

Curcumin: Old Spice, New Drug

BY JESSICA LEAR

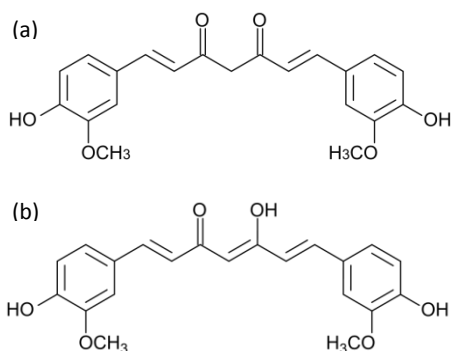
MENTOR: MARGARET HARRIS

Over the last decade, curcumin, best known as the yellow color of turmeric a spice in many Indian foods, has been shown to be an important ally in the fight against disease. Over the past few years, scientists have found that curcumin has antibacterial, antiviral, antifungal and antiprotozoal properties. In addition, it has been found to be a powerful anti-oxidant and anti-inflammatory drug. These properties allow curcumin to fight some of the most prevalent diseases in the world, including Alzheimer's disease, malaria and cancer.

CURCUMIN AND ALZHEIMER'S

Alzheimer's disease (AD) is an extremely devastating disease that has increased immensely over in the past few decades. AD patients have sticky, beta amyloid plaques that ruin their neurons. These plaques are increased by high cholesterol, which increases naturally as we age. Curcumin has been shown to fight the plaques directly while lowering cholesterol so future plaques are not formed. These findings and more have lent support to the idea that curcumin is a very promising AD drug.

In addition, when someone has AD, there is a lot of inflammation and reactive



Packing a punch. Curcumin, shown here in its (a) keto and (b) enol forms, has been found to exhibit properties that may help fight common human diseases, like Alzheimer's. Images obtained via Creative Commons license and can be found at <http://commons.wikimedia.org/w/index.php?title=Special%3ASearch&search=curcumin>.

oxygen species in their brains, which destroys them. Curcumin has shown to successfully fight both inflammation and reactive oxygen species in the brain in mice. Curcumin achieves this is by blocking, or inhibiting, a pathway that causes inflammation called the NF-kB pathway. "Curcumin regulates multiple cell signaling pathways. It especially inhibits NF-kB activation, related to the reduction of many diseases," said Sukshanti Prakobwong, a graduate student at Rajabhat Udonthani University in Thailand who is actively involved in curcumin research. When a signal induces the NF-kB pathway, inflammatory molecules and reactive oxygen species are produced, which can cause AD, cancer and more. Curcumin blocks this pathway so no inflammatory molecules and reactive oxygen species are produced and no disease develops.

COMMON USES

Although curcumin has just recently gained a lot of attention, it is anything but new. Bharat B Aggarwal, a professor of cancer medicine at the University of Texas MD Anderson Cancer Center, points out that pure curcumin was isolated from the flavor-free curry spice turmeric (figure 2) more than 100 years ago. It also has a medical history dating back to 1900 BC. "Curcumin has been used in ayurvedic medicine since ancient times, with various biological applications," said Haritha Nair, a graduate student at the Integrated Cancer Research Program in India. In addition, curcumin has been used as a food coloring for centuries, especially in India and south-east Asia. "You can see turmeric anywhere if you visit a Southeast Asian country," said Prakobwong.

That raises an interesting question: might people in India and south Asia already be benefiting from curcumin's medicinal properties? Interestingly, despite India being one of the most populated counties in the world, it has one of the lowest occurrences of cancer and Alzheimer's disease. Though significant



Spice it up. Turmeric, most commonly found in its powder form, owes its golden color to the presence of curcumin. Image obtained via Creative Commons license and can be found at <http://www.flickr.com/photos/ciamabue/4571802106/lightbox/>.

studies still must be done, there is a possibility that this is partly due to the high amounts of curcumin the people of India are exposed to throughout their lives. This statistic lends weight to the idea that curcumin can fight cancer, disease, and injury. If curcumin studies continue to support its use of fighting numerous diseases, it could change the way the Western world eats as Eastern foods become more popular in order to reap the benefits of spices like curcumin.

RECENT & NOVEL DEVELOPMENTS

Curcumin has also been shown to fight malaria, another worldwide killer. Twenty-one days after curcumin was administered to mice with malaria, 29% were still alive, while 0% of mice with malaria that were not given curcumin were alive. These odds are not great, but they show that curcumin does fight malaria to some extent. This is useful because although current antimalarials are available and successful, they are expensive and not available in most third world countries where malaria is prevalent. Future research will assess the effects of linking curcumin with current antimalarials, hoping to increase the efficiency of treatment while decreasing the cost.

In the past year, significant research has shown that curcumin may be an ideal form of birth control - one that not only prevents pregnancy, but also fights cervical cancer and sexually transmitted diseases due to its anticancer and antiviral properties. Studies have also shown that curcumin causes sperm to stop moving forward -- a crucial part of conception -- while mice that were given curcumin intravaginally became infertile.

Studies on mice have also shown that curcumin may help fight depression. Mice that were given curcumin showed much less depressed behavior than mice without curcumin. In addition, curcumin significantly increased molecules in the brain such as noradrenaline and dopamine, which are contained in antidepressants.

Some of these treatments are many years off, but one novel use of curcumin has already been commercialized. "There is numerous experimental data that suggest that curcumin can accelerate wound healing," said Aggarwal. This has led Johnson & Johnson to supply a curcumin-containing band-aid, he added.

ABSORPTION WOES

While curcumin is being actively studied by dozens of labs around the world, research was not always easy going. Curcumin does not dissolve in water. This is problematic because in order for a drug to be utilized, it must be absorbed into the cell, making it bioavailable. In a recent study, patients ingested 10g of curcumin. It was expected that large amounts of curcumin would be detected in the blood since 10g is a large amount. However, only very low, almost undetectable, amounts of curcumin were detected, supporting the idea that curcumin is not absorbed into the body, but lost as waste.

This was a big challenge for scientists to overcome as it is imperative that curcumin be absorbed to be utilized as a potential drug. To overcome this problem, scientists first tried dissolving curcumin in dimethyl sulfoxide (DMSO). This worked, but unfortunately, DMSO can cause side effects such as hypertension, so better methods were needed before curcumin could be widely distributed. Very recently, curcumin nanoparticles, or nanocurcumin, have been developed.

Since these particles have diameters of only 10-1000nm (compared to ordinary curcumin particles, which are in the micrometer range) they are much more soluble than natural curcumin, and they do not produce the side effects of DMSO.

ASSOCIATED RISKS

While studies on curcumin seem promising, it is still important to understand its possible side effects. So far, it has shown to be non-toxic in all animal models tested. The FDA generally recognizes curcumin as safe and a daily intake of 0.1-3mg/kg-body weight has been approved. Prakobwong reported that in a cancer clinical trial, patients received over 8g per day and did not experience any side effects. Over forty clinical trials have been completed and the only side effects reported when ingesting between 2-12g were nausea and diarrhea. Though these are nuisances, they are not major side effects compared to those associated with other cancer drugs. In fact, curcumin capsules are already available for purchase. "Studies suggest that curcumin is safe in human subjects even when consumed up to 12 grams per day for three months," said Aggarwal.

There have, however, been a few studies that have noted potential risks of curcumin. One study has suggested that curcumin could interfere with a powerful tumor suppressor gene known as the p53 pathway. Despite this, Nair still thinks curcumin does not cause cancer, but fights it; "the ability of curcumin to induce apoptosis [cell death] in cancer cells without cytotoxic effects on healthy cells contributes to the understanding of the anti-cancer potential of curcumin." Another research group from Wake Forest University has found that curcumin could alter iron metabolism, leading to iron deficiency. While it is important to note these findings, it is also important to know that these studies are very limited compared to the amount of studies that have indicated that curcumin is safe.

WHAT'S NEXT?

The future of curcumin seems to be promising. "It is expected that curcumin may find application as a novel drug in the near future to control various diseases," said Nair. Over forty clinical

trials of curcumin have already been concluded, and forty more are currently ongoing. One direction curcumin research is going is the aforementioned nanocurcumin, which has shown to be immensely powerful and soluble. "In the new era for curcumin research, we are focusing on the improvement of its bioavailability in many ways such as using the nanoparticle or nanotechnology," said Prakobwong.

Another route that curcumin research is going is using antibodies to target certain types of cells. Antibodies that target specific cancer cell types have been linked to curcumin. When released into the body, the antibody finds the specific cells, curcumin moves into the cell, and the cell is destroyed so the cancer cannot spread. Only time will tell if curcumin is the answer to cancer, Alzheimer's disease, malaria, and more. Yet whether it is natural, nano, or antibody linked, curcumin is surely one of the most promising drugs of the 21st century. ■

Jessica Lear is a student at West Virginia University.