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A single dose of kudzu extract reduces alcohol consumption in a binge drinking paradigm

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ABSTRACT

Background: Overconsumption of alcohol has significant negative effects on an individual's health and contributes to an enormous economic impact on society as a whole. Pharmacotherapies to curb excessive drinking are important for treating alcohol use disorders.
Methods: Twenty (20) men participated in a placebo-controlled, double-blind, between subjects design experiment ($n = 10$/group) that tested the effects of kudzu extract (Alkontrol-Herbal™) for its ability to alter alcohol consumption in a natural settings laboratory. A single dose of kudzu extract (2 g total with an active isoflavone content of 520 mg) or placebo was administered 2.5 h before the onset of a 90 min afternoon drinking session during which participants had the opportunity to drink up to 6 beers *ad libitum*; water and juice were always available as alternative beverages.
Results: During the baseline session, the placebo-randomized group consumed 2.7 ± 0.78 beers before treatment and increased consumption to 3.4 ± 1.1 beers after treatment. The kudzu group significantly reduced consumption from 3.0 ± 1.7 at baseline to 1.9 ± 1.3 beers after treatment. The placebo-treated group opened 33 beers during baseline conditions and 38 following treatment whereas the kudzu-treated group opened 32 beers during baseline conditions and only 21 following treatment. Additionally, kudzu-treated participants drank slower.
Conclusion: This is the first demonstration that a *single* dose of kudzu extract quickly reduces alcohol consumption in a binge drinking paradigm. These data add to the mounting clinical evidence that kudzu extract may be a safe and effective adjunctive pharmacotherapy for alcohol abuse and dependence.

1. Introduction

Excessive alcohol consumption is a leading cause of illness worldwide (Shield et al., 2013) and has a significant impact on the health of millions people. Over the past two decades, alcohol abuse has affected the national economy and is on the rise as analysis of the estimated cost of alcohol abuse in the US has risen from $148 billion in 1992 (Harwood et al., 1998) to $184.6 billion in 1998 (Harwood, 2000), and to $223.5 billion in 2006 (Bouchery et al., 2011). The impact of excessive alcohol consumption results in increased healthcare costs, loss of productivity, alcohol-related crime (including assault and sexual abuse), and motor vehicle accidents.

Patterns of alcohol consumption vary, but one of the more pervasive types in the younger population is binge drinking. Binge drinking is defined as the consumption of 5 or more drinks for men, and 4 or more drinks for women, in a 2-h period (National Institute on Alcohol Abuse and Alcoholism (NIAAA), 2015). (A standard drink in the US is defined as containing 14 g of alcohol, an amount found in 12 oz of beer, 5 oz of wine, and 1.5 oz of 80-proof liquor.) This pattern of rapid drinking typically produces a blood alcohol level above the legal driving limit of 0.08%, and is associated with many alcohol-related problems (including accidents, injuries, crime, and lost productivity; Bouchery et al., 2011; Center for Disease Control and Prevention (CDC), 2004; NIAAA, 2000). The CDC reports that in 2001, binge drinking was responsible for approximately half of the alcohol-related deaths and two-thirds of the economic costs (as measured in years of potential life lost; CDC, 2004). A recent

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government survey found that 23% (58.6 million) of persons 12 years of age and older engaged in binge drinking in the 30 days prior to the survey (Substance Abuse and Mental Health Services Administration (SAMSHA), 2011). Other surveys have found that 17% of adults engage in a binge drinking episode 4 times per month and consume ~8 drinks per episode (CDC, 2012) and 50% of college-aged drinkers report binge drinking in the past two weeks (NIAAA, 2014).

There are currently three FDA-approved medications for alcohol use disorders: disulfiram (Antabuse®), naltrexone (in both an oral formulation [ReVia®] and a sustained-release injectable formulation [Vivitrol®]), and acamprosate (Campral®) (Friedmann, 2013; Williams, 2005). All are available only by prescription. While they are effective for some individuals, they are not universally useful or well tolerated for all patients. Currently, we do not know which treatment strategy is useful for an individual patient population (Kranzler, 2000) and the many side effects often limit their acceptance and adherence (Edwards et al., 2011). There are no over-the-counter medications or preparations that are proven to reduce alcohol consumption, and no medication has been evaluated specifically to treat binge drinking patterns of consumption.

Readings of historical Chinese texts (Li, 1590–1596; Sun, circa 600 AD) reveal that extracts of the kudzu root have been used to treat alcoholism and drunkenness since at least 600 AD. Recent analysis of the kudzu root has revealed it contains 3 active isoflavones that have antidipsotropic activity: daidzin, daidzein, and puerarin. Studies with these components demonstrated significant reductions in alcohol consumption in animal models. Heyman et al. (1996) showed that daidzin-treated rats had a dose-related decrease in lever pressing reinforced by oral alcohol consumption. Keung and co-workers showed the effectiveness of daidzin and daidzein to suppress ethanol consumption in Syrian golden hamsters (Keung et al., 1995; Keung and Vallee, 1993a,b). Lin et al. (1996) showed dose-related reductions in alcohol consumption of 40 to 65% with oral ingestion of puerarin (100–300 mg/kg/day). Benlhabib et al.'s (2004) work with puerarin showed not only a 50% reduction in alcohol intake, but a suppression of alcohol withdrawal symptoms in alcohol preferring rats.

Our laboratory has been involved in assessing an extract of the kudzu root (*Pueraria lobata*) for its ability to reduce alcohol consumption in humans. In the first study, kudzu extract was administered for 7 days and acute binge drinking was suppressed (Lukas et al., 2005). In the second study, participants who were treated for 4 weeks with kudzu extract significantly reduced their alcohol consumption during weeks 2 through 4 of the study (Lukas et al., 2013). We have subsequently shown that puerarin is the major active isoflavone because 7 days treatment with this compound alone (1200 mg/day) produced a similar reduction of binge drinking as the extract (Penetar et al., 2012). Given that a week of preplanning is unlikely before a binge drinking episode or opportunity, we built on our previous findings to explore in the present experiment if a *single dose* of kudzu extract taken shortly before a drinking session would reduce alcohol consumption.

2. Materials and methods

2.1. Participants

A total of 32 participants (28 men, 4 women) between the ages of 21 and 40 years old were recruited through advertisements in local newspapers and on the internet (e.g., CraigsList and local University websites) to participate in this study. Inclusion criteria included good physical and mental health, a body mass index (BMI) between 18 and 30, ages between 21 and 40 yrs, and a self-reported drinking pattern of 15 drinks per week or incidences of binge drinking 2 or more times per week. Exclusion criteria included a diagnosis of an Axis I disorder (as assessed through the Structured Clinical Interview for DSM disorders (DSM-IV-TR; First et al., 2002), psychoactive prescription medication, current or past alcohol dependence, cigarette consumption greater than 5 per day, and heavy caffeine use (defined as greater than 500 mg of consumption per day). Four participants failed to meet inclusion criteria and 8 participants dropped out of the study before completion (1 after the first drinking session and was lost to follow-up; 7 due to schedule conflicts with work, school or family emergencies and were not interested in continuing). Twenty men (18 Caucasian [1 Hispanic] and 2 multiracial) completed both sessions of the study and were used in the analysis. They were physically and mentally healthy individuals, 23.6 ± 3.6 years old, with a BMI between 22 and 30 ($M = 25.4 \pm 2.5$) and reported drinking on average 3.4 ± 0.9 days/week and consumed on average 18.5 ± 6.2 drinks per week with an average of 5.7 ± 2.0 drinks per drinking day (demographics reported in Table 1). All participants were primarily beer drinkers, only occasionally consuming other types of alcoholic drinks. None of the participants met criteria for alcohol abuse or dependence, nor had current psychiatric disorders. Seven were light cigarette smokers (less than 1 to 4 cigarettes per day), 13 used marijuana recreationally (up to 2 times per month), and none were heavy users of caffeinated beverages. The McLean Hospital Institutional Review Board reviewed and approved the study and related documents (advertisements, informed consent, protocol). Participants provided written informed consent and were financially compensated for their time.

2.2. Materials and medication

Drinking sessions were conducted in a modified laboratory room decorated to simulate a dormitory or small apartment (the 'natural settings') room and included carpeting, wall hangings, an overstuffed reclining chair, end tables, lamp, television with satellite connections, DVD player and stereo equipment, and bookcases. The room contained a small sink with an under-the-counter refrigerator where the beverages (beer, juice, and water) were kept.

Kudzu extract was administered in gelatin capsules containing 500 mg of extract (Alkontrol-Herbal™; NPI-031) prepared by Natural Pharmacia International, Inc., Burlington, MA. The extract contained 26% (130 mg) active isoflavones (20% puerarin, 4% daidzin, 2% daidzein; an improved HPLC analysis revealed

Table 1
Demographic profiles of participants. Values are averages ± sd.

	Placebo ($n = 10$)	Kudzu ($n = 10$)	p Value
Age (years)	24.6 ± 3.3	22.6 ± 3.7	0.785
Weight (pounds)	181.3 ± 9.5	176.3 ± 22.5	0.529
Body mass index (BMI)	26.1 ± 2.2	24.6 ± 2.6	0.192
Race (Ethnicity)	9 Caucasians; 1 Multiracial	9 Caucasians; 1 Multiracial; (1 Hispanic)	
Age of first drink	16.2 ± 2.0	16.2 ± 1.9	>0.99
Years drinking regularly	5.3 ± 3.5	4.6 ± 3.5	0.661
No. of drinks/week	15.8 ± 5.6	21.1 ± 5.8	0.054
No. of drinking days/week	3.4 ± 0.94	3.5 ± 0.96	0.817
No. of drinks/drinking day	4.9 ± 1.6	6.5 ± 2.1	0.068
Tobacco smokers[1]	0	1	
Marijuana users[2]	6	7	

[1] Those reporting daily smoking (participant reported smoking ~4 cigarettes/day).
[2] All users reported 2 times per month or less.