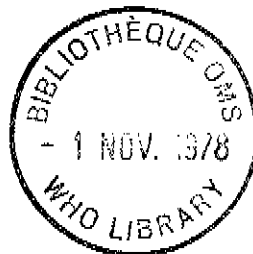




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TRANSLATION

THE INFLUENCE OF ALCOHOL AND DRUGS ON ROAD SAFETY

INDEXED

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This article presents information on the effects that the interaction of drugs and alcohol may have on road safety.

1. Epidemiology

During the past six years there has been an increase of 23% in the number of motor cars in the Federal Republic of Germany; during the same period, the consumption of alcohol rose by 30% and between 1971 and 1975 an increase of 120% in drug consumption was recorded by health insurance societies (1). Rates of increase are probably similar in other highly industrialized countries. Thus, in 1973, Joachim (2) noted that in the United States 79% of men and 63% of women regularly consumed alcohol; in Australia the rates were as high as 85% for men and 71% for women. The rates of increase for drug consumption are still higher. Thus, Ackermann et al. (3) found that in 1957 only 3% of drivers stated that they had taken drugs in the 24 hours preceding the offence, whereas in 1967 the percentage had risen to 20%. Various authors reported similar results up to the start of the nineteen-seventies: according to Wagner (4), investigation of some 5000 drivers showed that between 10% and 13% of those questioned had taken drugs in the preceding 24-hour period. Krelenburg (5) estimates that the proportion of traffic accidents involving drugs is between 15% and 20%. In systematic surveys carried out among the population of San Francisco, Mannheimer & Mellinger (6) established that 17% regularly took analgesics, tranquillizers or stimulants. Bonnicksen et al. (7) note that, of 50 000 drivers, 12% admit to having taken drugs. Kapur (8) found in 1973 that, out of 1560 persons, as many as 60% had taken one or more drugs; in 48% a combination of drugs and alcohol was found. Mallach & Seitz (9), in sample surveys conducted in 1975, found that 24% of blood tests ordered by the police showed that drugs were present. With regard to drug abuse, a distinction can undoubtedly be made between urban and rural areas, for Bäumler (6) found that in an agricultural region of Switzerland only 4% of those investigated abused drugs.

Many authors have found that, as opposed to the situation with regard to alcohol consumption, in which the male sex is clearly in the majority, women are two and a half times more often under the influence of drugs (3, 6, 12, 14); however, it should be taken into account that a large proportion of women take contraceptive drugs only.

Moreover, the frequency of drug consumption increases with age (3, 12, 14), while the use of alcohol most often involves younger persons (10, 11). According to various authors (1, 3, 6, 12), analgesics are the pharmaceutical products most often consumed by drivers. Next in order come sedatives, hypnotic drugs, psychotropic substances, stimulants, drugs to improve blood circulation, etc.; but the distribution of drug categories varies from one country to another and from one year

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to another (3, 7, 8, 11, 13). It is also evident that certain groups of drug are typical for certain age-groups. Thus, Ladewig (6) found that persons aged between 20 and 30 years frequently took amines to induce wakefulness, and Mannheimer & Mellinger (6) determined that a preponderant number of middle-aged persons took sedatives and tranquillizers.

Combined drug and alcohol use is particularly frequent. More than 10 years ago, Wangel (4) found that, of 4891 drivers whose blood alcohol level was around 1.5%, 16% were at the same time under the influence of a drug, while in a control group of 1226 subjects who had not taken alcohol, only 10% were under the influence of a drug. Moreover, the "alcohol" group consumed drugs more frequently and in significantly higher quantities than the control group. Osterhaus states in (12) that of 5200 drivers under the influence of alcohol, 14.5% had also taken drugs. Klein arrived at similar results (2): 10%-15% of drivers who had consumed alcohol stated that they had also taken drugs. "In 1968, Finkle et al. conducted a questionnaire survey together with chemical analysis of the body fluids of persons involved in traffic accidents. They showed that 21% of the 3409 drivers who had consumed alcohol also took drugs regularly" (8). Van Ooijen has also found that the combination of drugs and alcohol has increased substantially in the past 10 years, having risen from 8.8% in 1965 to 23.1% in 1975/76 (14).

Physicians, pharmacists and users should constantly bear in mind that the increased consumption of alcohol and drugs is prejudicial to driving ability. A distinction should be made here between the effects of the following combinations:

- a) alcohol incompatibility due to drugs;
- b) effects of alcohol intensified by drugs;
- c) effects of alcohol modified by drugs.

In particular, mention should be made of the effect of Antabuse (disulfirame), which varies from person to person and is unpredictable.

2. Results of experimental research

Experimental research has also been conducted on the combined effect of alcohol and drugs on road safety. As far as method is concerned, the experiments carried out relate mainly to healthy male and/or female subjects who, in a double blind test, are given certain drugs and alcohol by random distribution. Their performance is then monitored by means of psychomotor tests of behaviour, coordination and attention, and also by subjective evaluation and behaviour simulator tests (15, 16). Only a few isolated experimental behaviour tests have been conducted (17).

Analgesics form the majority of the drugs most often found in drivers (see above). However, in view of the fact that these substances, taken in therapeutic doses, should, with a few rare exceptions, have scarcely any influence on the effect of alcohol, a large number of experimental studies are now concerned with psychotropic and hypnotic drugs. The greatest danger as far as psychotropic drugs is concerned is that they intensify the effect of alcohol (18).

With regard to psychotropics, Linnoila and Mattila (19) have, inter alia, obtained the following results:

- "Diazepam taken with alcohol reduces all parameters except the subjective performance capacity;
- chlordiazepoxide does not aggravate the reduction in attention resulting from alcohol;
- weak doses of neuroleptics appear to reduce attention but are less likely than diazepam to have a potentiating effect on alcohol" (see also (20) and (21)).

Landauer et al. (22) point out that medazepam, which is a benzodiazepine derivative, lessens the subject's capacity when administered with alcohol.

Taken as a whole, the results of experimental research on tranquilizers are not in agreement. Thus, Kielholz et al. have found, unlike Linnoila (19), that chlordiazepoxide reacts synergistically with alcohol. Milner et al. state that "anxiolytics such as benzodiazepines can have a potentiating effect when combined with alcohol" (23). Benzocetamine shows no interaction, either synergistic or antagonistic, with alcohol (24). According to Richter & Hobi (21), benzodiazepine derivatives taken with alcohol diminish coordination and attention. Palva et al. (25) state that the interaction between diazepam and alcohol is attributable mainly to the constituents of the diazepam itself and hardly at all to the resultant metabolites. Staak et al. (9) show that alcohol has a noticeable effect in retarding intestinal resorption of oxazepam. The simultaneous effect of alcohol and oxazepam leads to an additive or superadditive reduction in the subject's capacities (see also (26)).

With regard to antidepressants, Patmann et al. (27) found that the combination of amitriptyline and alcohol produced no reduction in capacity. Imipramine, too, does not increase the effect of alcohol in any significant manner. It is probable that these drugs intensify the effect of alcohol only to the extent that they act as sedatives. Thus amitriptyline enhances the effect of alcohol only at the start of a treatment, for a sedative effect can be established at that point. Adverse effects in the event of extended medication are not known (21).

With regard to hypnotic drugs, Saario et al. (28) state that:

"Flurazepam, with alcohol, reduces psychomotor performance the most;

- glutethimide and methaqualone have no interaction with alcohol in the morning;
this is possibly due to the circadian rhythm."

Saario (29) found that nitrazepam was less additive in its effect than bromvalerone. All published research on animals (30) show that barbiturates have a strong alcohol-potentiating action. Burford (15) also writes of this interaction between phenobarbital and alcohol. According to (19) and (21), hypnotics in general have a considerable alcohol-potentiating effect.

As far as neuroleptics are concerned, Seppälä et al. (31) state that "thioridazine and alcohol do not have major combined effects on the subject's ability, whereas chlorpromazine has a reciprocal effect with alcohol. The interaction between sulphiride and alcohol is weak". According to Richter & Hobi (15), the chief danger with regard to neuroleptics also lies in their alcohol-potentiating action.

3. Results of pharmacokinetic and pharmacodynamic studies on the interaction between alcohol and drugs

While pharmacokinetic changes caused by drugs in ethyl alcohol are rare, the reverse situation is of special importance. As far as existing knowledge goes (32), it seems possible that ethyl alcohol, by influencing drug metabolism selectively, triggers basically similar pharmacokinetic interactions with drugs.

So far, considerable changes in resorption have not been found either in man or in animals. Furthermore, Mallach et al. (33) show that alcohol slows down intestinal resorption of oxazepam without the rate of conjugation being altered (see also (9)). Investigations of changes in the diffusion of drugs by alcohol do not produce concordant results.

Research on drug metabolism has shown that acute doses of ethyl alcohol selectively inhibit hydroxylation reactions, while hydrolysis and conjugation reactions are not affected. Hydroxylation reactions, including hydroxylation in closed chains, hydroxylation in lateral chains, N-demethylation, N-hydroxylation, and O-dealkylation are catalysed by an enzymatic system, included in a membrane of the endoplasmic reticulum; this enzymatic system is reversibly inhibited by alcohol.

Because of this change, elimination is retarded and the half-life period is extended. There are noticeably fewer metabolites in the urea. As the alcohol is eliminated, this inhibition effect diminishes and formation and evacuation of metabolites proceeds with some delay.

These inhibition reactions are not so pronounced with regard to drugs for which several metabolic paths are possible.

However, it is impossible to understand all the interactions so far known at the level of metabolism. Because of the effect of the alcohol itself on the central nervous system, a combination with drugs acting on the central nervous system leads to phenomena of addition or potentiation. This "central nervous interference" is produced with sedatives, hypnotics, narcotics, anticonvulsants, antihistamines, neuroleptics, tranquilizers, antidepressants, morphine, morphine derivatives and certain antihypertensives (34). For other pharmacokinetic studies, see (35, 36, 37).

4. Summary

Within the framework of this survey it has not been possible to deal with the complex questions of analysis. Among the most recent methods of detection, gas phase chromatography and mass spectroscopy have proved to be of particular interest (see, inter alia, (38, 39, 40, 41)).

Pharmacokinetic studies, clinical investigations and the expertise derived from legal medicine case histories show that, in respect of many of the very common drugs, when there is an interaction with alcohol, a potentiating effect of the latter has to be taken into account (see also (11)). In summary, the following indications may be given (34):

<u>Drugs</u>	<u>Effect of alcohol</u>
1. Tranquillizers, sedatives, hypnotics, anticonvulsants, antihistamines	Intensification of sedative and hypnotic effect
2. Neuroleptics, thymoleptics, analgesics	Intensification of the effects
3. Analgesics of the morphine type	Intensification of the effect of morphine
4. Oral antidiabetics (sulfonylurea derivatives)	Intensification of effect of reducing blood sugar
5. Isocinizids and other monoamine oxydase inhibitors	Intensification of monoamine oxydase inhibition Increase in arterial tension

Unlike the potentiation of the effect of alcohol caused by many drugs during the acute period of alcohol ingestion, chronic alcohol consumption produces an induction of the metabolizing enzyme into the endoplasmic reticulum and thus leads to an increase in this metabolism. The following indications are given in (34):

<u>Drugs</u>	<u>Effects of alcohol in cases of chronic consumption</u>
1. Sedatives, hypnotics (barbiturates)	Weakening of sedative and hypnotic effect
2. Anticonvulsants	Weakening of anticonvulsant effect Convulsions
3. Antidiabetics (sulfonylurea derivatives)	Hyperglycaemia
4. Anticoagulants (coumarin)	Weakening of coagulation-inhibiting effect

In order to improve road safety, it is essential to make a constant check of the extent to which critical situations and traffic accidents are attributable to the interactions between alcohol and drugs described above.

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