

Chemistry and Pharmacology of Kinkéliba (*Combretum micranthum*), a West African Medicinal Plant

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Kinkéliba (*Combretum micranthum*, Fam. Combretaceae) is an undomesticated shrub species of western Africa and is one of the most popular traditional bush teas of Senegal. The herbal beverage is traditionally used for weight loss, digestion, as a diuretic and mild antibiotic, to relieve pain. The fresh leaves are used to treat malarial fever. As part of our program in validating traditional medicinal uses, this dissertation research examined the natural products chemistry and biologically active constituents in kinkéliba. Leaf extracts, as the most biologically active plant tissue relative to stem, bark and roots, were screened for antioxidant capacity, measuring the removal of a radical by UV/VIS spectrophotometry, anti-inflammatory activity, measuring inducible nitric oxide synthase (iNOS) in RAW 264.7 macrophage cells, and glucose-lowering activity, measuring both phosphoenolpyruvate carboxykinase (PEPCK) mRNA expression and glucose production in an H4IIE rat hepatoma cell line. Radical oxygen scavenging activity, or antioxidant capacity, was utilized for initially directing the fractionation; highlighted subfractions and isolated compounds were subsequently tested for anti-inflammatory and glucose-lowering activities. The ethyl acetate and *n*-butanol fractions of the crude leaf extract were fractionated leading to the isolation and identification of a number of polyphenolic compounds. Some of these compounds, the catechins and glycosylflavones, were previously reported in kinkéliba or other species in Combretaceae. Other compounds, the flavans and galloylated *C*-glycosylflavone derivatives, are being reported for the first time in this species and family. Finally, a group of major constituents in the kinkéliba leaves were discovered to be a series of compounds with a new skeleton, a flavan-piperidine alkaloid. The kinkéloids, as they are named here, were isolated and structurally elucidated by 1- and 2-D NMR spectroscopy and HRMS spectrometry. The positive glucose-lowering activities led to an animal study that tested the activity of the crude extract and fractions in mice fed a high-fat diet, resulting in the development of a diabetic model. The treated groups showed lowered baseline blood glucose measurements as well as decreased PEPCK levels in the liver, strongly suggesting that kinkéliba constituents may be beneficial in the treatment of Type 2 diabetes.