Incidence of type 2 diabetes (T2D) is rising dramatically. In 2015, ~ 415 million people had T2D (8.8% of the world's population), with 46.5% unaware of their illness. It is estimated that T2D will affect 439 million people by 2030; by 2040, 642 million. T2D has genetic, environmental, and lifestyle contributors. These cause poor insulin production or impair the body's ability to use insulin properly. Chronic hyperglycemia, with increasing oxidative stress and inflammation, can cause macro- and microvascular complications.

Chamomile (CH; *Matricaria chamomilla* syn. *Chamomilla recutita*, Asteraceae) has anti-inflammatory, antioxidant, anticancer, antimicrobial, antispasmodic, and sedative effects. Its apigenin, quercetin, esculetin, luteolin, and chlorogenic acid impact many cellular processes. They may regulate carbohydrate digestion and absorption. In vitro evidence suggests apigenin as CH's main inhibitor of α-amylase. Chamazulene, its major terpenoid, scavenges free radicals, inhibiting chain formation and lipid peroxidation. In vivo and in vitro studies suggest hypocholesterolemic and anti-platelet activities, supporting CH's cardioprotective potential. Among herbs studied for effects in T2D, CH has not previously been reviewed systematically. The authors searched electronic databases for in vivo and human clinical trials. In vitro studies, reviews, letters, etc., and non-English language publications or those unavailable in full text were excluded. Of 208 records yielded, 87 were duplicates, and 102 were excluded based on title or abstract. Of 19 assessed in full text, four did not meet criteria. Of 15 included in this systematic review (SR), six were human trials; nine, in vivo. No evaluation of potential bias or study quality is mentioned, nor any reports of CH adverse effects.

Human trials' endpoints included blood glucose (BG), insulin, HbA1c, inflammation, lipid profile, oxidative stress, hepatic enzymes involved in glucose metabolism, liver and renal function, and weight changes in T2D. Details of most study designs are unclear. Patients received 2.5-10 g/d CH infused in hot water.* Interventions lasted 4-12 weeks. Four compared CH to placebo (PL); two, to black tea (*Camellia sinensis*, Theaceae) with patients who were also depressed. Three assessed CH in hyperglycemia; three, dyslipidemia. One glycemic study reported CH post-prandial and fasting blood glucose (FBG) levels were lower than but not significantly different from PL. In two trials, CH "markedly" reduced HbA1c vs.
PL or black tea. In one of these, CH also reduced serum insulin levels and insulin resistance and significantly reduced FBG < 11%; between group changes were not significant. Two dyslipidemia studies reported significant lipid profile changes; one did not. Of two trials assessing CH’s antioxidative and anti-inflammatory effects, one found improved antioxidant capacity; the other, reduced inflammatory factors. One trial studied effects of CH on T2D complications, reporting significant decreases in serum creatinine without changes in urea.

All in vivo studies included rats with variously induced diabetes. Three used a methanolic extract of CH; the rest, water extracts/infusions. Most administered 20-500 mg/kg/d extract for 2-14 weeks; one used 1 g/kg/d for 8 weeks. CH extracts were given orally via feeding cannels, drinking water, or gavage. All in vivo studies assessed glycemic results. Main outcomes were FBG, post-prandial BG, HbA1c, and serum insulin levels, and insulin resistance. Amylase activity; glycan-4, hepatic glycogen phosphorylase, and phosphatidylinositol-glycan-specific-phospholipase (GPL) D1 levels; and β-cells of pancreatic islets were reported by one study each. CH alone or with exercise produced higher levels of insulin (61%) and lower FBG (53%) vs. controls in one study. Another compared an aqueous solution of CH aerial parts to a similar solution of oregano (Origanum spp., Lamiaceae) at 150 and 300 mg/kg/d for six weeks. The high dose of each extract and combined low doses of both "remarkably" improved serum insulin levels and reduced amylase activity and HbA1c. While both CH doses improved FBG, 300 mg/kg/d was more beneficial (57% reduction vs. 20% for 150 mg/kg/d). One study found significant reductions in BG after 4 weeks with no effect on insulin levels. In another, 14 days CH administration increased insulin-positive β-cells of pancreatic islets and dose-dependently reduced BG. Another study reported significantly reduced BG (4.0%) after administration of an acute dose of CH extract. Other glycemic results were also encouraging. Two in vivo studies assessing the effects of CH (combined with oregano in one case) on blood lipids had promising but inconclusive results.

Oxidative stress and inflammation are highly related. Four in vivo studies reported CH's effects on oxidative stress markers in diabetic animals; none, on inflammatory response. Improved total antioxidant capacity, inhibition of liver and kidney lipid peroxidation, and enhanced superoxide dismutase and catalase activity were among the results reported. The three in vivo studies reporting on CH and T2D complications all reported significant changes in relevant outcomes. Higher doses were more efficacious than lower ones. One study reported a "remarkable" decrease in hepatic enzyme serum activity with CH supplementation; another, restoration of renal profiles in diabetic animals. Combined with oregano, CH significantly reduced apoptosis in renal cells.

While the evidence presented indicates that CH substantially lowers FBG and HbA1c, its regulation of lipid profiles remains inconclusive. Inconsistent results in many endpoints, often dramatically better in rats than in humans, were potentially due to many factors. More epidemiological studies are needed to better establish evidence for CH's properties and effects in T2D. Proposed mechanisms of action need in vitro and in vivo study.

—Mariann Garner-Wizard

*As still seen all too often in peer-reviewed journals, the authors refer throughout to this infusion as CH "tea." "Tea" properly refers only to Camellia sinensis, Theaceae.