

**PHARMACOLOGICAL AND CLINICAL PROFILE OF ACAMPROSATE-A DRUG
USED FOR ALCOHOL ABUSE: A REVIEW****SATYANAND TYAGI*¹, SACHIN KUMAR¹, AMIT KUMAR² AND MOHIT
SINGLA¹.**¹K.N.G.D Modi Institute of Pharmaceutical Education & Research, Modinagar, Uttar Pradesh, India.²M S Ramaiah College of Pharmacy, Bengaluru, Karnataka**Corresponding Author*

sntyagi9@yahoo.com

ABSTRACT

Alcoholism, also known as alcohol dependence is a disabling addictive disorder. It is characterized by compulsive and uncontrolled consumption of alcohol despite its negative effects on the drinker's health and social standing. Similar to other drug addictions, alcoholism is medically defined as a treatable disease. The term 'alcoholism' is a widely used term, first coined in 1849 by Magnus Huss, but in medicine was replaced in by 'alcohol abuse' and 'alcohol dependence' in the 1980s DSM (Diagnostic and Statistical Manual of Mental Disorders) Similarly in 1979 an expert World Health Organization committee disfavored the use of 'alcoholism' as a diagnostic entity, preferring the category of "alcohol dependence syndrome". FDA approved drug Acamprosate is used for treating alcohol dependent individuals seeking to continue to remain alcohol-free after they have stopped drinking. Acamprosate may not be effective in patients who are actively drinking at the start of treatment, or in patients who abuse other substance in addition of alcohol. In the present article, we have focused on pharmacological profile of drug Acamprosate along with its clinical utility in the treatment of alcohol abuse.

KEYWORDS

Alcohol dependence syndrome, Alcoholism, Acamprosate, Campral and DSM

INTRODUCTON

Alcohol abuse, as described in the DSM-IV, is a psychiatric diagnosis describing the recurring use of alcoholic beverages despite negative consequences¹. It is differentiated from alcohol dependence by the lack of symptoms such as tolerance and withdrawal. Alcohol abuse is sometimes referred to by the less specific term alcoholism. However, many definitions of alcoholism exist, and only some are compatible with alcohol abuse. Alcohol abuse is highly

associated with adolescent suicide. Adolescents who abuse alcohol are 17 times more likely to commit suicide than adolescents who don't drink².

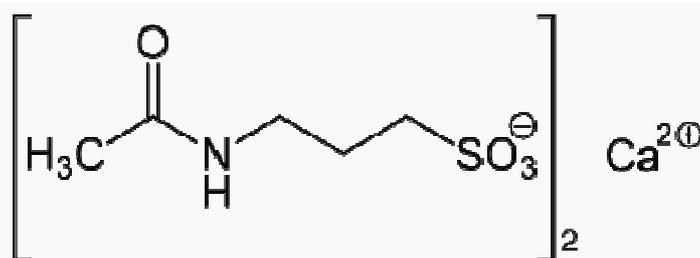
Alcohol abuse during adolescence may lead to long-term changes in the brain which leaves them at increased risk of alcoholism in later years; genetic factors also influence age of onset of alcohol abuse and risk of alcoholism. About 40 percent of those who begin abusing alcohol before age 14 develop alcohol dependence in

later life, whereas only 10 percent of those who did not begin drinking until 20 years or older developed an alcohol problem in later life³.

Alcohol abuse is significantly associated with suicide and violence. Alcohol is the most significant health concern in Native American communities because of very high rates of alcohol dependence and abuse; up to 80 percent of suicides and 60 percent of violent acts are a result of alcohol abuse in Native American communities⁴. Alcohol dependence, as described in the DSM-IV, is a psychiatric diagnosis (a mental illness) describing an entity in which an individual uses alcohol despite significant areas of dysfunction, evidence of physical dependence, and/or related hardship.

DESCRIPTION OF ACAMPROSATE

Acamprosate, also known by the brand name Campral, is a drug used for treating alcohol dependence. Acamprosate is thought to stabilize the chemical balance in the brain that would otherwise be disrupted by alcoholism, possibly by blocking glutamatergic *N*-methyl-D-aspartate receptors, while gamma-aminobutyric acid (GABA) type A receptors are activated⁵. Reports indicate that acamprosate only works with a combination of attending support groups and abstinence from alcohol⁶. Certain serious side effects include allergic reactions, irregular heartbeats, and low or high blood pressure, while less serious side effects include headaches, insomnia, and impotence. Acamprosate should not be taken by people with kidney problems or allergies to the drug.



Acamprosate calcium

While the Food and Drug Administration (FDA) in the United States approved this drug in July 2004, it has been legal in Europe since 1989. After it approved the drug, the FDA released this statement:

"While its mechanism of action is not fully understood, Campral is thought to act on the brain pathways related to alcohol abuse. Campral was demonstrated to be safe and effective by multiple placebo-controlled clinical studies involving alcohol-dependent patients who had already been withdrawn from alcohol, (i.e., detoxified). Campral proved superior to placebo in maintaining abstinence (keeping patients off alcohol consumption), as indicated by a greater percentage of acamprosate-treated subjects being assessed as continuously abstinent throughout treatment. Campral is not addicting and was generally well-tolerated in

clinical trials. The most common adverse events reported for patients taking Campral included headache, diarrhea, flatulence, and nausea."

The Scripps Research Institute conducted a double blind study comparing the effectiveness between using acamprosate and placebos in combination with psychotherapy. The primary end-point evaluated was percentage of alcohol-free days. The researchers concluded that acamprosate is "safe and effective"⁷.

PHYSIOLOGICAL ACTION OF ACAMPROSATE

Alcohol inhibits activity of biochemical receptors called *N*-methyl-D-aspartate receptors, or NMDARs, so that chronic alcohol consumption

leads to the overproduction of these receptors. Thus, sudden alcohol abstinence causes these excessive numbers of NMDARs to be more active than normal and to produce the symptoms of delirium tremens and excitotoxic neuronal death⁸. Withdrawal from alcohol induces a surge in release of excitatory neurotransmitters like glutamate, which activates NMDARs⁹. Acamprosate reduces this glutamate surge¹⁰. The drug also protects cultured cells in excitotoxicity induced by ethanol withdrawal¹¹ and by glutamate exposure combined with ethanol withdrawal¹².

SIDE EFFECTS OF ACAMPROSATE

The most common side effects of acamprosate, occurring in 3% or more of people, are the following:

- accidental injury
- feelings of weakness
- pain
- anorexia (loss of appetite)
- diarrhea
- flatulence
- nausea
- anxiety
- depression
- dizziness
- dry mouth
- insomnia
- tingling sensations
- itching
- sweating

RISKS AND PRECAUTIONS

Drugs like acamprosate that affect the brain's chemistry may impair judgment, thinking, or motor skills. The effects of acamprosate on the fetus are not known. Similarly, it is not known if acamprosate crosses into breast milk.

DRUG INTERACTIONS

Co-administered naltrexone increases the blood concentration of acamprosate, probably by slowing the emptying of stomach contents into the small intestine. This interaction is unlikely to

change the safety or effectiveness of acamprosate.

ALTERNATIVES

In the United States, only two other drugs, disulfiram (Antibuse) and naltrexone (Revia) are approved to treat alcohol dependence. Disulfiram is used less frequently today because of side effects and high discontinuation rate among users. A multicenter study of people recovering from alcohol dependence found that acamprosate had no influence on recovery, whereas naltrexone improved symptoms of depression and anxiety and lengthened time to relapse in patients with low-depression and low-dependence¹³.

RESEARCH

In three of four trials, acamprosate plus support group therapy proved more effective to support group therapy alone in maintaining alcohol abstinence. The combine trial was a large, multicenter study that looked at the effectiveness of medications and behavioral therapies, or the combination of these, in the management of recovery from alcohol dependence¹⁴. Interventions with acamprosate, naltrexone, behavioral therapy, or placebo all had reduced the amount of drinking. Acamprosate, either alone or in combination with behavioral therapy or other medical management, had no effect on the number of days before relapse or the number of heavy drinking days. However, naltrexone treatment alone or in combination with other medical management or behavioral therapy improved both these outcomes significantly.

CONCLUSION

It may be concluded that alcoholism, or alcohol dependence is a disease. The consequences of alcohol misuse are serious and in many cases, life threatening. Heavy drinking can increase the risk for certain cancers, especially those of the liver, esophagus, throat, and larynx. Heavy drinking can also cause liver cirrhosis, immune system problems, brain damage, and harm to the fetus during pregnancy. Chronic alcoholism continues to be wide spread and debilitating

disorder that places a tremendous burden on society in terms of health care costs, lost wages and personal suffering. Acamprosate is a prescription drug used for the treatment of alcohol dependence. It is thought to balance neurotransmission in the brain. Neurotransmission is the process by which neurons communicate with one another. Acamprosate was used in Europe for several years before the U.S. Administration approved acamprosate in September 2004. It is only one of three drugs approved in the United States for this condition. Acamprosate is used along with counseling and social support to help people who have stopped drinking large amounts of alcohol (alcoholism) to avoid drinking alcohol again. Drinking alcohol for a long time changes the way the brain works. Acamprosate works by helping the brains of people who have drunk large amounts of alcohol to work normally again. Acamprosate does not prevent the withdrawal symptoms that people may experience when they stop drinking alcohol. Acamprosate has not been shown to work in people who have not stopped drinking alcohol or in people who drink large amounts of alcohol and also overuse or abuse other substances such as street drugs or prescription medications.

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