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Sinclair

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[54] **METHOD FOR TREATING ALCOHOL-DRINKING RESPONSE**

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[51] **Int. Cl.**[4] **A61K 31/44**

[52] **U.S. Cl.** **514/282;** 514/811

[58] **Field of Search** 514/810, 811, 812, 282

[56] **References Cited**

PUBLICATIONS

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"Feasibility of Effective Psychopharmacological Treatments for Alcoholism", J. D. Sinclair, Ph.D, British Journal of Addition, 1987, 82, 1213–1223.

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Attorney, Agent, or Firm—Armstrong, Nikaido, Marmelstein, Kubovcik & Murray

[57] **ABSTRACT**

A therapeutic method is provided for use as an adjunct in the treatment of alcoholism. The method consists of extinguishing the alcohol-drinking response of alcoholics during a relatively short period of time by having them drink alcoholic beverage repeatedly while an opiate antagonist blocks the positive reinforcement effects of ethanol in the brain.

8 Claims, 3 Drawing Sheets

Fig. 1

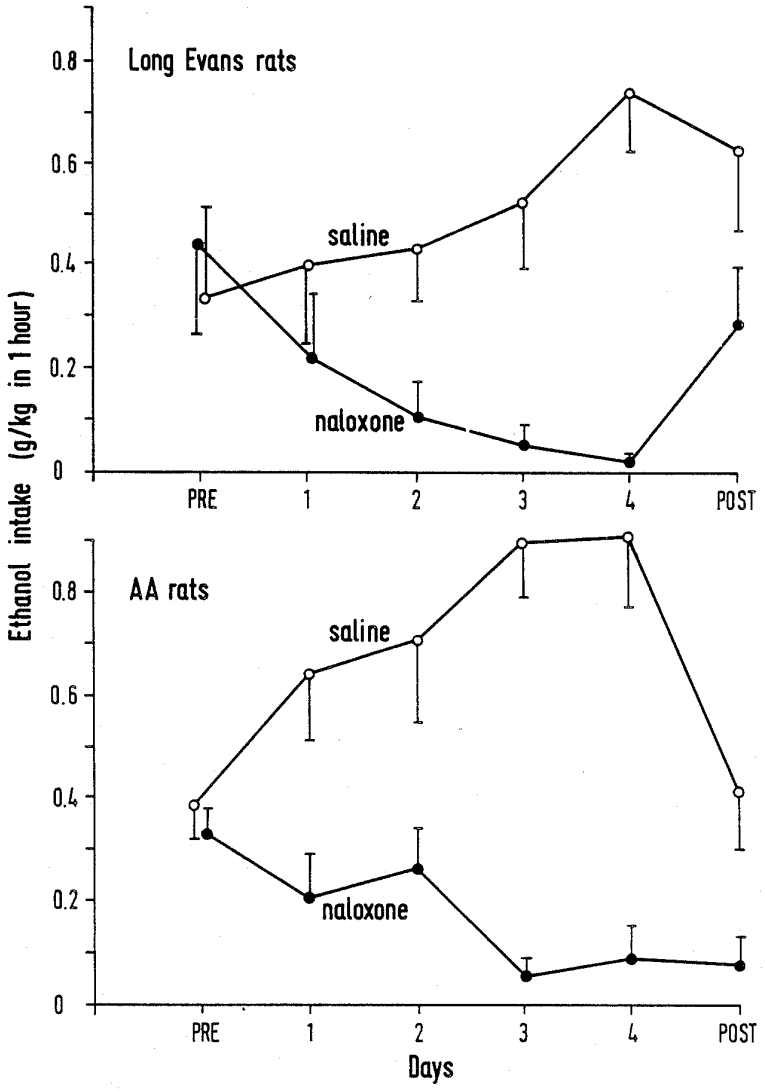
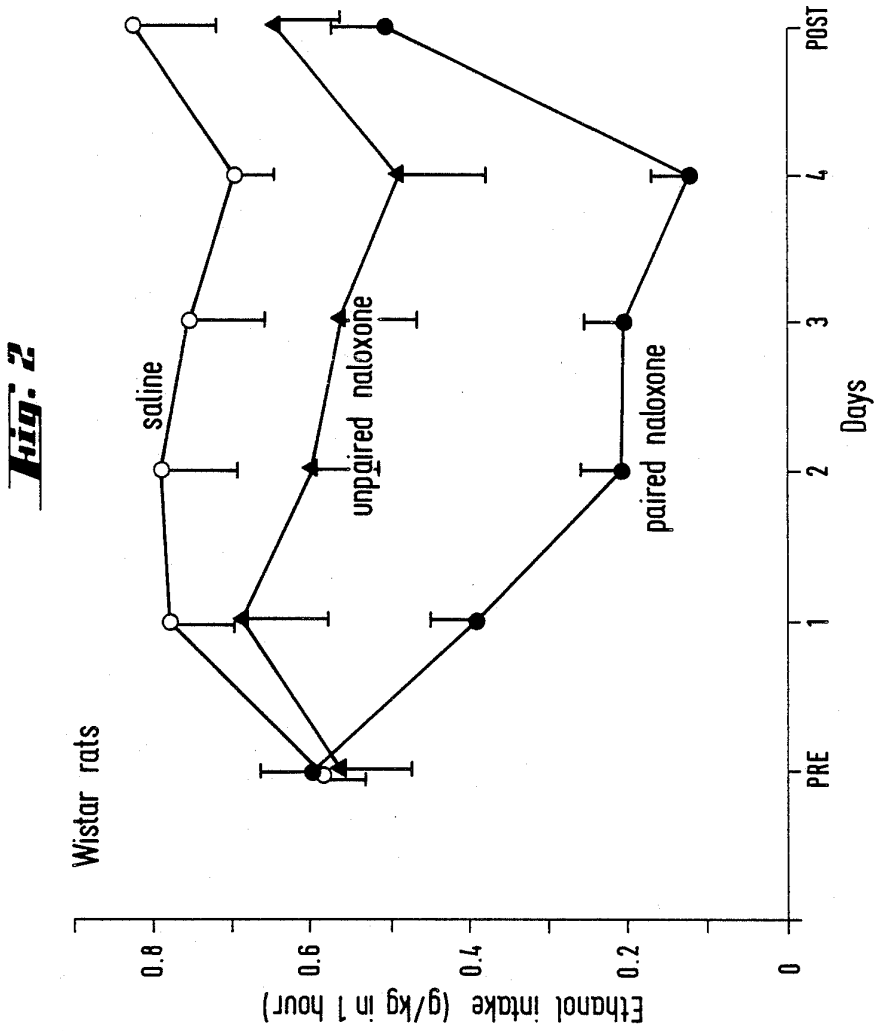


Fig. 2



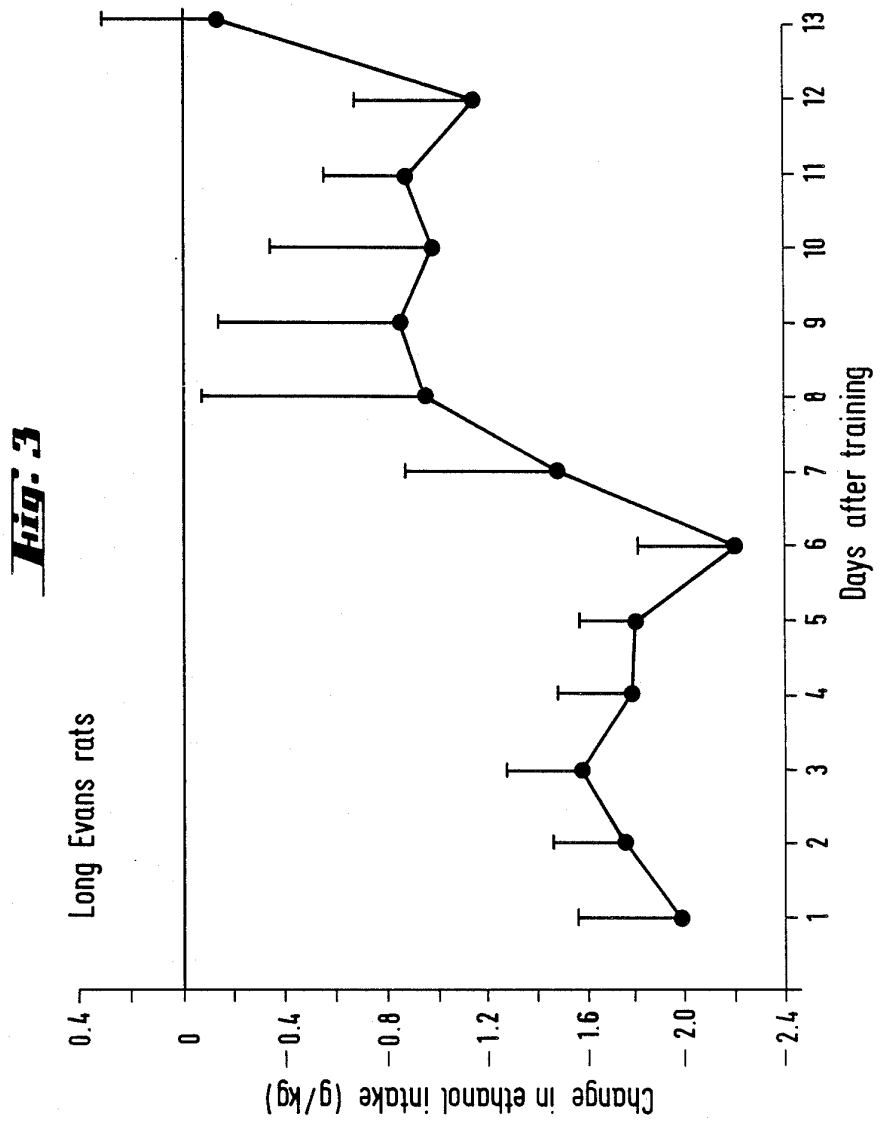


Fig. 3

METHOD FOR TREATING ALCOHOL-DRINKING RESPONSE

FIELD OF THE INVENTION

The invention is a treatment for alcohol abuse in which the alcohol-drinking response is extinguished over a limited number of sessions by being emitted while the reinforcement from alcohol is blocked with an opiate antagonist such as naloxone or naltrexone.

BACKGROUND OF THE INVENTION

Alcoholism is the most costly health problem in many countries. The cost, e.g., in America is estimated to be about $117,000,000,000 per year. The treatment methods currently used are not very effective. Most alcoholics drop out of treatment within a month or two. Few alcoholics, regardless of the type of treatment, are able to avoid relapses and renewed alcohol abuse.

No one is born an alcoholic. The drinking of alcohol (ethanol or ethyl alcohol) is a learned response, reinforced largely by the rewarding effects of alcohol in the central nervous system—the euphoria from lower, stimulatory doses of ethanol. An alcoholic is a person who, through an interplay of genetic and environmental factors, has had the alcohol-drinking response reinforced so often and so well that it becomes too strong for the individual to continue functioning properly in society. The strong alcohol-drinking response—i.e., the drive for alcohol—then dominates the person's behavior and life.

The current methods for treating alcoholism are not very successful probably because they do not effectively weaken the alcoholic's alcohol-drinking response. Some methods (e.g., counselling, Alcoholics Anonymous) are aimed at increasing the alcoholic's ability or will power to withstand the drive for alcohol. The drive, however, is not weakened and the patient is told that he will remain an alcoholic, that is, a person with an overly strong alcohol-drinking response, for the rest of his life. These methods succeed in some alcoholics, but in most the time eventually comes when a momentary decrease in will power causes a resumption of alcohol drinking and alcohol abuse.

Other treatments use punishment of various sorts (e.g., electric shock, disulfiram reactions, loss of a job) to try to stop alcohol drinking. Punishment is, however, a poor method for changing behavior and has many limitations. In particular, it is ineffective when positive reinforcement is still being received for the same response that is punished. Since the treatments that punish alcohol drinking do not block the positive reinforcement of the same response coming from alcohol in the brain, they should not be expected to be very effective.

A third type of treatment has been proposed. Alcohol and opiates appear to cause positive reinforcement largely through the same neuronal system in the brain. Consequently, opiates such as morphine or methadone might be able to satisfy the drive for alcohol and thus abolish alcohol drinking. This does indeed occur in rats and other animals, and there is evidence suggesting opiates could also succeed in making alcoholics stop drinking alcohol. The treatment probably would, however, turn alcoholics into opiate addicts, which is, of course, not a good solution.

Instead of counteracting the drive for alcohol or temporarily satisfying it, a successful treatment for alcoholics should permanently weaken the alcohol-drinking response. Fortunately, there is a well-established method for weakening a learned response: "extinction". Extinction consists of having the response emitted repeatedly in the absence of positive reinforcement.

It is relatively simple to remove external sources of positive reinforcement, such as the food a rat gets for pressing a lever or even the social reinforcement a person sometimes gets for drinking alcohol. But much of the positive reinforcement for alcohol drinking is internal, from the rewarding effects of alcohol in the brain.

The results showing that alcohol and opiates share a common mechanism of reinforcement show how the internal positive reinforcement from alcohol might be blocked. Various substances, called opiate antagonists, are able to block the receptors for opiates and thus prevent the effects of, e.g. morphine. Furthermore, there is already evidence that the two most commonly used opiate antagonists, naloxone and naltrexone, do block positive reinforcement from alcohol. First, they block the stimulatory effect of alcohol which is generally thought to be related to the euphoria and positive reinforcement. Second, it has been shown that while they are in the body they reduce voluntary alcohol drinking and intragastric self-administration of alcohol by animals.

Naloxone and naltrexone were originally intended for use in treating overdoses of opiates. They have since been suggested for use against a wide variety of problems including respiratory failure, anorexia nervosa, bulimia, obesity, emesis and nausea, shock, severe itching, constipation, growth of neoplasms, and sexual impotence and frigidity. There have been many studies attempting to use naloxone to reverse alcohol intoxication and especially the coma produced by very large amounts of alcohol; although the results have been mixed and there is still controversy as to whether naloxone can antagonize severe alcohol intoxication, it is important to note that none of these studies reported any bad effects from giving naloxone in conjunction with alcohol. The doses of naloxone have ranged between about 0.2 and 30 mg daily, and naltrexone from about 20 to 300 mg daily. Other suggested uses are for the opiate antagonists in conjunction with other drugs, particularly, opiate agonists. For instance, U.S. Pat. No. 3,966,940 is for a compound containing narcotics or analgesics plus naloxone to be given especially to narcotic addicts. In these cases the opiate or other drug is seen to be active pharmacological agent and the opiate antagonist is included to counteract some of its effects.

Continual treatment with opiate antagonists should reduce the alcohol intake of alcoholics: so long as the antagonist is in the body, the alcoholic should have little incentive for drinking because alcohol is not rewarding. This maintenance treatment, however, has the same problem found with other long-term deterrent treatments, such as that with disulfiram: how to keep the alcoholic on the medication. Since there is still a strong drive for alcohol, the alcoholic is likely to drop out of treatment and stop taking the antagonist so that he or she can satisfy the drive by drinking again.

However, combining the well-established procedure of extinction from psychology with the pharmacological findings that opiate antagonists block reinforcement from alcohol provides a new and much more promising way of treating alcoholism. Indeed, it provides what could be called the first true cure for alcoholism. After a relatively short period of treatment during which an

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