

# Old gastrointestinal drug slows aging

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Recent animal studies have shown that clioquinol - an 80-year old drug once used to treat diarrhea and other gastrointestinal disorders - can reverse the progression of Alzheimer's, Parkinson's and Huntington's diseases. Scientists, however, had a variety of theories to attempt to explain how a single compound could have such similar effects on three unrelated neurodegenerative disorders.

Researchers at McGill University have discovered a dramatic possible new answer: According to Dr. Siegfried Hekimi and colleagues at McGill's Department of Biology, clioquinol acts directly on a protein called CLK-1, often informally called "clock-1," and might slow down the aging process. The advance online edition of their study was published in Oct. 2008 in the *Journal of Biological Chemistry*.

"Clioquinol is a very powerful inhibitor of clock-1," explained Hekimi, McGill's Strathcona Chair of Zoology and Robert Archibald & Catherine Louise Campbell Chair in Developmental Biology. "Because clock-1 affects longevity in invertebrates and mice, and because we're talking about three age-dependent neurodegenerative diseases, we hypothesize that clioquinol affects them by slowing down the rate of aging."

Once commonly prescribed in Europe and Asia for gastrointestinal problems like diarrhea and shigella, clioquinol was withdrawn from the market after being blamed for a devastating outbreak of subacute myelo-optic neuropathy (SMON) in Japan in the 1960s. However, because no rigorous scientific study was conducted at the time, and because

clioquinol was used safely by millions before and after the Japanese outbreak, some researchers think its connection to SMON has yet to be proven.

The exact mechanism of how clioquinol inhibits CLK-1 is still under investigation, Hekimi said. "One possibility is that metals are involved as clioquinol is a metal chelator," he explained. Chelation is a type of binding to metal ions and is often used to treat heavy metal poisoning.

Hekimi is optimistic but cautious when asked whether clioquinol could eventually become an anti-aging treatment.

"The drug affects a gene which when inhibited can slow down aging," he said. "The implication is that we can change the rate of aging. This might be why clioquinol is able to work on this diversity of diseases that are all age-dependent."

However, he admits to being concerned about how people may interpret his results.

"The danger is that you can buy a kilogram of this compound at a chemical wholesaler, but we don't want people to start experimenting on themselves. Clioquinol can be a very toxic substance if abused, and far more research is required."

Source: McGill University

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