Curcumin – A Novel Treatment for Depression

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Depression: Common and Difficult to Treat

About 1 in 10 Americans report symptoms of depression, and the causes can be as varied as the individuals reporting them.[1]

Unfortunately, many of the current therapeutic drugs for depression are only effective – and safe- for short periods. However, because of the cyclical and chronic nature of depression, dysthymia, and other depression-like illnesses, these medications are often *required* to be taken long term. This is when the worst aspects of conventional prescription drugs come into play. Many have a marked sedative effect and can cause weight gain, insomnia, hypersomnia, and loss of libido. Others – in a frightening reversal of their intended use – can actually cause greater feelings of hopelessness and suicidal thoughts.

Natural Approaches to Depression: A Challenge

The challenges of finding an effective, long-term, and *natural* therapeutic agent,whether as a stand-alone or add-on therapy, is not lost on practitioners. While St. John's Wort (*Hypericum perferatum*) has solid studies supporting its use in cases of mild and moderate depression and even alcoholism, it has not been shown as effective for helping those with Major Depressive Disorder.[2,3,4, 5, 6, 7, 8]

Other botanical extracts, effective at reducing stress or anxiety, often fall short of the mark when targeting dysthymia or depression.

However, current research and traditional practice point to an alternative – if novel – botanical compound: curcumin from turmeric.

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Curcumin: A Long History of Healing

Curcumin, the active compound in turmeric (*Curcuma longa*) has well-noted anti-inflammatory abilities. Turmeric, and by extension curcumin, has a long history in Ayurvedic and Traditional Chinese Medicine. It has been used for stress, mania, and other depression-like conditions for centuries.[9,10,11]

In more recent years, it has been frequently investigated for a variety of conditions, including pain relief in rheumatoid arthritis and osteoarthritis, tumor inhibition in colorectal cancer cells, and supporting cognitive capacity in scientific models and clinical cases of Alzheimer's disease.[11,12,13,14,15]

Aside from curcumin's ability as a strong anti-inflammatory and antioxidant, which reduces DNA damage to cells throughout the body, curcumin reverses other physical effects of stress and depression. It reduces inflammatory markers in the bloodstream, which travel to the brain, and it helps prevent low levels of serotonin, noradrenaline, and dopamine. Additionally, laboratory research shows that curcumin promotes neurogenesis – brain cell formation- notably in the frontal cortex and hippocampal regions of the brain.[16,17,18]

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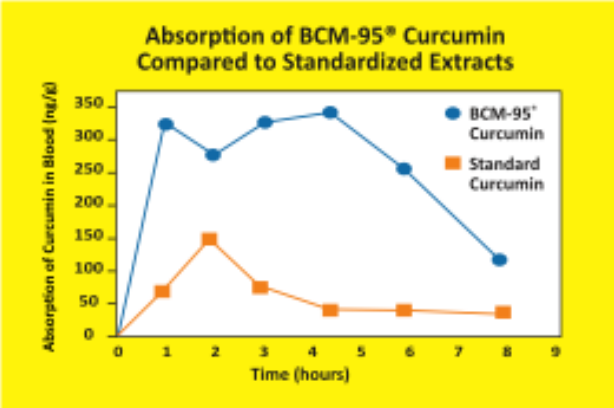
Better Absorption and Greater Efficacy

Although curcumin has historically been singled out as the compound in turmeric doing most of the "heavy lifting", in its plain extract form it can still be difficult for the body to absorb and use. Additionally, turmeric contains only 2-5 % actual curcumin.

However, there have been improvements and enhancements in curcumin extracts that help extend the reach of the compound beyond that seen in standard 95% extracts. One of the most highly regarded is BCM-95® curcumin.

BCM-95 combines high quality curcumin with turmeric essential oils in a patented process. It has ***up to 10 times*** the absorption and greater blood retention time than standard 95% curcumin extracts. It has been the subject of 15 published studies, 10 of them human clinical trials. That is why this specific high absorption curcumin was chosen in laboratory models of depression, and a recent human clinical study of Major Depressive Disorder (MMD).[9, 19, 20, 21, 22]



BCM-95 curcumin shows impressive absorption and blood retention, making the compound much more beneficial at lower doses.

Source*: Antony B, Merina B, Iyer VS, Judy N, Lennertz K, Joyal S. A pilot cross-over study to evaluate human oral bioavailability of BCM-95 CG (Biocurcumax™) a novel bioenhanced preparation of curcumin. Ind J Pharm Sci. 2008:445-449.*

Scientific Research

In a published laboratory study, BCM-95 was compared to fluoxetine (one brand name is Prozac®) and imipramine (one brand name is Tofranil®) in a scientific model of depression.[21]

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The study was an initial gauge into the antidepressant potential of curcumin. It tested two different doses and also noted how well BCM-95® curcumin worked as an "add on" therapy with these two commonly prescribed drugs. All the tests were carried out with the drugs given orally to mice and rats.

The effect of curcumin (100mg/kg) was similar to that of fluoxetine and imipramine ($p > 0.05$). Interestingly, its addition to fluoxetine and imipramine did not improve their antidepressant activity, nor was it able to alleviate the drugs' marked sedative qualities.

The study authors indicated that curcumin's antidepressant like activity could be due to an increase in serotonin, norepinephrine and dopamine levels in the brain.

Major Depressive Disorder

More recently, a clinical study using BCM-95® curcumin was conducted with individuals with Major Depressive Disorder (MDD). The objective of this trial – the first randomized, controlled clinical trial to compare the efficacy and safety of curcumin with fluoxetine (alone or in combination) – was to determine whether curcumin could be a viable therapeutic treatment for patients with MDD.[22]

To qualify for inclusion in the trial, the patients were required to be 18 years or older and diagnosed with MDD according to criteria of *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (American Psychiatric Association) and needed to have scored more than seven on the Hamilton Depression Rating Scale, (HAM-D17), a standard diagnostic tool used for interviewing and screening patients with possible depression. The clinically validated 17 item questionnaire examines physiological and physical symptoms of each patient, including feelings of guilt, sadness, sleep loss, anxiety, and motor skills.

Individuals in the study were also required to have caregivers, and not have suicidal ideation, schizophrenia, bipolar disorder, or other psychotic disorders or hypersensitivity to the study medications.

Sixty patients met the eligibility criteria and were randomized into groups of twenty. The three treatment groups were comparable for baseline demographics and clinical characteristics.

Table 1 - Baseline charateristics of patients randomized in the study.	Group 1: Fluoxetine (n=20)	Group 2: Curcumin (n=20)	Group 3: Fluoxetine and curcumin (n=20)	P value
Age (years), mean	33.6	37.8	40.4	0.21~
(95% CI)	(28.9 – 38.3)	(31.9 – 43.8)	(34.1 – 46.7)	
Sex, n (%)				
Male	10 (50)	5 (25)	6 (30)	0.22§
(95% CI)	(29.9 – 70.0)	(11.3 – 46.8)	(14.6 – 51.9)	
Females	10 (50)	15 (75)	14 (70)	
(95% CI)	(29.9 – 70.0)	(53.1–88.8)	(48.1 – 45.5)	
Previous episode of depressive illness, n (%)				0.62§
Yes	4 (20)	4 (20)	2 (10)	
(95% CI)	(8.0 – 41.6)	(8.0 – 41.6)	(2.8 – 30.1)	
No	16 (80)	16 (80)	18 (90)	
(95% CI)	(58.4 – 91.9)	(58.4 – 91.9)	(69.9 – 97.2)	
Duration of current episode				0.61~
(months), mean	5.1	8.0	5.0	
(95% CI)	(0.05 – 10.1)	(2.3 – 13.6)	(1.4 – 8.6)	
Baseline HAM-D17* total score,				0.43~
Mean	21.0	19.3	21.9	
(95% CI)	(17.6 – 24.4)	(16.4 – 22.1)	(18.9 – 24.8)	
Baseline CGI-S† score,				0.96~
Mean	4.2	4.1	4.2	
(95% CI)	(3.8 – 4.6)	(3.8 – 4.4)	(3.9 – 4.5)	

*Hamilton Depression Rating Scale, 17-item version †Clinical Global Impression-Severity of Illness ~Analysis of variance §Chi-square test

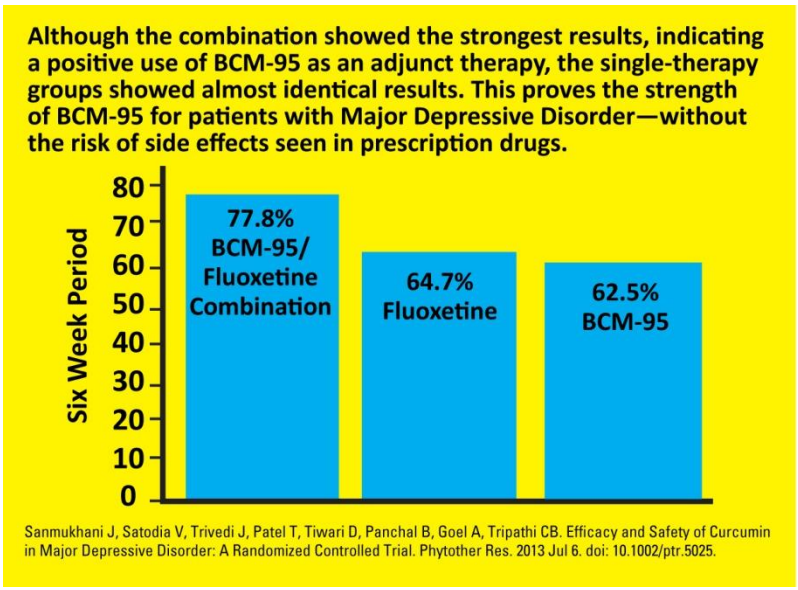
Overall, 45 patients completed the six week study per protocol, with no significant difference in the dropout rate in each group. Nine patients abandoned treatment and were lost to follow-up before the first follow-up visit, so a total of 51 patients were included in the intent-to-treat (ITT) analysis (n = 17, fluoxetine; n = 16, curcumin; n = 18, fluoxetine and curcumin).[22]

Only three patients were judged to be noncompliant (each for only a single episode) during their study period, so the overall compliance of the patients was excellent.

The results of the study were quite significant.

The highest proportion of response, measured by the HAM-D(17) scale was in the group using the combination of fluoxetine and BCM-95® curcumin at 77.8%.[22]

Interestingly, the single-therapy groups scored almost exactly the same, with fluoxetine at 64.7% and BCM-95 curcumin at 62.5% -- numbers so close that the data is not statistically significant from one another.[22] Of even greater interest, the mean change in the HAM-D(17) was almost the same in each group as well, meaning that for those who benefited, their improvement was equally as good whether they took the drug or curcumin.[22]



There are two important conclusions from the result of this study. First, BCM-95® curcumin worked as well as the prescription drug fluoxetine in terms of the measurable changes in the HAM-D(17) score from baseline to six weeks of treatment. Second, this study provides the first human clinical indication that curcumin may be used as an effective and safe treatment for patients with MDD without concurrent suicidal ideation or other psychotic disorders (excluded from the study criteria).[22]

Future Treatment and Hope

People with depression have higher levels of inflammation in the brain. Also, people with depression have lower levels of neurogenesis in the brain, meaning they make fewer new brain cells than people with no history of depression. Curcumin is both a potent anti-inflammatory agent and a powerful stimulator for neurogenesis.

This clinical trial justifies the need for further investigations and human studies that incorporate curcumin into responsible treatment plans that ameliorate the inflammation in the brain and primary symptoms of depression without the risks and side effects common to many anti-depressant drugs.

As curcumin was found to have good efficacy and a benign safety profile in patients of depression, it should be further studied on its own and in combination with fluoxetine or other antidepressants. Future trials, with larger sample sizes, longer duration and higher dosage levels will be able to detect smaller, clinically meaningful differences as well.

Conclusion

Depression is a major global public health issue leading to substantial disability. The pharmaceutical interventions can be quite costly, and have many potentially serious adverse effects. There are also many people whose disease does not fully respond to treatment. The BCM-95® curcumin used in this study shows efficacy on major depression on its own at the same level as the drug, and even better results when combined with the drug.

The results of this study – and further studies to come – have incredible potential. They will be meaningful for the health and hope of millions of people worldwide.

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Dr. Ajay Goel is Director of Epigenetics and Cancer Prevention at Baylor University Medical Center in Dallas, TX. He has spent more than 20 years researching cancer and has been the lead author or contributor to over 150 scientific articles published in peer reviewed international journals and several book chapters. He is currently researching the prevention of gastrointestinal cancers using integrative and alternative approaches, including botanical products. Two of the primary botanicals he is investigating are curcumin (from turmeric) and boswellia.
Dr. Goel is also a member of the American Association for Cancer Research and the American Gastroenterology Association and is on the international editorial boards of *Gastroenterology, Clinical Cancer Research, PLoS One, Digestive Diseases and Sciences* and *World Journal of Gastrointestinal Oncology*. He also performs peer-reviewing activities for almost 75 scientific journals, as well as serves on various grant funding committees of the National Institutes of Health.