NATURAL INHIBITORS OF ALDH2 (ISOFLAVONES) AND ITS POSSIBLE EFFICACY IN SUBSTANCE USE DISORDERS

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INTRODUCTION

Isoflavones (specifically daidzein) are specifically reversible inhibitors of aldehyde dehydrogenase-2. Its use in the treatment of alcohol use disorder has been associated with a reduction of cocaine use in animal reports but not in humans. Its mechanism of action, differs from disulfiram (the drug that has more positive outcomes for the treatment of cocaine use disorder) because it inhibits aldehyde dehydrogenase-1 (ALDH1) and aldehyde dehydrogenase-2 (ALDH2) irreversibly and produces an accumulation of acetaldehyde in blood, leading to undesirable effects if alcohol is consumed simultaneously. The high prevalence of alcohol-cocaine simultaneous consumption (higher than 60%), requests drugs well tolerated if alcohol is consumed.

OBJECTIVES

To evaluate if a natural inhibitor of ALDH2 (daidzein) is well tolerated if alcohol is taken and its possible positive effects in cocaine use disorder.

METHODS

Two phases of the study were carried out:

The first, is a crossover-single blind-randomized, with ten healthy male volunteers (mean age of 23.9), going through two experimental sessions: one taking single dose of alcohol (0.5 g/kg, Vodka Absolut, Sweden) and other taking four capsules of soy extract product (Super-Absorbable Soy Isoflavones, Life-Extension, United States) and 2h later, the same dose of alcohol.

The second one, is a unicentric-open-uncontrolled with nine subjects (mean age of 48+9.27) with Cocaine Use Disorder, going through 12 weeks of treatment with Super-Absorbable Soy Isoflavones and 4 weeks of follow up. An intention to treat analysis was performed.

Data were analyzed with SPSS 18.0 statistical package.

RESULTS

The first phase of the study, did not presented differences between sessions in vital signs (except slightly higher significative reduction in diastolic blood pressure at 2, 3, 4, and 8 h after administration with alcohol alone) and subjective and adverse effects (except headache higher at 8h after alcohol alone administration) (Figure 1). No differences were found in blood ethanol concentrations (Figure 2).

In the second phase, 77.8%(7) of volunteers ended the study, the Severity Dependence Scale (SDS) had a significant decrease between weeks 0-12 (p=0.024) and weeks 0-16 (p=0.002); according to the Substance Use Report (SUR), 3(33.3%) of them consumed less than 20% of the days during the last three weeks; but during the last three weeks of the treatment no one reached the abstinence (Table 1).

Figure 1. Time course of the physiological and subjective effects after administration of ethanol and soy isoflavones + ethanol. Mean values and standard error (n=10). Figures correspond to systolic and diastolic blood pressure (mmHg), heart rate (beats/min), and drunkenness (mm)

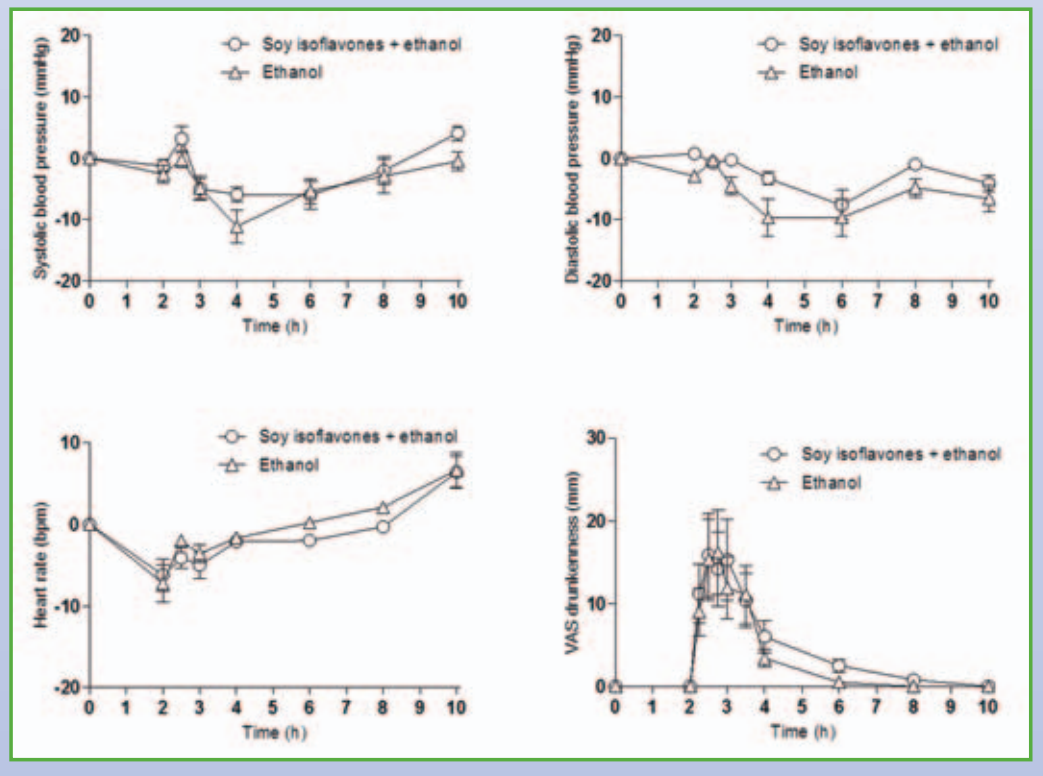

Figure 2. Plasma concentrations of alcohol after the administration of alcohol and soy extract + alcohol. Mean values and standard error (n=10).

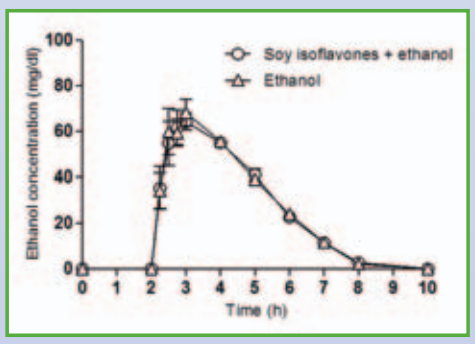

Table1. Results of the Severity Scales . Severity Dependence Scale(SDS), Brief Substance Craving Scale (BSCS) and Cocaine Selective Severity Assessment (CSSA).

Main Scales Results SCALES	SCORES	N=9 P
BSCS(mean, SD)		
Week 0-12	1.89±3.95	0.1
Week 0-16	2.44±4.36	0.1
Week 12-16	0.55±2.55	0.5
SDS(mean, SD)		
Week 0-12	4±4.33	0.024
Week 0-16	5.77±3.8	0.002
Week 12-16	1.78±2.59	0.073
CSSA(mean, SD)		
Week 0-12	1±1.56	0.8
Week 0-16	1.78±17.3	0.76
Week 12-16	0.78±15.4	0.88

CONCLUSIONS

Results demonstrate that soy isoflavone extract did not interfere in the acetaldehid metabolism. Also, preliminary data suggests that in the treatment of cocaine use disorder, isoflavones could decrease the severity of cocaine consumption and increase retention. Cocaine-alcohol comorbidity has a high prevalence, it is important the availability of treatments that do not interact with alcohol consumption.

Literature Reference

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Supported in part by grants of Ministerio de Sanidad (Investigación Clínica Independiente, EC-10-166) and Instituto de Salud Carlos III (ISCIII-UE-FEDER: Red de Trastornos Adictivos-RTA, RD12/0028/0009; RD16/0017/0003 and RD16/0017/0010; L. Galindo is a Rio Hortega fellowship, CM14/00111).