences Center in the USA.

Parkinson's disease is a degenerative neurological disorder that mostly influences a person's movement and motor skills, with symptoms including shaking, rigidity and difficulty in walking. These effects are a result of lower than normal production of dopamine, a chemical that sends behavioural signals from the brain to the body.

While there is currently no cure for the condition, there are a number of treatments that act to reduce the severity of the symptoms of Parkinson's disease. Dopamine itself cannot be used as a drug, as it will not cross the blood-brain barrier. However, one of the chemicals that forms dopamine - levodopa or L-DOPA - can cross into the brain and is converted into

dopamine once there.

L-DOPA has been used to treat Parkinson's disease symptoms for many years, but when used alone can result in side effects such as nausea. This is because only 5-10% of levodopa taken as a drug crosses the blood-brain barrier, with the rest being converted into dopamine elsewhere in the body. The drug carbidopa does not cross into the brain, but when taken with L-DOPA prevents its conversion into dopamine outside the brain and reduces side effects for patients.

Many studies show that patients with Parkinson's disease have a lower rate of most cancers compared with the general population. As most patients in these studies were treated with a combination of L-DOPA and carbidopa, it is possible that one or both of these drugs could exhibit anti-cancer properties and contribute to the lower incidence of cancer observed in these patients.

Earlier studies showed that L-DOPA does not have anticancer properties, but until now the potential anticancer properties of carbidopa have not been investigated.

"Interestingly, no one has previously suspected carbidopa as a potential player in this phenomenon," said Bhutia. "Carbidopa is never used by itself as a drug for any disease. But our data show that carbidopa by itself possesses the anticancer effect. We believe that the reduced incidence of most cancers in Parkinson's disease patients is due to carbidopa."

She added: "We also postulate that the increased incidence of melanoma in Parkinson's disease patients is most likely due to L-DOPA, and not due to carbidopa, because L-DOPA is the precursor for melanin synthesis, a metabolic pathway that occurs exclusively in melanocytes."

In the current study, Bhutia and her team, as well as collaborators from Japan and India, tested the effects of carbidopa on a human pancreatic cancer cell line and also in mouse models of pancreatic cancer. They found that carbidopa significantly inhibited cancer cell growth both in the cell line and in the mice.

The researchers believe that carbidopa is likely to have wide ranging anticancer effects, but chose to focus on pancreatic cancer for this study because of the low survival rate and limited treatment options for this form of the disease.

"Pancreatic cancer, especially the pancreatic ductal adenocarcinoma, is the most lethal of all cancers with a dismal survival rate," commented Bhutia. "Carbidopa as an anti-cancer agent to treat pancreatic cancer would be something truly amazing. Given the fact that it is an FDA-approved drug, re-purposing the same drug for cancer treatment would be tremendously cost- and time-saving."

The recommended dose of carbidopa for Parkinson's disease patients is 200 mg/day, but when given at a dose even as high as 450 mg/day, there are no side effects. While this study was not carried out in humans, the dose of carbidopa given to the mice that stopped tumour growth was equivalent to a dose in humans of less than 400 mg/day, which is within the dose range considered to be safe for patients.

The aryl hydrocarbon receptor (AhR) protein plays a critical role in cancer and activation of this protein has shown promise for treating a variety of different cancers including breast, colon and pancreatic cancer. Bhutia and colleagues showed that carbidopa activates AhR and believe this may explain, at least in part, its anticancer properties.

"Our laboratory is actively working to determine if there are additional targets for this drug related to its potency as an anticancer drug," Bhutia

added.

The author of an accompanying commentary to the research article Professor Stephen Safe, Texas A&M University, remarked: "This receptor was initially identified as the critical target that mediates the toxicity of "dioxin" and related compounds; however, results of this study with carbidopa and several other reports are demonstrating that the AhR is a therapeutic target not only for cancer but many other diseases."

The authors acknowledge that the role of AhR in cancer is complex, but suggest that as carbidopa is already in use by Parkinson's disease patients, further investigations into its role as a potential anticancer drug should be carried out.

"We would like to partner with oncologists to design and conduct clinical trials in cancer patients to establish whether or not carbidopa would be useful as an anticancer drug in humans," said Bhutia.

Professor Aideen Sullivan (University College Cork) is a Parkinson's disease expert who was not involved in the research. When asked about the current study, she commented: "With increasing interest in the re-purposing of drugs, to reduce costs and time needed to get a drug to market, it is timely for investigators to explore the potential anticancer properties of anti-Parkinson's therapies."

She added: "Since carbidopa has already been proven to be safe and well-tolerated by people with Parkinson's, its application in cancer treatment, where most current therapies are associated with severe and long-lasting side-effects, will be welcomed by patients. Nevertheless, due to the complexity of cancer cell biology, it will be important to firstly conduct studies on the effectiveness of carbidopa in specific types of cancer."

More information: *Biochemical Journal* (2017). DOI:

10.1042/BCJ20170583