Chemicals found in fruit and veg offer dementia hope

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A group of chemicals found in many fruits and vegetables, as well as tea, cocoa and red wine, could protect the brain from Alzheimer's disease, a dementia expert will tell scientists at a conference today (Friday).

Speaking at the British Pharmacological Society's Summer Meeting in Edinburgh, Dr Robert Williams will argue that, while much more research needs to be done, there is mounting evidence that certain flavonoids - chemicals found in plants and food derived from plants - might provide therapeutic benefit for Alzheimer's sufferers.

"There have been some intriguing epidemiological studies that the consumption of flavonoid-rich vegetables, fruit juices and red wine delays the onset of the disease," says Dr Williams, a Biochemist working at Kings College London. "These reports, while not as powerful as controlled, randomised clinical trials, have encouraged a number of research groups, including our own, to investigate the biology of flavonoids in more detail."

Dr Williams says that a lack of good research and clinical trial data meant this field of research had suffered from a lack of scientific credibility, not helped by early positive health claims for flavonoids that cannot access the brain or are broken down too rapidly by the body to be of any benefit. Scepticism also persists because flavonoids are known antioxidants and yet clinical trials with other antioxidants, such as vitamin E, showed no reported benefit on either symptoms or disease progression in dementia.

However, a new concept is emerging that suggests flavonoids do not act simply as antioxidants but exert their biological effects through other mechanisms. A small number of recent studies carried out in models of Alzheimer's disease have found that oral administration of green tea flavonoids or grape flavonoids reduces brain pathology and, in some cases, improves cognition. Dr Williams and colleagues have focused their own cellular studies on a flavonoid called epicatechin, which is abundant in a number of foodstuffs, including cocoa.

"We have found that epicatechin protects brain cells from damage but through a mechanism unrelated to its antioxidant activity and shown in laboratory tests that it can also reduce some aspects of Alzheimer's disease pathology.

"This is interesting because epicatechin and its breakdown products are measurable in the bloodstream of humans for a number of hours after ingestion and it is one of the relatively few flavonoids known to access the brain suggesting it has the potential to be bioactive in humans."

Alzheimer's disease is a devastating, progressive disorder affecting an estimated 15-20 million people worldwide. Over the past four decades, through worldwide research efforts, it is now known that in the brains of people with Alzheimer's disease there are abnormal cellular processes which lead to neurodegeneration and dementia. Understanding these disease processes at the molecular level will allow the development of pharmacological agents to block these processes, and lead the way for effective therapies in Alzheimer's disease.

Central to the development of Alzheimer's disease is toxic beta-amyloid peptide, a substance that is normally produced in the brain but, in this disease, is deposited abnormally as amyloid plaques. Dr Williams has shown that flavonoids can protect brain cells against the toxic actions of beta-amyloid.

He adds: “Although our findings support the general concept that dietary intake of flavonoid-rich foods or supplements could impact on the development and progression of dementia, they are clearly insufficient to make any sort of nutritional recommendations at this stage.

“The challenge now is to identify the single flavonoid or combination of flavonoids that exert the most positive effects and to define the mechanisms of action and optimal quantity required before embarking on clinical trials to treat their effectiveness in dementia.”

The British Pharmacological Society Summer Meeting in Edinburgh will also highlight the work of three other scientists who are working on different aspects of Alzheimer’s disease. They will present their latest research findings showing that insight into disease mechanisms is leading to the development of agents with the potential to become new and effective therapies for Alzheimer’s disease.

Dr Tiziana Borsello, from the Mario Negri Institute of Pharmacological Research in Milan, Italy, will present data which show that cell death in Alzheimer’s disease and other neurodegenerative states involves the activation of a protein called JNK. Over a number of years, she and her team have developed the powerful and specific cell-permeable inhibitor of JNK (D-JNKI1). In her talk, Dr Borsello will show that D-JNKI1 can reduce production of beta-amyloid and amyloid plaques and improve memory in mice. This exciting research opens up new prospects for the treatment of Alzheimer’s disease.

Professor Michael Rowan, from University College Dublin, Ireland, will present data showing that beta-amyloid can directly affect the physiological processes involved in memory formation. His research has identified therapeutic agents that target the cytokine system in the brain and are able to prevent this detrimental effect of beta-amyloid. This line of enquiry suggests that agents that remove cytokines could improve

cognitive function in Alzheimer's disease.

Dr Warren Hirst, from Wyeth Pharmaceuticals, Princeton, USA, will outline two potential therapeutic strategies. The first is the discovery and development of novel potent, selective and brain-penetrant small molecule beta-secretase inhibitors. These investigational small molecules have the potential to prevent the accumulation of beta-amyloid in the brain. The second strategy addresses the cognitive deficits associated with the disease, which are only partially addressed by current therapies. Neurotransmitter receptors in the brain play an important role in cognitive processes and new evidence suggests that blocking a specific class of receptors, the 5-HT_{1A} receptors, can improve learning and memory in rats and mice. These, or similar molecules, may improve cognitive function in Alzheimer's disease patients.

In summary, the symposium highlights how basic molecular and pharmacological research, including the work presented here, has enabled the identification and development of agents with promise to treat this devastating disease. Turning the findings from research into new medicines which are effective to treat Alzheimer's disease is some way off, but is within reach.

Source: British Pharmacological Society