Since World War II there has been a massive increase in the use of drugs, physician prescribed, over the counter, and illicit. Simultaneously, a large increase has occurred in the use of alcohol. The likelihood of combined use of alcohol and another drug has substantially increased. Moreover, epidemiological studies in the United States indicate that alcohol drinkers are more likely to use psychoactive drugs than are non-drinkers (Abelson & Fishburn, 1976).

There is epidemiological evidence that such combined use is reflected in roadside accident rates. For example, Bø, et al. (1975) determined diazepam and alcohol blood levels both in drivers hospitalized after accidents and in control drivers. For the accident drivers, 41.8% had alcohol alone present, 9.5% had diazepam alone present, and 10.8% had both drugs present. This compared with 1.5% of the control group having alcohol alone, 2% having diazepam alone and no members of the control group with both drugs present.

Similarly, a study of fatally injured drivers and pedestrians (Traffic Injury Research Foundation of Canada, 1980) found alcohol alone present in 41% of the fatalities, drugs alone in 12% and drugs with alcohol in 14%. Clearly, the few epidemiological studies available suggest that alcohol alone, drugs alone, or drugs in combination with alcohol are all overrepresented with respect to their likely distribution in the general population of drivers.

Given the sparseness of epidemiological studies in this area, can the experimental literature on combined alcohol-drug administration permit us to state which drugs in combination with alcohol...
present a threat to the driving public? This paper will examine this issue by a brief review of studies of joint alcohol-drug use on driving-related behavior. The review cannot claim to be inclusive but represents the results of a computer search and the availability of periodicals in a major university library.

Specifically excluded from this review were studies primarily concerned with physiological side effects. Excellent reviews of such studies can be found in reviews by Coleman and Evans (1975) and Kissin (1974).

Clearly, responses such as vomiting, cramps, breathing difficulties, etc. found in joint alcohol-disulfiram use, will seriously impair driving. Such impairment will in many cases be obvious to the user. What is less obvious are the dangers involved in the joint use of alcohol with drugs where the prime symptoms are predominantly behavioral.

In the following, reference will be made only to whether joint use results in greater impairment than associated with either drug alone. No attempt will be made to describe the results as sub-additive, additive or supra-additive. This position has been taken because nearly all the studies utilized only one active dose level of the drug and alcohol. Accurate determination of the linearity or non-linearity of drug interactions requires several dose levels. As examples of the complexity of such interactions, I refer you to the paper by Carpenter, et al. (1975) on meprobamate-alcohol interaction and by Moskowitz and Burns (1980) on caffeine-alcohol interaction.

**Minor Tranquilizers**

This class of psychotropic drugs is most likely to be found in combined use with alcohol among the general population. Many are unaware that these are CNS depressants that can increase the effects of alcohol on performance skills and alertness. For example, meprobamate and alcohol have been shown to impair performance skills. Goldberg (1963) reported decreased oculomotor control and body steadiness as well as drowsiness and fatigue after combined alcohol-meprobamate use. Loomis (1963) found increased impairment of tracking and reaction time measures in a driving simulator.
Zirkle, et al. (1960) reported increased impairment on tasks ranging from simple arithmetic to accuracy of visual illusions. Forney and Hughes (1964) found increased impairment of cognitive tasks such as arithmetic and mental tests. Reisby and Theilgaard (1960) obtained increased impairment in time estimation, attention, reaction time, body steadiness, oculomotor control and alertness.

The two most prominent minor tranquilizers are the benzodiazepines, diazepam and chlordiazepoxide. While alcohol appears to increase impairment in combination with diazepam, there is little evidence for such an effect with chlordiazepoxide.

Thus, although Goldberg (1963) examining chlordiazepoxide and alcohol found increased decrements in oculomotor control and standing steadiness, Hughes, et al. (1965) failed to find increased impairment on pursuit tracking tasks or on subjective symptoms. Nor did Miller, et al. (1963) find impairment increased on a digit symbol task.

On the other hand, abundant evidence exists for increased skills decrement following joint diazepam-alcohol use. Burford, et al. (1975) found increased impairment of reaction time on a step pursuit tracking task. Smiley, et al. (1975) reported decreased ability to stop accurately while driving an instrumented car as well as impaired control of steering wheel movements.

Franks, et al. (1975) examined both chlordiazepoxide and diazepam on a battery of sensory perceptual motor tasks and found enhanced deficits for diazepam but not for chlordiazepoxide. Molander and Duvhok (1976) studied diazepam, oxazepam and methylperone effects on critical flicker fusion frequency and physical coordination, and mood. Diazepam-alcohol produced increased deficits on the objective measures but not in mood. This suggests that subjective judgments may be inadequate to evaluate degree of impairment. The other drugs had lesser effects on the response variables.

Linnoila, et al. (1974) found increased impairment by diazepam and alcohol on choice reaction time, attention and coordination. Morland, et al. (1974) reported increased impairment on time estimation, letter cancellation, sorting task, complex coordination, mirror tracking and a clinical examination. Linnoila and Mattila (1973) found increased deficits in collision frequency, ignoring of instruction and steering errors in a driving simulator. Linnoila and
Hakkinen (1974) using professional drivers of considerable experience reported similar results. Diazepam-alcohol combination produced greater impairment of driving skills than either diazepam or alcohol alone. Moskowitz and Burns (1977) found increased impairment of tracking, visual search, attention and information processing.

While earlier studies (e.g., Lawton and Cahn, 1963) failed to find greater deficits under the combined diazepam and alcohol, evidence from recent research has pointed to enhancement of impairment, suggesting more sensitive and relevant behavior variables are being examined.

It has been argued that laboratory studies of volunteer subjects for possible behavioral decrement produced by tranquilizers, alone or in combination with alcohol, may not be relevant for emotionally disturbed patients who are drivers. The assumption is that the emotionally disturbed individual would be more likely to be involved in traffic accidents due to his emotional state and that the sedating role of the tranquilizers in alleviating his symptoms would produce an improved safety record. These contentions have been inadequately examined. However, a study by Finnish psychiatric outpatients by Maki and Linnoila (1976) found that drug-treated outpatients had an accident record nearly double the non-drug-treated subjects or the controls. This study can only be considered suggestive until it is replicated with control, to ensure that subjects on drug and non-drug treatments do not differ in terms of their illness.

**Major Tranquilizers**

The major tranquilizers are greater potency compounds used for more seriously emotionally disturbed patients. The two most prominent members of this drug category are the phenothiazines (e.g., chlorpromazine, thioridazine) and the Alkaloids of Rauwolfa (e.g., reserpine).

Zirkle, et al. (1959) reported mental arithmetic, visual perceptions of illusions and a digit symbol test significantly more impaired by joint chlorpromazine-alcohol treatments. Goldberg (1961) reported increased deficits in body sway. Loomis (1963) presented evidence for impairment on a driving simulator. Milner and Landauer
(1971) reported chlorpromazine and thioridazine increased reaction time, with chlorpromazine having the greater effect. However, Saario (1976) failed to find any interactions between thioridazine and alcohol on complex reaction time, coordination or attention tests.

Even fewer human studies are available to evaluate reserpine interactions with alcohol. Burger (1961) reported increased reaction time, as did Feldmann (1962).

Marihuana

Recent studies present evidence that combined alcohol-marihuana produces increased impairment of skills performance. Manno, et al. (1971) found increased impairment of both pursuit tracking and scores on mental arithmetic. Macavoy and Marks (1975) also reported increased deficits in monitoring visual signals in central and peripheral vision while in a divided-attention situation. Chesher, et al. (1976) examined combined marihuana-alcohol treatments on a test battery and found increased impairment on standing steadiness, manual dexterity, and psychomotor skills. Moskowitz (1977) and Burns and Moskowitz (1980) reported increased impairment of vigilance, information processing and oculomotor control.

All reported studies appear to agree with increased impairment under combined marihuana-alcohol and the need for alerting users to this danger.

Barbiturates

Joyce, et al. (1959) examined the interaction of alcohol and phenobarbital and found greatly increased complex reaction times. Doenicke and Kugler (1965) and Doenicke, et al. (1966) examined the effects of consuming alcohol at various intervals up to 24 hours after administration of various medium- and short-acting barbiturates. A markedly increased tendency to fall asleep and impaired motor performance were noted, even at these delayed intervals.

Loomis (1963) examined secobarbital in a driving simulator where measures of tracking and reaction time were secured. Results demonstrated increased impairment of performance under the combined dose.
A series of studies by Osterhaus (1964) demonstrated signs of severe intoxication when barbital was combined with blood alcohol concentrations in the .06% to .16% range. Symptoms included unconsciousness and extended sleep, vomiting and severe motor impairment.

Chloral hydrate frequently is used as a hypnotic to induce sleep. Sellers, et al. (1965) examined the effects of chloral hydrate and alcohol on simple and complex choice reaction times, a rotary pursuit task and a vigilance task. Combined administration decreased performance on the pursuit rotor and vigilance.

Stimulants

It would be anticipated that stimulants would antagonize alcohol, a CNS depressant. In general, some of the effects of alcohol were opposed, although results are rather variable and appear quite dependent on dose levels and behaviors examined.

Newman and Newman (1956) examined the ability of 15 mg dextro-amphetamine and 300 mg of caffeine to counteract the influence of alcohol on measures of handsteadiness, flicker fusion and body balance. Only the latter behavior showed a slightly greater resistance to impairment under caffeine. Hughes and Forney (1964) administered dextro-amphetamine and alcohol to subjects performing a battery of mental tests while in a stressful, delayed auditory feedback situation. No evidence was found for improved performance on either verbal or arithmetic tests. Forney and Hughes (1965) utilized the same technique of examining mental performance under the stress of auditory feedback while under the influence of caffeine and alcohol. Of the nine mental performance tasks, only two simple arithmetic tests and a color discrimination task show evidence of caffeine mitigating the decrement produced by alcohol.

Brown, et al. (1966) examined the effect of d-amphetamine on pursuit tracking tasks over 3-1/2 hours. The tracking task was administered at four levels of difficulty, and the ability of the stimulant to counteract some of the effects of the alcohol was a function of the difficulty level of the task, so that at some levels the amphetamine improved performance, but not at other levels. Similar interactions with the response measure were exhibited in a
study by Wilson, et al. (1966) on amphetamine-alcohol combinations. Whereas antagonism was found in three tests of mental performance, none was found in measures of intellectual or psychomotor performance.

Moskowitz and Burns (1980) examining four dose levels of caffeine and alcohol, found an extremely complex interaction dependent upon both dose levels and response measures. Low levels of caffeine counteracted low levels of alcohol on attention, perception and tracking, but higher levels of caffeine were relatively less effective in offsetting higher levels of alcohol. At no level was caffeine able to counteract alcohol's impairment of information processing rate as measured by backward masking.

Thus, overall, the anticipated antagonism between alcohol and stimulants occurs only on some behaviors and not on others. No stimulant appears to have the property of counteracting all of the deficits induced in performance by alcohol. Perhaps the difficulty lies in the broad labels of depressant and stimulant being inadequate to deal with the highly selective nature of the specific behaviors which are either impaired or improved.

Antidepressant Drugs

Few human behavioral studies have examined this class of psychoactive drugs. Landauer, et al. (1969) determined that alcohol-amitriptyline increased impairment on a step pursuit tracking task, the pursuit rotor and a dot-tracking task. Seppala, et al. (1975) similarly reported increased deficits for the combined amitriptyline treatment on choice reaction time. In addition, doxepin with alcohol increased times and number of errors in a reaction time task. However, nortriptyline and chlorimipramine showed no interactions with alcohol. Moreover, Hughes and Forney (1963) reported a nonsignificant tendency towards antagonism between alcohol and nortriptyline on mental tasks performed under auditory delayed feedback.

Antihistamines

Hughes and Forney (1964) examined the effects of clemizole, diphenhydramine and tripelennamine on a battery of nine mental tasks
performed under the stress of delayed auditory feedback and a pursuit tracking task. While there were no additional performance decrements under the combined dosages for the mental tests, the pursuit tracking task was significantly further impaired by the diphenhydramine-alcohol treatment.

Linnoila (1973) examined the effects of diphenhydramine and meclastine on a choice reaction time test, two coordination tests and an attention task. The diphenhydramine-alcohol combination produced significant impairment on the objective tests, notably the coordination test.

Although the above review does not include all possible relevant studies on combined drug-alcohol effects on driving-related behavior, it does contain a good portion of the literature available in major libraries. If, nevertheless, the number of articles examined appears few, this is an accurate reflection of the rather sparse literature available.

Despite the obvious social and economic consequences of joint alcohol-drug use for safety in driving and in industry, this review suggests that, for most drug categories, only a few specimen drugs have been examined for possible interaction effects with alcohol. Typically, only one active dose level of alcohol and drug has been examined. Moreover, the range of behaviors examined has been limited. This last issue is of considerable concern since it is clear that psychoactive drugs affect specific behavioral mechanisms, and defining their potential effects requires sampling a set of behaviors.

The overall impression created by this review is that most combined drug-alcohol use results in increased impairment over that from either substance alone. This may be because drugs were selected for study based on clinical impressions of increased impairment. In no drug category has there been a systematic examination of drugs to give insights into what drug characteristics are likely to be associated with a greater risk of alcohol interaction.

The failure to examine the problem of alcohol-drug interaction more thoroughly reflects the resources allocated by society for this research. Regretfully, support for examination of the behavioral toxicology of drugs has failed to keep abreast of the increasingly
complex demands placed on humans for man-machine interactions amidst the increasingly frequent use of psychoactive substances.

If governments in a period of economic stress cannot fully support the efforts required in this field, they should at least utilize their drug licensing authorities to require that information regarding the behavioral side effects of drugs, by themselves and in use with the common solvent alcohol, be submitted by the drug suppliers. Moreover, such a move would spur consideration of the behavioral side effects of drugs as an issue in drug development and selection.

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ACKNOWLEDGMENT

This study has been sponsored by grants from the National Institute on Alcohol Abuse and Alcoholism, National Institute on Drug Abuse, and Insurance Institute for Highway Safety.