

# The Four-Loko Effect

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## Abstract

There have been recent reports of mass hospitalizations for alcohol intoxication following consumption of fruit-flavored, caffeinated, alcoholic drinks—especially concerning one brand in particular: Four Loko. Caffeine was quickly determined to be the culprit. In accordance with a directive by the Food and Drug Administration, caffeine was removed from Four Loko and similar beverages. However, the evidence that caffeine played a prominent role in widespread displays of intoxication is far from clear. Rather, it is likely that Four Loko-type drinks are especially effective as intoxicants because they provide alcohol in an unusual context. It has been known for many years that drug tolerance partially results from an association between drug-paired stimuli and the drug effect. When these stimuli are altered, the drug-experienced individual does not display the expected tolerant response to the drug—rather, an enhanced (i.e., nontolerant) response is seen. Four Loko and similar beverages may be especially effective intoxicants because they provide a very novel flavor context for alcohol. A recent announcement by the manufacturer of Four Loko suggests (either by design or happenstance) appreciation of the contribution of alcohol-associated cues to alcohol tolerance.

## Keywords

alcohol, tolerance, energy drink, intoxication

In September 2010, 23 students at Ramapo College in Mahwah, NJ, were hospitalized for alcohol intoxication. The next month, after a party in Ellensburg, WA, attended by Central Washington State College students, 12 partygoers had to be hospitalized for alcohol intoxication. A beverage named Four Loko was identified as the culprit in these and other instances of mass intoxication. In many news reports and websites, Four Loko was labeled “blackout in a can” and “liquid cocaine.” Phusion Projects, the manufacturer of Four Loko, is the defendant in several unlawful death lawsuits.

Four Loko was the invention of three students at Ohio State University in 2005. The product they developed was a fruit-flavored, caffeinated, alcoholic drink that also contained guarana (a South American caffeine-containing plant) and taurine (an amino acid derivative). The “Four” in Four Loko originally referred to the four primary ingredients: alcohol, caffeine, taurine, and guarana. Almost all discussions of the baneful effects of Four Loko have focused on the mischievous effects of combining alcohol with caffeine. Some have claimed that the stimulant masked the intoxicating effects of alcohol, thus encouraging excess alcohol consumption. Ramapo College, Central Washington State University, and many other colleges and universities quickly banned the drink, as did many states.

The Food and Drug Administration (FDA) decided that caffeine was an illegal additive to an alcoholic beverage. As stated in a November 18, 2010, letter to several companies making such drinks (including Phusion Projects), the FDA said that consumption of caffeine-containing alcoholic beverages could lead to “hazardous and life-threatening situations” (United States Food and Drug Administration, 2010). The manufacturers were given 15 days to remove caffeine from their drinks, and they complied.

## Why the Hyperintoxicating Effect of Four Loko?

Prior to coerced decaffeination, Four Loko contained 12% alcohol (6% in some jurisdictions) and an undisclosed amount of caffeine. According to the manufacturer, the caffeine content was comparable to that found in a cup of coffee. Although

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caffeine was the designated villain in the Four Loko story, the evidence that the stimulant modulates either the physiological, objective behavioral, or subjectively rated effects of alcohol is far from clear.

### **The role of caffeine**

Some clinicians have suggested that the stimulant effect of caffeine may antagonize the soporific effect of alcohol and that “lengthened time awake theoretically allows greater alcohol intake before loss of consciousness” (Weldy, 2010, p. 556). Not surprisingly, this theoretical possibility has not been evaluated. There do not appear to be published findings comparing time-to-unconsciousness in people permitted to freely consume caffeinated and noncaffeinated versions of alcoholic drinks. There are, however, many other studies of caffeine–alcohol interactions.

Caffeine does not affect the pharmacokinetics of alcohol—breath and blood alcohol concentrations are similar following ingestion of alcohol alone or caffeine and alcohol together (e.g., Azcona, Barbanoj, Torrent, & Jané, 1995; Ferreira, de Mello, Rossi, & de Souza-Formigoni, 2004). Interpretation of the various behavioral studies of caffeine–alcohol interactions is complicated by the fact that they have used different drug doses and different tasks (e.g., pursuit rotor, reaction time). Some have reported that caffeine offsets the debilitating effects of alcohol (e.g., Hasennfratz, Bunge, Prá, & Bättig, 1993; Rush, Higgins, Hughes, Bickel, & Wiegner, 1993), and others reported that caffeine has no effect (e.g., Ferreira et al., 2004; Nuotto, Mattila, Seppälä, & Konno, 1982). When participants simply are asked to rate their level of intoxication, the addition of caffeine to alcohol may decrease (e.g., Ferreira, de Mello, Pompéia, & de Souza-Formigoni, 2006), increase (e.g., Fillmore, Roach, & Rice, 2002), or have no effect (e.g., Azcona et al., 1995) on subjective drunkenness.

As an additional complication, when any effect of caffeine on alcohol-induced impairment is noted, it may be due not to the pharmacological interaction of the stimulant and depressive drugs, but rather to “the ironic effects of expectancy” (Fillmore et al., 2002). Fillmore and colleagues demonstrated that participants that drank coffee immediately after drinking an alcoholic beverage were more impaired on a psychomotor task than those who consumed alcohol alone if, and only if, the participants were led to believe that caffeine counteracted the effects of alcohol. According to Fillmore et al., these participants did not compensate for the impairing effects of alcohol because they relied on caffeine to attenuate alcohol’s effects. The expectation manipulation, rather than caffeine, was responsible for the effects of coffee because similar results were obtained with caffeinated and decaffeinated coffee. According to Fillmore et al., their results suggest that caffeine itself does little to modify the effects of alcohol and that any apparent effects of the stimulant are manifestations of the drinker’s expectancies concerning caffeine–alcohol interactions.

In summary, the evidence that caffeine is the agent responsible for the alleged displays of excessive intoxication seen following

consumption of the original formulation of Four Loko and similar beverages is not overwhelming. Not surprisingly, Phusion Projects minimized any harmful consequences of combining alcohol with caffeine, noting that the combination “is comparable to having coffee after a meal with a couple glasses of wine” (Phusion Projects, 2010). Indeed, based strictly on pharmacology, Four Loko should have about the same effect as a bottle of wine and some coffee. Even the cost of Four Loko (about \$3.00 to \$4.00) is comparable with wine and coffee (if you buy Trader Joe’s “Two Buck Chuck”). Why did this particular beverage cause so many people to become so inebriated that they required hospitalization?

### **The situational-specificity of tolerance**

One reason why Four Loko and similar beverages may be especially effective intoxicants was intuited by the New York Times columnist, Frank Bruni: “If you set out to engineer a booze delivery system that is as cloying, deceptive and divorced from the usual smells, tastes and presentation of alcohol as possible, you’d be hard pressed to come up with something more impressive than Four Loko” (Bruni, 2010). Four Loko (and similar beverages) induce an exaggerated effect because they provide alcohol in an unusual context.

It has been known for many years that drugs in general, and alcohol in particular, have a greater effect if they are administered in the presence of unusual cues rather than in the presence of cues typically associated with the drug. Thus, if you present alcohol in a manner divorced from the usual alcohol-associated stimuli, the effects of the alcohol are enhanced. That is, the drug-experienced individual does not display the expected tolerant response to the drug when it is administered in the presence of cues not previously associated with the drug. Rather, a large response to the drug, typically seen in the drug-inexperienced individual, is displayed. The phenomenon has been termed “the situational specificity of tolerance” (Siegel, 1976).

Although experimental studies of the situational specificity of tolerance typically have manipulated environmental cues (e.g., the room where the drug is administered), there is evidence that a variety of stimuli may become associated with a drug and control the display of tolerance. Ambient temperatures (Kavaliers & Hirst, 1986) or magnetic fields (Kavaliers & Ossenkopp, 1985) may, after being paired with drug administration, influence the display of tolerance. Flavor cues also may serve as effective drug-associated cues that modulate the display of tolerance (e.g., McNally & Westbrook, 1998). For example, most experienced coffee drinkers are tolerant to many effects of caffeine. Thus, drinking a cup of coffee has a comparatively smaller effect on blood pressure in individuals who routinely drink caffeinated coffee than it does in caffeine-inexperienced individuals. However, if the caffeine is administered to the caffeine-tolerant individual in a manner circumventing the usual caffeine predictive cues (i.e., blood levels similar to those obtained by drinking coffee are achieved by intravenous caffeine administration), the elevated blood

pressure response is apparent (Siegel, Kim, & Sokolowska, 2003).

The most dramatic demonstrations of situation specificity of tolerance concern tolerance to the lethal effects of drugs. Opiate addicts (or patients receiving medically prescribed opiates) who become tolerant to the respiratory-depressive effects of the drug, may experience a (so-called) “overdose” if they take the usual dose of the drug in an unusual setting (e.g., Gerevich, Bácskai, Farkas, & Danics, 2005; Gerevich, Bácskai, & Kurimay, 2004; Gutiérrez-Cebollada, de la Torre, Ortuño, Garcés, & Camí, 1994; Siegel, 2001). In studies with rats and mice, situational-specificity of tolerance to drug lethality has been demonstrated with a variety of drugs (see Siegel, 2001) including alcohol (Melchior, 1990).

In summary, situational specificity of tolerance is very general. It has been seen with respect to tolerance to a variety of effects of various drugs and in many species, from snails to humans, suggesting that such specificity “may be a general phenomenon having an early evolutionary development and broad phylogenetic continuity” (Kavaliers & Hirst, 1986, p. 1201).

Tolerance situational-specificity results because we prepare for the physiological changes produced by a drug when we are provided with cues that a drug effect is imminent. It has been known at least since the time of Ivan Pavlov that our bodies prepare for food when it is time to eat, or when we smell the food cooking, or when we perceive other signals that a meal is imminent. More recently, it has been determined that we similarly prepare for a drug. Generally, this preparation tends to lessen the drug effect (and thus is one mechanism of drug tolerance). However, if the drug is presented in a manner that does not allow for such anticipatory responding, we experience the full drug affect unmodulated by any preparatory response. Evidence in support of this associative account of drug tolerance has been extensively reviewed elsewhere (e.g., Dworkin, 1993; Siegel, 2005; Siegel, Baptista, Kim, McDonald, & Weise-Kelly, 2000).

We may surmise that the Four Loko experience for many undergraduates would involve receiving alcohol in an unusual context. As noted by Bruni (2010), Four Loko—a “biliously colored,” sweet, synthetically fruity beverage—is an unusual medium for alcohol: “It’s a malt liquor in confectionary drag.” The results of studies of situational-specificity of tolerance suggest that Four Loko and similar drinks are especially effective as intoxicants because these beverages provide an unusual context for the intoxicating drug that they deliver.

There are several reports of situational-specificity of alcohol tolerance in humans. Some studies are experiments that have cues explicitly paired with a drug effect. Others have used opportunistic designs that rely on the participants’ extraexperimental conditioning histories.

For example, Shapiro and Nathan (1986) reported results of an experiment in which certain environmental cues were explicitly paired with alcohol. Men (aged 19–36), identified as “light to moderate drinkers,” consumed an alcohol-*tonic* mixture on five occasions, once every other day for 10 days. On those alternate days when they did not consume the alcohol

beverage, they consumed unadulterated tonic. Each beverage was presented in the context of different visual and gustatory cues. In the “lab” environment, the beverage was offered in a large room filled with a variety of laboratory paraphernalia. In this environment, just before drinking the beverage, participants gargled with a green, menthol-flavored mouthwash. The alternative “home” environment was set up as a small bedroom, equipped with a television, bed, dresser, table, and chair. Prior to consuming the beverage in this environment, participants gargled with a red, cherry-flavored mouthwash. Half the participants consumed the alcohol-adulterated tonic in the lab environment and the unadulterated tonic in the home environment. The relationship between environmental cues and substance ingested was reversed for the remaining participants. Finally, in a test session, all participants consumed the tonic-alcohol mixture in the lab environment. Those who had previously consumed alcohol in this lab environment were less impaired in their performance on a coding-vigilance task than were those who consumed alcohol in the home environment. That is, tolerance was situationally specific to the environment where the alcohol had previously been consumed.

McCusker and Brown (1990) described the results of an opportunistic study concerning situational specificity of tolerance to alcohol in university students. All were experienced social drinkers (consuming, on average, about one-half pint of beer per day). These participants were divided into groups. One group was given alcohol in a familiar form and context (they consumed beer in a simulated bar), whereas a second group was administered the same dose of alcohol in a novel form and unusual context (the alcohol was mixed in artificially sweetened carbonated water and consumed in an office setting). Based on several objective measures of intoxication, the unusual context group became more inebriated than the usual context group.

McCusker and Brown (1990) manipulated context by controlling both external cues (the place where the alcohol was consumed) and cues inherent to the beverage (the flavor of the drink). In fact, it is possible to demonstrate the situational-specificity of alcohol tolerance merely by manipulating flavor cues. Remington, Roberts, and Glautier (1997) reported results that should have alerted alcohol beverage entrepreneurs to the possibility of enhancing the intoxicating effects of their products by simply using an unusual flavor. The Remington group demonstrated that their college-student volunteers became more intoxicated after consuming alcohol in a novel colored and flavored beverage (a blue-colored, peppermint-flavored drink) than they did consuming the same amount of alcohol in a more typical alcohol-associated beverage (a beer-colored and beer-flavored drink).

In summary, many people have become very drunk after consuming Four Loko because the drink provides a novel context for alcohol administration; alcohol tolerance, having been acquired in the context of different cues, may not be exhibited in the context of Four Loko cues. Perhaps the rather unwieldy phrase “situational-specificity of tolerance” should be renamed the “Four Loko effect.”

## The New “Four” in Four Loko

The “Four” in Four Loko no longer refers to the primary ingredients in the beverage (alcohol, caffeine, guarana, and taurine). As indicated, Phusion Projects announced the removal of the stimulants (in a press release dated November 16, 2010). Seven weeks later, the company issued another press release that gave a new meaning to the “Four.” This new marketing strategy appears relevant to a further implication of the associative analysis of tolerance.

On the basis of this associative analysis, an individual with considerable experience with a particular flavor of Four Loko should eventually acquire tolerance to the effects of alcohol consumed in conjunction with that flavor. Consider, for example, someone who frequently consumes watermelon-flavored Four Loko. This flavor, which likely would be experienced initially as an unusual cue for alcohol, has been described by Bruni (2010):

The watermelon-flavored Four Loko, for example, is a shade of rosy pink that puts me in mind of sherbet. Or bridesmaid dresses. Or maybe Bubble Yum bubblegum. In fact, the watermelon tasted somewhat like that too. It certainly didn't bear any relation to any melon that I've ever tripped across — or, for that matter, to any known fruit. Its sweetness is more generic and synthetic, and makes Hi-C seem like a blast of unsullied farm-to-table goodness. (p. WK5)

Because of the Four Loko effect, this individual would not display his usual level of alcohol tolerance when initially consuming this novel-flavored alcoholic beverage. However, as the individual continues to consume watermelon-flavored Four Loko, the association between this flavor and the systemic effects of alcohol would increase, and the alcohol-compensatory learned responses elicited by the predrug flavor cue would increasingly strengthen. Eventually, alcohol tolerance would be manifest when the alcohol is consumed in the context of the watermelon flavor.

According to the associative interpretation of tolerance, one way to attenuate the development of tolerance is to alter the predrug cues over the course of successive administrations (thus decreasing the number of pairings of any particular cue with the drug effect). That is, tolerance should be decreased if the Four Loko aficionado drank the various available flavors—first, the watermelon-flavored beverage, then the blue-raspberry-flavored beverage, then the cranberry-lemonade-flavored beverage, and so on.

The prediction that altering predrug cues should retard the development of tolerance is a straightforward implication of the associative interpretation of tolerance (Siegel, 2008). There is a report that the changing-cue procedure attenuates tolerance to the cardiac effects of nicotine. Epstein, Caggiula, Perkins, McKenzie, and Smith (1991) evaluated heart rate in two groups of participants who smoked cigarettes over five experimental sessions (following common instructions about when and how long to puff). For the “repeated” group, the same precigarette

cue was presented prior to each smoking session. For the “changing” group, a different predrug cue was presented prior to each smoking session. The results were clear: “The decreased heart rate to repeated bouts of smoking for subjects in the Repeated group suggests the development of acute tolerance. Tolerance to the heart rate effects of smoking did not develop for subjects who experienced smoking in a context that changed before each smoking bout, suggesting cardiovascular effects of smoking are influenced by the context of drug administration” (Epstein et al., 1991, p. 17). Some have suggested practical applications of the technique. In a webpage titled “Changing Environment to Prolong Drug Effectiveness: A Practical Application of Environmentally-Induced Drug Tolerance Theory” (Schueler & Schueler, 2002), varying predrug context is recommended as a strategy to minimize tolerance to therapeutically administered drugs and to thus avoid the necessity of increasing dosage. The patient is advised to “periodically change the environment where you take the medication . . . addictive behavior research indicates that changing environments should prolong a drug's effectiveness without having to increase dosage . . . Keep alternating where you take your medication so that psychological cues never have a chance to develop and no tolerance can set in.”

Such a changing-context procedure is now a feature of the newest Four Loko product. According to a press release dated January 4, 2011, the “Four” apparently now denotes the interval (in months) that the beverage will be available in a particular flavor before cycling to a different flavor:

Phusion Projects today announced the launch of its newest product: Four Loko XXX Limited Edition. The innovative product will feature a brand new Four Loko flavor profile every four months . . . “From our inception, Phusion Projects has always led the alcohol industry with new, innovative products, and we're building on that legacy with Four Loko XXX Limited Edition,” said Jeff Wright, a Phusion Projects co-founder . . . since each flavor will only be around for a limited time, we hope our customers will try each one while they can and then tell us what they think about it. (Phusion Projects, 2011)

## Giving Psychology Away

In perhaps the best known address by a president of the American Psychological Association, George Miller advocated that psychologists become more active in promoting their research to the general public as a way of addressing social problems: “I can imagine nothing we could do that would be more relevant to human welfare, and nothing that could pose a greater challenge to the next generation of psychologists, than to discover how best to give psychology away” (Miller, 1969, p. 1074). Subsequently, others similarly have suggested that basic research findings could be put to use to benefit society (Klatzky, 2009; Zimbardo, 2004). Of course, when we publish our results and “give psychology away,” some recipients may be more virtuous than others.



An entrepreneurially inclined reader of the extensive literature on associative drug tolerance, motivated to concoct an alcohol-containing beverage that would deliver maximal bang for the buck, might well decide to use bizarre flavors and then systematically vary the availability of these flavors. Coincidentally, that appears to be the strategy of Phusion Projects with respect to Four Loko and Four Loko XXX Limited Edition. However, as we teach our students, it is not easy to disentangle correlation from causation.

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