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File: ■ Turmeric (*Curcuma longa*, Zingiberaceae)
■ Curcumin
■ Major Depressive Disorder
■ Meta-analysis

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RE: Meta-analysis Finds Curcumin to Be an Effective Adjunct Treatment for Major Depressive Disorder

Al-Karawi D, Al Mamoori DA, Tayyar Y. The role of curcumin administration in patients with major depressive disorder: Mini meta-analysis of clinical trials. *Phytother Res*. 2016;30(2):175-183.

Nearly 50% of patients with major depressive disorders (MDDs) discontinue treatment due to adverse events. Therapies with better tolerability are needed to treat this chronic disease that negatively affects quality of life and increases morbidity. The antidepressant activity of curcumin, a component of turmeric (*Curcuma longa*, Zingiberaceae) rhizome, has been evaluated in numerous clinical trials. This meta-analysis evaluated the safety and efficacy of curcumin in the treatment of MDD.

The search of the literature and presentation of the results followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA). The following databases were searched from 1986 through 2016: PubMed, Scopus, PsycINFO, Evidence Based Medicine Guidelines, DynaMed, JAMA evidence, and the Cochrane Library. The following key words were used: curcumin, depression, MDD, efficacy, and effect. Reference lists of identified papers were hand-searched. Included articles met the following criteria: (1) human study, (2) quantitative analysis, (3) intervention and control group, (4) curcumin was an independent intervention, (5) study addressed only MDD, (6) depression was measured with standardized scales, and (7) in English. The Quality Assessment Tool for Quantitative Studies was used to assess study quality, and an overall rating of methodological quality was assigned; this rating classifies studies as strong (no weak ratings), moderate (1 weak rating), or weak (≥ 2 weak ratings). For the meta-analysis, the data from all studies were converted into Hamilton Depression Rating Scale scores according to published methods. Small sample sizes were adjusted with the Hedges' adjusted *g* formulation of standardized difference in means. Also, the random-effects model and generic inverse variance method were used to combine the results since the studies had different design characteristics.

A total of 1757 studies were identified, and six met all inclusion criteria (four randomized controlled trials, one crossover study, and one open-label study). The six studies included a total of 342 patients (n = 177, curcumin; n = 165, control). All patients received antidepressant therapy in addition to either curcumin (1 g/day, n = 5 studies or 500 mg/day, n = 1 study) or placebo. In regard to methodological quality, five were rated as strong, and one was rated as moderate. The meta-analysis showed that there was a significant reduction in MDD symptoms with curcumin treatment compared with control ($P = 0.002$). This outcome was not influenced by any single study. Several subgroup analyses were conducted with the following outcomes: (1) curcumin had a significant benefit in middle-aged patients ($P = 0.002$) but not older-aged patients (specific age ranges not described); (2) curcumin had a significant benefit in patients treated for > 6 weeks ($P = 0.001$) but not patients treated for < 6 weeks; (3) 1 g/day curcumin had a significant benefit ($P = 0.002$) but 500 mg/day curcumin did not; and (4) curcumin had a significantly greater benefit in patients with MDD only compared with patients with MDD plus comorbidities ($P = 0.002$).

In three of the studies, the curcumin treatment also contained piperine, a component of black pepper (*Piper nigrum*, Piperaceae) fruit which has been shown to increase the bioavailability of curcumin. Subgroup analysis showed that treatments containing piperine had smaller benefits than curcumin alone ($P = 0.05$). However, the authors note that two of these studies used a low (potentially subtherapeutic) dose of piperine, and the study that used a higher dose of piperine used a low dose of curcumin (which may have been too low to produce an effect). Therefore, the piperine meta-analysis should be viewed with caution.

The pooled data had minimal heterogeneity as assessed with the I^2 Index. Funnel plot analysis showed no publication bias. Adverse events were digestive/gastrointestinal complaints (e.g., gastritis, nausea), tachycardia, flushing, and giddiness. Two of the six studies reported no adverse events.

According to the authors, this is the first meta-analysis of the effect of curcumin on MDD. The authors conclude that curcumin is effective in reducing symptoms of depression in patients with MDD who are taking antidepressants, and curcumin is more effective in middle-aged patients, at a dose of 1 g/day, and when taken for > 6 weeks. The authors acknowledge that the results should be interpreted with caution because (1) there were only six studies, (2) only two doses of curcumin were evaluated, (3) the dose of piperine and/or curcumin may not have been optimal, and (4) long-term outcomes were not assessed despite that MDD is a chronic condition.

The authors used rigorous methodology in conducting the meta-analysis. These encouraging results indicate that larger and longer-duration clinical trials of curcumin in the treatment of MDD are warranted. There were no conflicts of interest.

—Heather S. Oliff, PhD

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