

Curcumin Study Validates Strategy of Pursuing Other LTR Inhibitors

by Peter Hale

Results of First In Vivo Test Show Antiviral Effect

Search Alliance, the Los Angeles community based research group, will report in this month's Searchlight the results of their 20-week pilot study of curcumin. The study was conducted to determine if curcumin, which has shown antiviral properties in vitro in both acutely and chronically HIV-infected cells, could achieve a reduction in viral load in people taking the substance.

The bottom line from the Search Alliance study; Curcumin exhibited no major toxicity at the dose used (2.6 grams per day), and was able to produce a mild antiviral effect in terms of reduction of viral load as measured by RNA PCR in all 11 of the 19 participants who completed the study.

Although no increase in CD4 cells were reported and there was no apparent reduction in p24 antigen, the results of this study are viewed as encouraging. While no-one is suggesting that curcumin be used as a monotherapy at this stage, for the first time we have evidence that compounds like curcumin can work in people. More importantly, there's the hope that eventually even stronger compounds that are also classified as LTR inhibitors, will serve as useful adjuncts to conventional antiretroviral therapy with drugs like AZT and ddI.

The Background

Curcumin is the main active ingredient found in the food spice turmeric. An orange-yellow crystalline substance (C₂₁H₂₀O₆), curcumin give turmeric powder-and thus curries, rice and other Indian dishes-its distinctive, mild flavor

and yellow color. Turmeric is an everyday spice in India that has been used for centuries. It is an essential ingredient in many curries and other Indian dishes and counts as one of the most prized of the cheaper, everyday Indian spices.

A study of East Africans and Indians in Kenya first alerted scientists to turmeric. In an examination of the two population groups, a stark difference was noted between infection rates. Africans were ten times more likely to be HIV-infected, despite comparable risk factors. The daily diet of the two groups were analyzed and the large amounts of turmeric ingested by the Indian population (up to 100 mg curcumin per day) suggested turmeric as a possible environmental factor that could be providing antiviral protection.

Subsequent reports from Trinidad where 40% of the population is of Indian descent (and eats curry), and 40% is African (and doesn't eat curry), showed the same pattern of HIV infection -with the Africans far more likely to develop HIV/AIDS.

Curcumin As An Anti-HIV Agent

We know now that curcumin is one of a new class of compounds found to inhibit the HIV LTR (long terminal repeat). The LTR is a sequence of HIV's viral DNA, often described as the 'on/off switch,' which activates the viral genome. If we can turn the switch off, we can deactivate the virus. More accurately, by inhibiting the LTR, the virus is not being stimulated to reproduce and thus cannot maintain replication.

In March 1993, researchers at Harvard Medical School reported in Proceedings of the National Academy of Sciences that three out of an initial 15 compounds tested, topotecan, β lapachone, and curcumin were "potent and selective inhibitors of HIV-1 LTR directed gene expression" in cells both acutely or chronically infected with HIV-1. Moreover, all three compounds were found to be effective at concentrations that have only minor effects on cells, suggesting that all three compounds might well be tolerated in humans.

Mechanism Of Action

Researchers have long known that curcumin has anti-inflammatory and antioxidant properties, but its precise mechanism of action in inhibiting the LTR is not yet known. It is possible that curcumin may block NF- κ B (NF-kappa B) from binding to its DNA binding site, like the drug pentoxifylline, thus inhibiting the LTR. Other anti-oxidants- such as vitamins C and E or the amino acid N-acetylcysteine (NAC)— may also block NF- κ B, and those which have been tested have been observed in the laboratory to partially inhibit the production of HIV.

Two recent studies suggest that curcumin may inhibit HIV in more ways than one: One group has shown that curcumin may inhibit protein kinase C, in addition to inhibiting LTR. Another paper suggests that curcumin may inhibit the HIV protease. (Scientists did a computer study of what the structure should be to block the HIV protease enzyme, and came up with a curcumin structure.)

Lipid peroxidation prevention by natural and synthetic antioxidants

