A drug identification system for intoxicated drivers based on a systematic review

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KEYWORD

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ABSTRACT

Tests to detect the use of illegal substances among drivers are becoming more common. During these tests, a saliva test is performed and agents observe the driver to determine whether or not they are driving under the influence of psychoactive substances. During the joint control of alcohol and drugs, a breath test is performed followed by a saliva test. In addition, agents use a previously established observation questionnaire to evaluate external signs that the driver may present. This review aims to help expand and improve the questionnaire administered by the traffic officer to the driver, so that upon completing the questionnaire as indicated, it is possible to determine which drug corresponds to the symptoms displayed by the driver. The diagnosis will be facilitated by a software tool that employs the use of decision trees whose gain function has been modified to give different weights to signs and methods. A study was conducted on the symptoms and observable and/or easily detectable signs of drugs detected at sobriety checkpoints. This has enabled the creation of a test that determines the substance consumed by the driver. The proposal facilitates the detection of drugs with the data gathered from the test.

1. Introduction

Traffic accidents are a major cause of mortality and morbidity, a major problem both regionally and globally. According to a report from the World Health Organization, road accidents are expected to become the fifth leading cause of death by 2030, up from its position as the ninth leading cause of death in 2004 (World Health Organization (Ed.). 2009. *Global status report on road safety: time for action*. World Health Organization.). Driving under the influence of alcohol and/or drugs is one of the most important reasons for this serious problem (Ojaniemi, K. K., Lintonen, T. P., Impinen, A. O., Lillsunde, P. M., Ostamo, A. I., 2009. Trends in driving under the influence of drugs: a register-based study of DUID suspects during 1977–2007. *Accident Analysis & Prevention*, *41*(1), 191-196. Rudisill, T. M., Zhao, S., Abate, M. A., Coben, J. H., Zhu, M., 2014. Trends in drug use among drivers killed in US traffic crashes, 1999–2010. *Accident Analysis & Prevention*, *70*, 178-187.).

Several studies have shown a connection between the effects of alcohol and drugs and the risk of a traffic accident, with an additional increase in the chances of a more severe or even fatal accident, com-

pared to a situation in which these substances have not been consumed (Rudisill, T. M., Zhao, S., Abate, M. A., Coben, J. H., Zhu, M., 2014. Trends in drug use among drivers killed in US traffic crashes, 1999–2010. *Accident Analysis & Prevention*, *70*, 178-187.). Alcohol is the most common substance involved in traffic accidents (Hingson, R., Winter, M., 2003. Epidemiology and consequences of drinking and driving. *Alcohol Research and Health*, *27*(1), 63-78. and was detected in 72% of the victims in a study by Ricci, G., Majori, S., Mantovani, W., Zappaterra, A., Rocca, G., Buonocore, F., 2008. Prevalence of alcohol and drugs in urine of patients involved in road accidents. *Journal of preventive medicine and hygiene*, *49*(2), 89-95. , which involved 100 accident victims in nonfatal traffic. In addition to alcohol, this study also showed the percentage of other drugs involved in traffic accidents, including benzodiazepines (42%), cannabis (21%) and cocaine (14%).

Studies have shown an increase in some countries in the rate of drivers who drive under the influence of alcohol and drugs (Ojaniemi, K. K., Lintonen, T. P., Impinen, A. O., Lillsunde, P. M., Ostamo, A. I., 2009. Trends in driving under the influence of drugs: a register-based study of DUID suspects during 1977–2007. *Accident Analysis & Prevention*, *41*(1), 191-196. Rudisill, T. M., Zhao, S., Abate, M. A., Coben, J. H., Zhu, M., 2014. Trends in drug use among drivers killed in US traffic crashes, 1999–2010. *Accident Analysis & Prevention*, *70*, 178-187. Chang, K., Wu, C. C., Ying, Y. H., 2012. The effectiveness of alcohol control policies on alcohol-related traffic fatalities in the United States. *Accident Analysis & Prevention*, *45*, 406-415. Woratanarat, P., Ingsathit, A., Suriyawongpaisal, P., Rattanasiri, S., Chatchaipun, P., Wattayakorn, K., Anukarahanonta, T., 2009. Alcohol, illicit and non-illicit psychoactive drug use and road traffic injury in Thailand: a case-control study. *Accident Analysis & Prevention*, *41*(3), 651-657. Mura, P., Chatelain, C., Dumestre, V., Gaulier, J. M., Ghysel, M. H., Lacroix, C., Kergueris, M. F., Lhermitte, M., Moulsma, M., Pépin, G., Vincent, F., Kintz, P., 2006. Use of drugs of abuse in less than 30-year-old drivers killed in a road crash in France: a spectacular increase for cannabis, cocaine and amphetamines. *Forensic Science International*, *160*(2), 168-172. Mørland, J., Steentoft, A., Simonsen, K. W., Ojanperä, I., Vuori, E., Magnusdottir, K., Kristinsson, J., Ceder, G., Kronstrand, R., Christophersen, A., 2011. Drugs related to motor vehicle crashes in northern European countries: A study of fatally injured drivers. *Accident Analysis & Prevention*, *43*(6), 1920-1926. Gjerde, H., Normann, P. T., Christophersen, A. S., Mørland, J. 2011. Prevalence of driving with blood drug concentrations above proposed new legal limits in Norway: estimations based on drug concentrations in oral fluid. *Forensic science international*, *210*(1), 221-227.). Many of these drivers are not under the influence of a single drug or alcohol, but of various substances commonly found at a checkpoint (Gjerde, H., Christophersen, A. S., Normann, P. T., & Mørland, J., 2013. Associations between substance use among car and van drivers in Norway and fatal injury in road traffic accidents: A case-control study. *Transportation research part F: traffic psychology and behaviour*, *17*, 134-144. Macdonald, S., Mann, R. E., Chipman, M., & Anglin-Bodrug, K., 2004. Collisions and traffic violations of alcohol, cannabis and cocaine abuse clients before and after treatment. *Accident Analysis & Prevention*, *36*(5), 795-800.). According to data provided by local police in Salamanca (Spain) the consumption of alcohol by drivers is decreasing, but very often a small percentage of these drivers test positive for drugs. It is therefore necessary to know the effects of these drugs and to be able to recognize them, so the traffic officer can run a toxicology screen and, if necessary, subsequent arrest, which would avoid a traffic accident.

The result has been an increase in the number of sobriety checkpoints for drivers to prevent driving under the influence of alcohol and drugs. These controls include a breath test performed on the air exhaled by the subject, and a saliva test. Officers also observed external signs to determine whether the subject was under the influence of these substances, impairing their ability to drive.

There are many signs that indicate drug use. While each drug has its characteristic manifestations, there are some general guidelines to indicate that a person is using drugs, including: a sudden change in behavior (Macdonald, S., Mann, R. E., Chipman, M., & Anglin-Bodrug, K., 2004. Collisions and traffic violations of alcohol, cannabis and cocaine abuse clients before and after treatment. *Accident Analysis & Prevention*, *36*(5), 795-800.; Graña, J. L., Muñoz, J. J., Navas, E., 2009. Normal and pathological personality characteristics in subtypes of drug addicts undergoing treatment. *Personality and Individual Differ-*

ences, *46*(4), 418-423.), mood swings – from irritable and grumpy to suddenly merry and bright (McAuley, J. W., Passen, N., Prusa, C., Dixon, J., Cotterman-Hart, S., Shneker, B. F., 2015. An evaluation of the impact of memory and mood on antiepileptic drug adherence. *Epilepsy & Behavior*, *43*, 61-65.), estrangement from family members; unkempt personal appearance; loss of interest in hobbies, favorite sports and other activities; change in sleeping pattern; awake at night and asleep during the day (Nettleton, S., Neale, J., Pickering, L., 2011. Techniques and transitions: A sociological analysis of sleeping practices amongst recovering heroin users. *Social Science & Medicine*, *72*(8), 1367-1373.), red or glassy eyes, runny nose.

This study aims to gather the symptoms produced by the main drugs detected in breath tests administered in Salamanca (Spain), without studying in depth the biochemical process reward circuit. The purpose of this review is to provide information to supplement and improve the tests carried out at sobriety checkpoints to detect whether a driver is under the influence of these substances. Moreover, the information retrieved from different scientific journals and publications will be used to develop a system to assist officers in detecting the specific drugs taken by a subject, further serving to contrast the test results with the published data. The system also will learn as more tests are generated, automatically calculating the applied weights.

The paper is organized as follows: section 2 describes the test methods, section 3 provides the results, and section 4 discusses the implications of the test and its application.

2. Methods

A systematic search on literature was performed to locate and review existing research on visible symptoms exhibited by a drug user. The review was designed to answer the following question:

What are the observable symptoms of alcohol or drug use that a user might present?

2.1. Search Strategy

Following the search strategy employed by Pidd, K., Roche, A. M., 2014. How effective is drug testing as a workplace safety strategy? A systematic review of the evidence. *Accident Analysis & Prevention*, *71*, 154-165. in their study How effective is drug testing as a workplace safety strategy?, additional searches were performed in MEDLINE, EMBASE and Web of Knowledge until February 20, 2015 for relevant publications using combinations of the keywords in **Table 1.** Search keywords:

Table 1. Search keywords

Drug	**Symptoms**	**Consumer**	**Addict**
Driver	**Crash**	**Deter***	**Detect***
Test*	**Death**	**Substance**	**Effects**
Risk*	**Opiates**	**Morphine**	**Codeine**
Alcohol	**Marijuana**	**Tetrahydrocannabinol**	**Cannabis**
Cocaine	**Benzodiazepines**	**Amphetamines**	**Methamphetamines**

Reference lists of identified articles were also examined in this search, and those deemed most appropriate were selected and included in the present study. In general, our focus was on recent publications (the vast majority are after 2000).

A total of 483 articles and manuals were identified (**Fig. 1.** Flowchart of search and exclusion process). Of the 469 articles, 94 duplicate articles were eliminated. A total of 14 manuals were detected, 2 diagnostic and 12 psycopharmacology handbooks. A total of 379 items, including both articles and manuals, fit the search criteria, 68 of which described symptoms. Of these 68 evaluations, 58 were articles, 10 of which were excluded because they referenced studies reporting on easily identifiable symptoms and signs. Of the 14 manuals, 4 were discarded because they focused on the psychological side effects, symp-toms and signs produced by drugs. Of the remaining 10, one was excluded because its publication was much earlier than the others, which deal with a much more advanced topic.

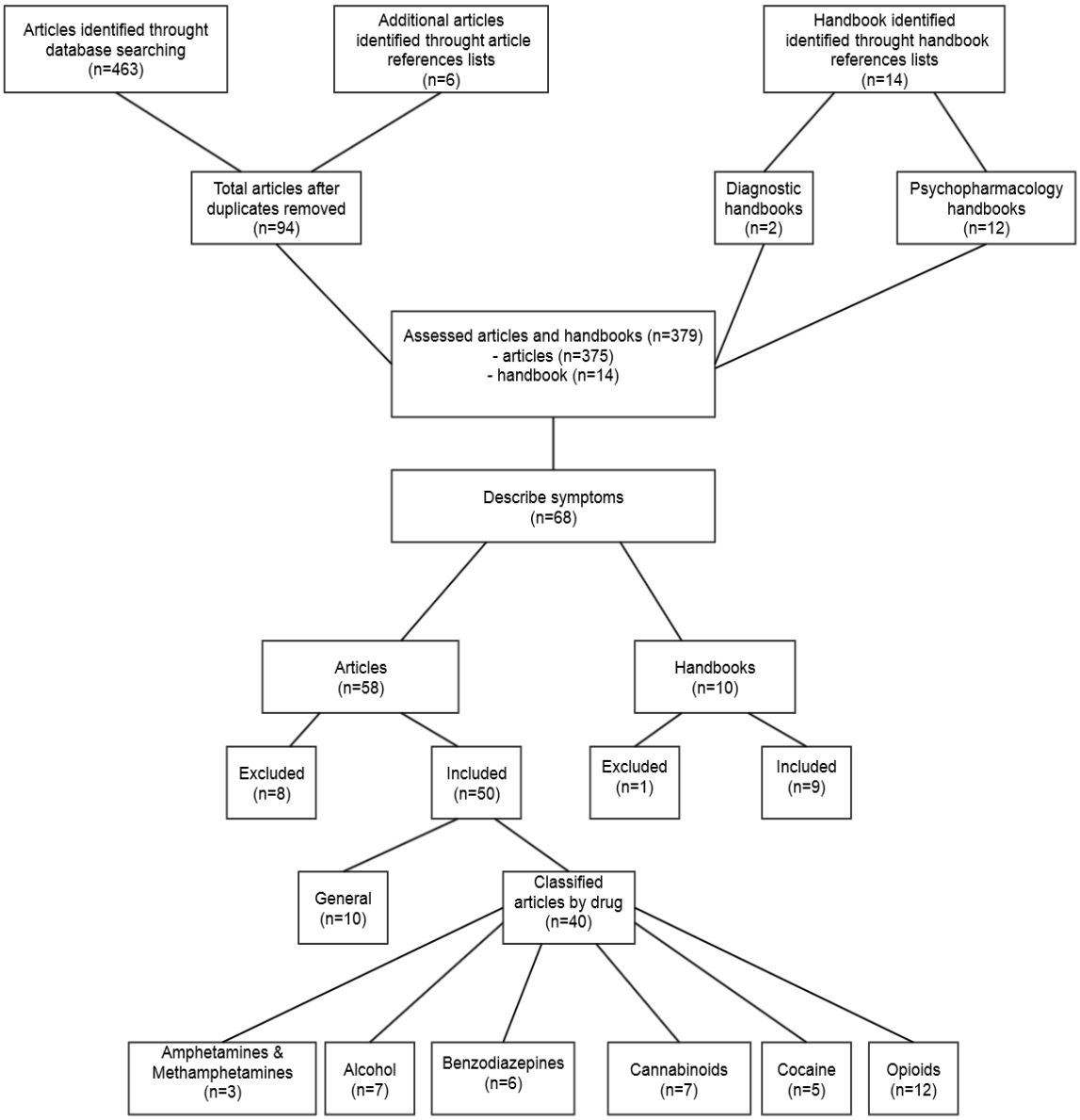

Fig. 1. Flowchart of search and exclusion process

2.2. Inclusion and exclusion criteria

The inclusion criteria consisted of articles based on controlled human testing (in individuals of both sexes) or experimental studies in animal models. The set of items was not restricted by demographic characteristics, nor was the selection limited by the nature of the use of the specific drug, or by the techniques used in the analysis.

3. Results

Of the 50 studies included in the review, three examine the symptoms and signs easily identified as part of the family of amphetamines, 7 of alcohol, six of benzodiazepines, seven of cannabinoids, five of cocaine and twelve of opioids.

On occasion, certain signs and symptoms mentioned in these studies were not identified by the same name, which is required to ensure some sort of uniformity when testing the signs and symptoms used by the software system developed. The guidelines used were in complete accordance with CIE-10 and DSM-IV-TR, both of which use very similar diagnostic criteria. In addition to all the signs and symptoms mentioned, it was also necessary to meet certain general criteria for the intoxication to be considered a diagnosis. More specifically, the criteria for acute intoxication were those of CIE -10.

The addictive power of many drugs is based in the mesolimbic dopamine reward pathway. Many daily life activities may provide a sense of gratification through the natural release of dopamine. The action on which many of these drugs are based, and their corresponding reward pathway, is geared toward producing this effect more sharply.

The rewarding effect produced by many psychotropic drugs is due to the fact that they do not use neurotransmitters to produce an effect on brain receptors, but act on them directly, resulting in a more noticeable effect in the release of dopamine.

This section is subdivided according to some of the drugs most commonly detected during sobriety checkpoints. Each subsection provides a contextualization of consumption from a physiological point of view and according to the symptoms and signs produced by these drugs.

3.1. Alcohol

Alcohol is undoubtedly the most widely used recreational drug (Spear, L. P., Swartzwelder, H. S., 2014. Adolescent alcohol exposure and persistence of adolescent-typical phenotypes into adulthood: a mini-review. *Neuroscience & Biobehavioral Reviews*, *45*, 1-8.). Alcohol is capable of binding to various receptors and triggers many different effects in various tissues. This, coupled with the large number of factors that can influence the intake of alcohol, makes it an extremely complex phenomenon, with areas yet to be defined. It also has a characteristic that sets it apart from many other drugs as it is a substance that seems to have a specific receptor. One of the major problems of this substance is that, unlike others, its action is not limited to a particular area of the body. Alcohol is a molecule of low molecular weight and is therefore able to cross lipid membranes (Zorumski, C. F., Mennerick, S., Izumi, Y. 2014. Acute and chronic effects of ethanol on learning-related synaptic plasticity. *Alcohol*, *48*(1), 1-17. Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia; Patiño, N. M., 2008. *Farmacologia medica/Medical Pharmacology, primera* ed. Médica Panamericana.), spread easily through tissue, and pass the blood-brain and placental barrier, which is one of its most dangerous aspects. It also interferes with many drugs, and its harmful long-term effects are gradually coming to light (Spear, L. P., Swartzwelder,

H. S., 2014. Adolescent alcohol exposure and persistence of adolescent-typical phenotypes into adulthood: a mini-review. *Neuroscience & Biobehavioral Reviews*, *45*, 1-8.). The most common causes of death in people with alcohol-related disorders are suicide, cancer, heart and liver disease (Vallejo, M. S., Vallejo, S., Rodrigo, P., Ruiz, P., 2010. *Tratado de Psicofarmacología*, sgunda ed. Médica Panamericana. Madrid).

Excessive alcohol consumption causes the user to experience a state of disinhibition and impaired judgment, a tendency toward argument and violence, and suddent mood swings. In addition, the individual may have an unsteady gait, experience nystagmus, depression of the sensorium, often slurred speech, and facial redness and conjunctival injection (Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia; Patiño, N. M., 2008. *Farmacologia medica/Medical Pharmacology, primera* ed. Médica Panamericana. ; Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York. ; American Psychiatric Association, 1994. Diagnostic and statistical manual of mental disorders (DSM). *American psychiatric association*, 143-7. *Washington, DC*).Alcohol is metabolized primarily by the liver and to a lesser extent by the kidney and lung. The Alcohol thins membranes, disrupting the normal functioning of the cell (Patiño, 2008 and Sadock et al., 2014). Alcohol significantly increases the activity of the channels associated with nicotinic acetylcholine, serotonin and GABA receptors, and inhibits those associated with glutamic acid, and calcium channels. Some effects are comparable to those produced by benzodiazepines.

Alcohol also can have severe effects when combined with other drugs (McDowell, D. M., Spitz, H. I., 1999. *Substance abuse: From principles to practice*. Psychology Press.), and not only in the short term. It is well known that people with alcohol-related disorders are often tolerant to many drugs. Using alcohol in combination with sedatives and analgesics can cause respiratory failure in high doses, and often lead to death. Its main reinforcing characteristics is the release of dopamine, as well as the release of endogenous opioids and endocannabinoids (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.).

Alcohol acts as a depressant in the central nervous system. Perhaps the lack of specificity of the mechanisms of the action of alcohol explains the many processes yet to be investigated.

3.2. Amphetamines and Methamphetamines

The main amphetamines and derivatives are psychostimulants such as dextroamphetamine and designer drugs such as MDMA and MDEA (N-ethyl-3, 4-methylenedioxymethamphetamine), consumed with the intent of improving performance or achieving a feeling of euphoria (Sadock et al., 2014). At present the differences between the action of amphetamine and methamphetamine have not been clearly defined, nor how the former differs from a methyl group. To date it has been observed that the physiological mechanisms are very similar, although slight quantitative differences have been reported whereby methamphetamine appears to be more powerful (Madras, B., Kuhar, M., 2014. *The Effects of Drug Abuse on the Human Nervous System*, first ed. Academic Press.). The therapeutic use of these drugs normally aims to maintain a waking state. Although the family of amphetamines has a considerable variety of abused substances, and are very different from cocaine, the effects are quite similar.

The consumption of amphetamine and its derivatives is often identified by psychomotor retardation, euphoria, hyper-alertness, abuse or aggression, a labile state of mind, repetitive stereotyped behaviors, noticeable weight loss, hallucinations, paranoid ideation, a tendency to argue, tachycardia (and sometimes bradycardia), mydriasis, increased or decreased blood pressure, sweating and chills, nausea and vomiting, muscle weakness, arrhythmia, chest pain ... (Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia; Madras, B., Kuhar, M., 2014. *The Effects of Drug Abuse on the Human Nervous System*, first ed. Academic Press. ; Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.).

Amphetamines produce a release of catecholamines, most sharply in the ventral tegmental area and limbic regions, stimulating the reward circuit. Designer amphetamines, while having an effect similar to that of the dopaminergic release, also cause the release of serotonin, which is linked to hallucinogenic effects. For example, 3,4-methylenedioxy-methamphetamine (MDMA or "ecstasy") reaches the serotonergic neurons and releases serotonin, which then inhibits the activity of the enzymes in the biosynthesis of serotonin (Madras, B., Kuhar, M., 2014. *The Effects of Drug Abuse on the Human Nervous System*, first ed. Academic Press. and Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia).
There are data indicating that the route of serotonergic stimulation causes an increase in metabolic rate, which is the reason body temperature increases (Gordon, C. J., Watkinson, W. P., O'Callaghan, J. P., Miller, D. B., 1991. Effects of 3, 4-methylenedioxymethamphetamine on autonomic thermoregulatory responses of the rat. *Pharmacology Biochemistry and Behavior*, *38*(2), 339-344.).
The abuse of amphetamine and its derivatives as a psychoactive drug causes damage to the dopamine system, and occasionally gliosis and other types of brain damage. To a lesser extent, they influence the noradrenergic synapses, and some even release serotonin derivatives (Patiño, N. M., 2008. *Farmacologia medica/Medical Pharmacology, primera* ed. Médica Panamericana.).

3.3. Benzodiazepines

These sedative hypnotics have the highest risk of addiction among prescription drugs in the world (Jones, J. D., Mogali, S., Comer, S. D., 2012. Polydrug abuse: a review of opioid and benzodiazepine combination use. *Drug and alcohol dependence*, *125*(1), 8-18. ; Licata, S. C., Rowlett, J. K., 2008. Abuse and dependence liability of benzodiazepine-type drugs: GABA A receptor modulation and beyond. *Pharmacology Biochemistry and Behavior*, *90*(1), 74-89.). These drugs are allosteric modulators of GABAA receptors. Benzodiazepines constituted a turning point in the treatment of anxiety.
Benzodiazepines have an anxiolytic and anticonvulsant effect and cause sedation and/or apathy, loss of attention span, altered psychomotor performance, nystagmus, slurred speech, unsteady gait, ataxia, and amnesia, which is why the medical sector has a set of guidelines for their responsible use(Jones, J. D., Mogali, S., Comer, S. D., 2012. Polydrug abuse: a review of opioid and benzodiazepine combination use. *Drug and alcohol dependence*, *125*(1), 8-18. ; Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York. ; Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia). The various effects (for example sedative/hypnotic or anxiolytic) that occur are attributed to the fact that different classes of these drugs bind to different subtypes of receptors (Hood, S. D., Norman, A., Hince, D. A., Melichar, J. K., Hulse, G. K., 2014. Benzodiazepine dependence and its treatment with low dose flumazenil. *British journal of clinical pharmacology*, *77*(2), 285-294.), which determines the use of other benzodiazepines as needed to treat anxiety or insomnia. When combined with alcohol, benzodiazepine may lead to violent behavior (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.). Generally speaking, an increase in the affinity for the neutransmitter itself is what causes the benzodiazepine to bind to its specific site in the GABA receptor. In addition, the various classes of these drugs also allow for a wide range of options with regard to half-life in the body and the start of the effects (Madras, B., Kuhar, M., 2014. *The Effects of Drug Abuse on the Human Nervous System*, first ed. Academic Press.).
By creating less dependence than existing drugs, they have rapidly replaced barbiturates and propanediols, such as meprobamate and tybamate of the 60s (Voshaar, R. C. O., Couvée, J. E., Van Balkom, A. J., Mulder, P. G., Zitman, F. G., 2006. Strategies for discontinuing long-term benzodiazepine use Meta-analysis. *The British Journal of Psychiatry*, *189*(3), 213-220. ; Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university

press, New York.). However, this success demands a need for responsible treatment. The risk of addiction to these drugs is often measured by the large number of people being treated with benzodiazepines for insomnia, anxiety, spasticity… (Sonnenberg, C. M., Bierman, E. J., Deeg, D. J., Comijs, H. C., van Tilburg, W., Beekman, A. T., 2012. Ten-year trends in benzodiazepine use in the Dutch population. *Social psychiatry and psychiatric epidemiology*, *47*(2), 293-301.). Prolonged use involes the risk of producing a tolerance for losing sensitivity of receptors. They do not tend to create dependency in the short term treatment of anxiet; however, if treatment lasts for months, the risk of dependency increases sharply (Woods, J. H., Winger, G., 1995. Current benzodiazepine issues. *Psychopharmacology*, *118*(2), 107-115. ; Griffiths, R. R., Weerts, E. M., 1997. Benzodiazepine self-administration in humans and laboratory animals–implications for problems of long-term use and abuse. *Psychopharmacology*, *134*(1), 1-37. ; Sonnenberg, C. M., Bierman, E. J., Deeg, D. J., Comijs, H. C., van Tilburg, W., Beekman, A. T., 2012. Ten-year trends in benzodiazepine use in the Dutch population. *Social psychiatry and psychiatric epidemiology*, *47*(2), 293-301.). Therefore, prolonged use of benzodiazepines should be avoided whenever possible, allowing the patient to use other methods that will be effective in reducing stress and anxiety-inducing situations of daily life.

Flumanezil is often used for detoxification therapy, since it is a benzodiazepine GABAA receptor antagonist (Woratanarat, P., Ingsathit, A., Suriyawongpaisal, P., Rattanasiri, S., Chatchaipun, P., Wattayakorn, K., Anukarahanonta, T., 2009. Alcohol, illicit and non-illicit psychoactive drug use and road traffic injury in Thailand: a case-control study. *Accident Analysis & Prevention*, *41*(3), 651-657. and Macdonald, S., Mann, R. E., Chipman, M., & Anglin-Bodrug, K., 2004. Collisions and traffic violations of alcohol, cannabis and cocaine abuse clients before and after treatment. *Accident Analysis & Prevention*, *36*(5), 795-800.), which reduces the effects of the withdrawal.

3.4. Cannabinoids

More specifically referred to as the Δ9-tetrahydrocannabinol, this highly lipophilic compound is the main psychoactive component in marijuana. Currently, marijuana is the most commonly used illegal drug in the world (Patiño, N. M., 2008. *Farmacologia medica/Medical Pharmacology, primera* ed. Médica Panamericana. ; Kedzior, K. K., Laeber, L. T., 2014. A positive association between anxiety disorders and cannabis use or cannabis use disorders in the general population-a meta-analysis of 31 studies. *BMC psychiatry*, *14*(1), 136. Wrege, J., Schmidt, A., Walter, A., Smieskova, R., Bendfeldt, K., Radue, E. W., Lang, U.E., Borgwardt, S., 2014. Effects of cannabis on impulsivity: a systematic review of neuroimaging findings. *Current pharmaceutical design*, *20*(13), 2126.). This situation is in large part due to the number of adolescents who start using cannabis. In adults there is a significant difference between the use of cannabis among men and women, with greater consumption recorded among the former (Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia).
In humans, Δ9-tetrahydrocannabinol is converted into 11-hydroxy-Δ9-tetrahydrocannabinol, the psychoactive metabolite. If doses are not very high, it produces a sense of well-being and euphoria, along with losing one's sense of time. Dry mouth and tachycardia may occur, but this is usually very mild (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York. and Vallejo, M. S., Vallejo, S., Rodrigo, P., Ruiz, P., 2010. *Tratado de Psicofarmacología*, sgunda ed. Médica Panamericana. Madrid). A 'deterioration' of short-term memory is observed. Usually the person will have a slower reasoning process (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York. and Radhakrishnan, R., Wilkinson, S. T., D'Souza, D. C., 2014. Gone to Pot – A Review of the Association between Cannabis and Psychosis. Frontiers in Psychiatry, 5, 54.), but often believes they have a unique approach. Reaction time is affected, and depersonalization

and derealization occurs. If the dose is excessive, it may cause the subject to experience delusions, panic and even psychosis (Radhakrishnan, R., Wilkinson, S. T., D'Souza, D. C., 2014. Gone to Pot – A Review of the Association between Cannabis and Psychosis. Frontiers in Psychiatry, 5, 54.), although there are not many recorded cases of the latter. Monoaminergic neurons and GABAergic are affected, and the involvement of dopaminergic neurons in the ventral tegmental area is currently a subject of debate. The majority of the cannabinoid receptors are grouped with the basal ganglia, hippocampus and cerebellum, although they can also be found to a lesser degree in the frontal cortex, and distribution varies when CB1 or CB2 are considered (Mackie, K., 2008. Cannabinoid receptors: where they are and what they do. Journal of neuroendocrinology, 20(s1), 10-14. [51]).
Although cannabinoids can produce tolerance and even psychological dependence, there is still no proof of a physio-logical dependency (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.), however, there are still not enough studies to solve the dispute. This is not to say, however, that cannabis is harmless in the long term. Regular consumption due to addiction is often reflected in a considerable loss of concentration, shorter attention span, and impaired judgment (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.). There may also be a dopaminergic dysfunction by which the synthesis of dopamine is markedly reduced (Bloomfield, M. A., Morgan, C. J., Egerton, A., Kapur, S., Curran, H. V., Howes, O. D., 2014. Dopaminergic function in cannabis users and its relationship to cannabis-induced psychotic symptoms. *Biological psychiatry*, *75*(6), 470-478. a), which explains a lack of motivation and apathy commonly observed among addicts (Bloomfield, M. A., Morgan, C. J., Kapur, S., Curran, H. V., & Howes, O. D., 2014. The link between dopamine function and apathy in cannabis users: an [18F]-DOPA PET imaging study. *Psychopharmacology*, *231*(11), 2251-2259.b).

3.5. Cocaine

Cocaine is a local anesthetic that modulates the dopaminergic neural system (Madras, B., Kuhar, M., 2014. *The Effects of Drug Abuse on the Human Nervous System*, first ed. Academic Press.). The main problem of cocaine addiction resides in the fact that withdrawal entails very high levels of anxiety, which results in frequent relapses (Coffey, S. F., Dansky, B. S., Carrigan, M. H., Brady, K. T., 2000. Acute and protracted cocaine abstinence in an outpatient population: a prospective study of mood, sleep and withdrawal symptoms. *Drug and Alcohol Dependence*, *59*(3), 277-286.).

Cocaine use is primarily evident through signs and symptoms such as: euphoria, hyper-alertness, tendency to discuss sudden changes in mood, abuse and aggression, repetitive stereotyped behaviors, hallucinations and paranoid ideation, tachycardia, arrhythmia, increased blood pressure (American Psychiatric Association, 1994. Diagnostic and statistical manual of mental disorders (DSM). *American psychiatric association*, 143-7. *Washington, DC* and Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia) sweating, nausea, mydriasis, seizures, chest pain and muscle weakness. Cocaine inhibits the reuptake of norepinephrine and dopamine in the presynaptic adrenergic terminals (McCord, J., Jneid, H., Hollander, J. E., de Lemos, J. A., Cercek, B., Hsue, P., Gibler, W.B., Ohman, E.M., Drew, B., Philippides, G,.Newby, L. K., 2008. Management of cocaine-associated chest pain and myocardial infarction a scientific statement from the American heart association acute cardiac care committee of the council on clinical cardiology. *Circulation*, *117*(14), 1897-1907.), resulting in the increased accumulation of catecholamines in the synaptic gap, causing a/the sympathomimetic effect (Muscholl, E., 1961. Effect of cocaine and related drugs on the uptake of noradrenaline by heart and spleen. *British journal of pharmacology and chemotherapy*, *16*(3), 352-359.). This also explains the increase in heart rate, which entails a series of risks. Cocaine has also been shown to impair the function of the left ventri-

cle and increase end-systolic wall stress (Mehta, P. M., Grainger, T. A., Lust, R. M., Movahed, A., Terry, J., Gilliland, M. G. F., Jolly, S. R., 1995. Effect of Cocaine on Left Ventricular Function Relation to Increased Wall Stress and Persistence After Treatment. *Circulation*, *91*(12), 3002-3009.). Cocaine is highly addictive, and psychological dependency occurs very easily (Madras, B., Kuhar, M., 2014. *The Effects of Drug Abuse on the Human Nervous System*, first ed. Academic Press.). This is because the reinforcing effect of the behavior is short and intense. However cocaine does not simply block the dopamine transporter, it is also capable of releasing dopamine (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.) by removing the neurotransmitter from the presynaptic neuron monoamine transporters.

With repeated abuse, the symptoms of intoxication during withdrawal are increasingly bothersome, and the person experiences fatigue and sleepiness, which is linked to a severe craving for cocaine, resulting in changes in behavior.

Cocaine can produce both tolerance and reverse tolerance; in the case of the latter, new doses of cocaine release further amounts of dopamine, which easily leads to episodes of paranoid psychosis, very similar and sometimes confused with paranoid schizophrenia (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.). This phenomenon usually occurs in people who have already been intoxicated several times. In these cases antipsychotics may be used in order to alleviate symptoms.

3.6. Opioids

Morphine and codeine are opioids with high affinity for the μ, δ and κ receptors (Patiño, N. M., 2008. *Farmacologia medica/Medical Pharmacology, primera* ed. Médica Panamericana.). Despite being widely studied, there are still questions about their strong influence on the sleep-wake cycle. In this respect, they have been shown to reduce the phases of deep sleep and REM in humans (Wang, Q., Yue, X. F., Qu, W. M., Tan, R., Zheng, P., Urade, Y., Huang, Z. L., 2013. Morphine inhibits sleep-promoting neurons in the ventrolateral preoptic area via mu receptors and induces wakefulness in rats. *Neuropsychopharmacology*, *38*(5), 791-801.).

In addition to analgesia, morphine produces pruritus, sedation, psychomotor retardation, lack of attention and impaired judgment, drowsiness, mood swings, and nausea, and usually produces miosis (mydriasis upon reaching a state of intoxication), dry mouth, produces a sense of heaviness, heat ... Excessive doses can occasionally cause hypotension and / or respiratory depression, the latter resulting from an inhibition, through the μ and δ receptors, of the medullary centers that control breathing (Leonard, B. E., 2004. *Fundamentals of psychopharmacology*. John Wiley & Sons. ; American Psychiatric Association, 1994. Diagnostic and statistical manual of mental disorders (DSM). *American psychiatric association*, 143-7. *Washington, DC*; Jones, J. D., Mogali, S., Comer, S. D., 2012. Polydrug abuse: a review of opioid and benzodiazepine combination use. *Drug and alcohol dependence*, *125*(1), 8-18. ; McDowell, D. M., Spitz, H. I., 1999. *Substance abuse: From principles to practice*. Psychology Press.). The metabolite produced by the analgesic effect of the drug is Morphine-6-glucuronide, which typically constitutes a maximum of about 10% of the drug.

The drug acts through the previously mentioned μ, κ and δ receptors. While they all appear to be associated with analgesia, the first also triggers respiratory depression, while the second triggers sedation diuresis (Sadock, B. J., Sadock, V. A., Ruiz, P., 2014. *Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry*, eleventh ed. Lippincott Williams & Wilkins. Philadelphia). The reward effect occurs upon activating the dopaminergic neurons of the ventral tegmental area that project to the cortex and the limbic system. The effects of bradycardia and respiratory depression have been linked to action on the μ receptors. Moreover, while morphine is an effective pain reliever, it is also known to frequently cause itching (Stahl, S. M., 2013. *Stahl's essential psychopharmacology: neuroscientific basis and practical applications, fourth ed*. Cambridge university press, New York.). When the opioid in ques-

tion is administered by epidural injection in the spinal cord, this effect is significantly more pronounced (Miyamoto, T., Patapoutian, A., 2011. Why does morphine make you itch?. *Cell*, *147*(2), 261-262.). Liu, X. Y., Liu, Z. C., Sun, Y. G., Ross, M., Kim, S., Tsai, F. F., Li, Q.F., Jeffry, J., Kim, J.Y., Loh, H.H., Chen, Z. F., 2011. Unidirectional cross-activation of GRPR by MOR1D uncouples itch and analgesia induced by opioids. *Cell*, *147*(2), 447-458. provide evidence that this itching is produced independently of the analgesic effect of morphine. This does not imply, however, that there is no interaction between the responses of itching and pain (Miyamoto, T., Patapoutian, A., 2011. Why does morphine make you itch?. *Cell*, *147*(2), 261-262.). It is suggested, therefore, that there are painful stimuli that can inhibit itching and that the inhibition of pain may result in itching. Naltrexone and clonidine, an antagonist of opioid receptors (Lorenzo, L., Leza, L. H., Fernandez, P. L., 2003. *Drogodependencias, tercera ed*. Médica Panamericana.), are often used as detoxification therapy, (the latter is also used for detoxification amphetamine) although there are various investigations on possible substitutes, derivatives and alternatives to these compounds (Yuan, Y., Zaidi, S. A., Elbegdorj, O., Aschenbach, L. C. K., Li, G., Stevens, D. L., Scoggins, K.L., Dewey, W.L., Selley, D,E., Zhang, Y., 2013. Design, Syntheses, and Biological Evaluation of 14-Heteroaromatic Substituted Naltrexone Derivatives: Pharmacological Profile Switch from Mu Opioid Receptor Selectivity to Mu/Kappa Opioid Receptor Dual Selectivity. Journal of Medicinal Chemistry, 56(22), 9156–9169.). To date, clonidine, an α2 adrenergic agonist, has been used as support for detoxification because of its action on the activity and release of norepinephrine. However, as it is not free from side effects such as sedation and hypotension, which preclude the use of high doses, the present study will investigate its possible combination with low dose naltrexone (Mannelli, P., Peindl, K., Wu, L. T., Patkar, A. A., Gorelick, D. A., 2012. The combination very low-dose naltrexone-clonidine in the management of opioid withdrawal. *The American journal of drug and alcohol abuse*, *38*(3), 200-205.; Motaghinejad, M., Motevalian, M., Asadi-Ghalehni, M., & Motaghinejad, O., 2014. Attenuation of morphine withdrawal signs, blood cortisol and glucose level with forced exercise in comparison with clonidine. *Advanced biomedical research*, *3*, 171.).

In general, opioids easily produce tolerance and dependence. This is why many people who abuse the drug will tend to increase the dosage, since anxiety is higher and it is increasingly difficult to alleviate pain or induce the state of euphoria and subsequent tranquility typical of morphine, which often leads to overdose (Matinfar, M., Esfahani, M. M., Aslany, N., Davoodi, S. H., Parsaei, P., Zarei, G., Reisi, P., 2013. Effect of repeated morphine withdrawal on spatial learning, memory and serum cortisol level in mice. *Advanced biomedical research*, *2*(1), 80.). At present, opioid dependence is a major cause of mortality and morbidity (Sullivan, J. G., Webster, L., 2015. Novel Buccal Film Formulation of Buprenorphine-Naloxone for the Maintenance Treatment of Opioid Dependence: A 12-Week Conversion Study. *Clinical therapeutics*.). Morphine dependence was associated with alterations in the G Neuropeptide S receptor (NPSR) bprotein. Experiments conducted by Ghazal, P., Ciccocioppo, R., Ubaldi, M., 2013. Morphine dependence is associated with changes in neuropeptide S receptor expression and function in rat brain. *Peptides*, *46*, 6-12. clearly demonstrate a change in the NPSR mRNA expression in rats after the withdrawl of morphine and the induction of withdrawal, and that anxiety is higher in morfino- dependent rats. During withdrawal, a person can experience tremors and palpitations, and tend to be more irritable and anxious.

While naltrexone restores the sensitivity of opioid receptors, it precipitates withdrawal symptoms, which is why it makes sense to combine it with clonidine, since the latter is for relieving symptoms (Kosten, T. R., O'Connor, P. G., 2003. Management of drug and alcohol withdrawal. *New England Journal of Medicine*, *348*(18), 1786-1795.).

4. Discussion

The results of this test also have important implications for the policy and practice of alcohol and drug controls by the police as a measure of safety on our roads.

4.1. Limitations

Although the present study is a comprehensive systematic review of research on the symptoms produced by major drugs, it is not without limitations. First, the criticism is mainly qualitative and, due to the number of different kinds of experiments that have been consulted, does not provide detailed results of these studies. It should also be noted that, upon reflecting the current consumption of the various drugs, there is no place for a thorough review of the biochemical mechanisms, which would be more appropriate for a specific study.
Secondly, there are a number of assessment tools available from intervention studies that can be used to conduct systematic reviews, although the quality of reviews may vary according to the type of assessment instrument used. Such tools could have been used for the evaluation of these studies, selecting a tool that has been developed to assess a variety of study designs.
A portion of the studies that were reviewed were conducted on humans, but some animal studies were performed due to the difficulty of conducting such studies on humans.

4.2. Data Minning

The test identifies the substance taken by the driver as the traffic officer checks for observable signs and symptoms presented by the subject. Symptoms and signs strengthen the development of a predictive model such as decision trees. The marked attributes (entries) travel through the tree until reaching a substance (decision). The remaining attributes (leaf nodes) are crossed during the process as well, which is why data mining techniques were used for this test.
The AttributeSelectedClassifier algorithm (dimensionality of training and test data is reduced by attribute selection before being passed on to a classifier) using the J48 classification algorithm to generate a decision tree from the relevant attributes obtained from the application of GainRatioAttributeEval evaluator and the search Ranker.
S is the consistent set of data samples with m different classes. The expected information needs to be classified with respect to the sample given by

$$I(S) = -\sum_{i=1}^{m} \rho_i \, log_2 \, \rho_i \qquad (1)$$

where ρ_i is the probability that a random sample belongs to class Ci and is estimated by s_i / s.
Attribute A has distinct values v, while s_{ij} is the number of samples in class C_i subset S_j. S_j contains those samples in S having value aj of A. The entropy, or the expected information based on the division of A into subsets, is given by

$$E(A) = -\sum_{i=1}^{m} I(S) \frac{s_{1i} + s_{2i} + \dots s_{mi}}{s} \qquad (2)$$

The encoding information that would be gained by branching on A is

$$\text{Gain } (A) = \text{I}(S) - \text{E}(A) \qquad (3)$$

J48 uses gain ratio which applies normalization to information gain using a value defined as

$$\text{SplitInfo}_A(S) = -\sum_{i=1}^{v}(|S_i|/|S|)\, log_2\,(|S_i|/|S|) \quad (4)$$

The gain ratio is defined as

$$\text{SplitInfo}_A(S) = -\sum_{i=1}^{v}(|S_i|/|S|)\, log_2\,(|S_i|/|S|) \quad ()$$

A decision tree is therefore generated based on the attributes that have obtained a greater value by measuring the ratio of gain with respect to the class.

Because the signs are more observable and recognizable symptoms, it seemed appropriate to assign them different weights to differentiate them when selecting the attributes for generating the decision tree. To do so, it was necessary to modify the GainRatioAttributeEval evaluator to employ the use of weights in the selection of attributes.

$$\text{Gain Ratio}(A) = (\text{ Gain }(A)/\text{SplitInfo}_A(S)\ )\ (A_{weight})$$

Equation **Eq. 6** introduces this new feature, allowing the measurement of gain with respect to class to be performed according to the weights that have been assigned to the attributes, where A_{weight} is the weight of each attribute.

The initial weights were taken from the results obtained in the previous section according to ICD-10 and DSM-IV-TR. The weights of the attributes corresponding to the symptoms, shown in **Table 2.** Attributes of sympton**,** have been given a weight of 0.5, due to the difficulty in observing them visually.

Table 2. Attributes of sympton

Attribute	Type of attribute	Weight of attribute
Tendency to discuss	Symptom	0.5
Aggression	Symptom	0.5
Labile state of mind	Symptom	0.5
Attention disorder	Symptom	0.5
Impaired judgment	Symptom	0.5
Interference with personal functioning	Symptom	0.5
Apathy	Symptom	0.5
Sedation (Deep)	Symptom	0.5
Psychomotor retardation	Symptom	0.5

Disturbance in attention	Symptom	0.5
Euphoria	Symptom	0.5
Anxiety or agitation	Symptom	0.5
Paranoid ideation	Symptom	0.5
Altered perception of time	Symptom	0.5
Alteration of reaction time	Symptom	0.5
Visual auditory or tactile illusions	Symptom	0.5
Hallucinations with preservation of orientation	Symptom	0.5
Depersonalization	Symptom	0.5
Derealization	Symptom	0.5
Abuse	Symptom	0.5
Anterograde amnesia	Symptom	0.5
Alteration of psychomotor performance	Symptom	0.5
Hyperarousal	Symptom	0.5
Grandiose beliefs or actions	Symptom	0.5
Stereotyped repetitive behaviors	Symptom	0.5
Feeling of great energy	Symptom	0.5

The weights of the attributes corresponding to the signs are shown in **Table 3.** Attributes of sign **Table 2.** Attributes of sympton**, Table 2.** Attributes of sympton weight of 0.7 was given to the signs that are more difficult to perceive, while a general weight 1.0 was assigned to the rest.

Table 3. Attributes of sign

Attribute	Type of attribute	Weight of attribute
Unsteady gait	Sign	0.7
Difficulty standing	Sign	0.7
Slurred speech	Sign	1.0
Nystagmus	Sign	0.7
Decreased awareness	Sign	1.0
Facial redness	Sign	1.0
Conjunctival injection	Sign	1.0
Sleepiness	Sign	1.0
Miosis	Sign	1.0
Midirasis	Sign	1.0
Hyperorexia	Sign	0.7
Dry mouth	Sign	1.0
Tachycardia	Sign	1.0
Erythematous skin lesions blister	Sign	1.0
Bradycardia	Sign	1.0
Cardiac arrhythmias	Sign	1.0
Hypertension	Sign	1.0
Hypotension	Sign	1.0
Sweating and chills	Sign	1.0
Nausea or vomiting	Sign	1.0
Evidence of weight loss	Sign	1.0
Psychomotor agitation	Sign	1.0
Muscle deblidad	Sign	1.0
Chest pain	Sign	1.0
Seizures	Sign	1.0

These initial weights can be incremented or decremented by the agent responsible for conducting the test, according to the agent's experience.

5. Conclusions and future works

There is growing international interest in conducting toxicology tests by traffic officers to reduce drug use, and hence reduce traffic accidents, resulting from the use of these substances by drivers.
This review was conducted to gather the main effects produced by these substances. The signs and symptoms that are gathered are those that directly and indirectly affect the subject's ability to drive, and tend to be observed visually.
This review is intended to serve as a compiled source of symptoms and signs that can assist in creating a more comprehensive questionnaire in which symptoms and signs exhibited by the driver can help to identify which substance has been taken.
It is also a way to recognize an individual who may test negative for alcohol, but nevertheless poses a threat to other drivers and citizens.
Given the growing use of sobriety checkpoints to detect drivers under the influence of alcohol and drugs as a strategy for preventing accidents, there is an urgent need for methodologically rigorous research to evaluate the effectiveness of drug tests as a tool to increase road safety. Therefore the questionnaire must be tested in a real environment in order to assess its effectiveness.
The weights given to the attributes corresponding to the symptoms and signs were developed according to the theoretical basis set out in the section on ¡Error! No se encuentra el origen de la referencia**.** Upon initiating the test phase, the data gathered from the test administered to drivers at sobriety checkpoints will be input as feedback for the test.

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