ABSTRACT OF THE DISCLOSURE

Covers a method for the treatment of drug addiction comprising administering to a drug addict a composition selected from the group consisting of 2-imino-5-phenyl-4-oxazolidinone, a pharmaceutically-acceptable salt thereof or a combined composition comprising 2-imino-5-phenyl-4-oxazolidinone or a salt thereof and an additional agent comprising an aluminum base, an aluminum salt, and an alkaline earth metal salt or an alkaline earth metal base. The method is particularly applicable to treatment of a drug addict dependent upon a stimulant-type addictive drug such as cocaine, amphetamine and the like.

BACKGROUND OF THE INVENTION

Field of the invention

This invention is concerned with alleviation of drug addiction by treating the drug addict such as a person dependent upon a stimulant-type addictive drug with a particular group of compounds. The treatment tends to draw the drug addict away from dependence upon the drug, at least in part.

Description of the prior art

Drug addiction, as defined by the Drug Addiction Committee of the National Research Council is a state of periodic or chronic intoxication detrimental to the individual and to society, produced by the repeated administration of a drug. Such addiction is characterized by a compulsion to continue to take the drug and to increase the dose with the development of psychic and sometimes physical dependence on the effects of the drug so that development of means to continue the administration of the drug becomes an important motive in the addict's existence. Thus, an addictive drug as the term is meant to be employed here is one used initially for the relief of physical or psychic pain, and if used consistently may lead to dependency on the part of the host because of an intractable craving and severe withdrawal symptoms which develop if the use of the drug is discontinued.

There are several types of drugs possessing addictive properties. The most common type includes the narcotics which possess the most potent addictive qualities. A narcotic is defined as any drug which produces sleep or stupor and at the same time relieves pain. Such drugs include opium alkaloids, as for example, morphine, heroin and codeine as well as synthetic narcotics not related to the opiates such as meperidine and methadone. Thus, any drug whether natural or synthetic, which is found to have addiction forming or addiction sustaining liability is a narcotic and any person who uses such drugs continuously for other than medicinal purposes to develop a state of euphoria is a narcotic addict.

Narcotic addiction is a sociological and economic problem not only in the United States but in many other countries of the world. There are untold thousands of narcotic addicts in the United States alone who are known and thousands more who are unreported. The total number of narcotic addicts in the world is estimated to be in the millions. These persons are a detriment to society, because once they develop the narcotic habit, they are no longer productive and will do anything including robbery and murder to obtain the funds with which to buy narcotics from nefarious peddlers. Despite strict government regulations and rigid law enforcement, the illegal use of narcotics continues virtually unabated.

The only known treatment for an addict is to place such a person in a clinic where the amount of narcotic is gradually reduced each day until the addict is no longer dependent upon the drug. At the present time, there is no absolute cure for the narcotic habit. It would, therefore, be extremely beneficial to mankind if a treatment for narcotic and other drug addiction could be developed which would destroy the innate craving of these unfortunate persons for addictive drugs and make them more useful members of society.

Another type of addictive drug includes the hypnotic and sedatives such as the barbiturates, bromides, choral hydrate, paraldehyde, camphor or marihuana and mesca-line as well as the so-called tranquilizers such as 2-methyl-2-n-propyl-1,3-propanediol dicarbamate. Short acting barbiturates such as pentobarbital or secobarbital are generally preferred by addicts rather than long acting agents such as phenobarbital. The barbiturates are often used by morphine addicts when the opiate is not readily available and combined addiction thus results, since both drugs must be taken in order to prevent withdrawal symptoms.

A third type of addictive drug includes the stimulants such as amphetamine and cocaine. Barbiturate addicts frequently abuse amphetamine. Although the excitement and exhilaration provided by the amphetamine drug is considered a factor in addiction, the many unpleasant side effects caused by large doses sometimes act as a deterrent to its continued use. Cocaine likewise causes euphoric excitement and pleasurable hallucinations which add to the satisfaction obtained. The cocaine addict is not a normal individual, but is often a dangerous and abused person.

SUMMARY OF THE INVENTION

In summary then the present invention comprises a method of treating drug addicts such as those persons dependent upon stimulant-type drugs such as cocaine, amphetamine and the like whereby such dependence is at a minimum advantage materially reduced in character. The compositions useful here comprise either 2-imino-5-phenyl-4-oxazolidinone, a pharmaceutically-acceptable salt thereof or a combination of one or either of the mentioned materials and an additional reagent comprising an aluminum base, an aluminum salt, an alkaline earth metal salt or an alkaline earth metal base.

It is therefore an object of this invention to provide a method of treating drug addicts through use of compositions which can be readily and conveniently administered to such addicts and which are very effective in the treatment of various types of drug addiction.

A further object of this invention is to provide a method for the treatment of drug addicts which substantially reduces or eliminates the craving for addictive drugs.

Yet another object of the invention is to provide a method for the treatment of drug addicts which is simple to perform, but effective in destroying the innate desire of such addicts for ever increasing amounts of narcotics.

A specific object of the invention is to provide a method of treating drug addicts particularly dependent upon stimulant-type addictive drugs such as cocaine and amphetamines.

Other objects will appear hereinafter.
DETAILED DESCRIPTION OF THE INVENTION

In more detail, the invention here comprises a method of treating addicts addicted to the above discussed classes of drugs or others, and particularly those addicted to stimulant-type drugs by administering to said drug addicts in daily dosages particular groups of compounds. These compounds reduce the craving for and dependence upon said drugs in some manner.

In more detail, the compositions found useful in the invention here comprise either 2-imino-5-phenyl-4-oxazolidinone, a pharmaceutically-acceptable salt thereof, or the combination of either of the just-mentioned two materials with an additional material comprising either a base or salt selected from the group consisting of aluminum bases, aluminum salts, alkaline earth metal salts and alkaline earth metal bases.

Thus, 2-imino-5-phenyl-4-oxazolidinone itself is effective here. Likewise salts of the oxazolidinone compound may also be employed here. Since this particular oxazolidinone is a relatively weak acid, salts may be formed via combination with a strong base. For example, alkali metal salts may be formed such as the sodium, lithium etc. salts. In addition alkaline earth metal salts such as the calcium salt may also be formed. Normally these salts are formed by reacting the oxazolidinone with a strong alkali metal or alkaline earth metal base or amphotride such as sodium hydroxide, potassium hydroxide, lithium hydroxide, calcium hydroxide etc. or sodium hydride, calcium hydride etc.

Likewise a third class of compounds found useful here comprises an additional agent in combination with the oxazolidinone or oxazolidinone salt or both. The combined compound includes the oxazolidinone and/or salt thereof and an aluminum or alkaline earth metal salt or base. Such salts or bases include aluminum, magnesium and calcium carbonates, hydroxides, sulfates, chlorides, bicarbonates, phosphates, citrates, thiosulfates, iodides, bromides, carbonate-hydroxides, acetates, propionates, lactates, benzoates, tartrates, etc. One particularly preferred composition comprises the combination of the oxazolidinone and/or salt thereof and a magnesium salt or base such as magnesium hydroxide, magnesium sulfate, magnesium chloride etc. One specific useful composition comprises the combination of 75% by weight of oxazolidinone and 25% by weight of magnesium hydroxide, wherein approximately equimolar compounds of each are present.

In the typical situation the combined compositions employed here which are useful in treatment of a drug addiction are formed by combining one or more of the just described aluminum or alkaline earth salts or bases with the oxazolidinone or salt thereof in a ratio of at least 0.05 mole of base or salt to 1 mole of oxazolidinone or oxazolidinone salt. While no upper limit of said ratio is to be construed, as a practical matter, up to about 50 or more moles of bases or salts per mole of oxazolidinone or oxazolidinone salt may be combined to form compositions useful in combating drug addiction.

The above compositions can be administered orally or by injection though the former is preferred. For oral administration, tablets, pills, or capsules are easily prepared. Tablets may be prepared to contain between 5 and 25 mg. of the active material together with the usual tableting adjuvants, e.g., coloring agents, flavoring agents, diluents, lubricants, carriers, and, if desired, dispersing agents or release retardants.

The materials disclosed here are useful in treating human drug addiction at a daily dosage ranging from about 0.1 to about 10 mg./kg. of body weight daily, either in single or divided doses.

As noted above, it has been found that the just disclosed compositions are particularly useful in treating those drug addicts who are dependent upon stimulant-type drugs such as cocaine, amphetamine, amphetamine derivatives, and the like.

The following example amply illustrates the efficacy of the invention.

EXAMPLE

It has been recognized since 1929 that the biological factors involved in drug dependence can be studied in infra-human organisms. In addition, it has recently been accepted that the behavioral aspects of drug dependence can be studied in infra-human organisms. An excellent treatise with respect to this is that entitled Self-Administration of and Behavioral Dependence on Drugs, by C. R. Shuster and T. M. Thompson Schuster, Annual Review of Pharmacology, Volume 9, 1969.

In essence then, study of drug addiction and its alleviation in animals such as monkeys is directly applicable to treatment of humans, and an excellent way to determine initial efficacy of any drug treatment useful in combating drug addiction.

Here the following studies were made. A Rhesus monkey was conditioned to press a bar in order to obtain cocaine. In this case, 100 micrograms per kg. of body weight of cocaine was injected into the monkey's jugular vein when he pressed the bar. After the monkey had become habituated, controls were set up. This involved allowing the habituated animal to press the bar freely for two hours per day. This was allowed to proceed for a period of five days. In this period of five days the monkey pressed the bar 96 times the first day, 111 times the second day, 92 times the third day, 78 times the fourth day and 89 times the fifth day for a mean pressing rate of 93.2 presses per two hour test session per day.

Two days later the monkey was intravenously administered 4 mg./kg. of body weight of a typical composition of this invention comprising a mixture of 2-imino-5-phenyl-4-oxazolidinone and magnesium hydroxide (75.3% and 24.7% by weight respectively) in a saline carrier. Thirty minutes later, the monkey was placed back in the self-administration chamber and allowed to press the bar for the two hour period. The composition of the invention was administered prior to each day's test session. In this instance after treatment the monkey pressed the bar 53 times the first day, 59 times the second and 50 times the third, for a mean average of 54 times per test session.

When the concentration of the inventive composition pretreatment was reduced to 1 mg./kg. and 2 mg./kg., a dose response curve was seen. At 1 mg./kg., cocaine self-administration was reduced from the average control level of 93.2 to 83 presses per session and at 2 mg./kg. reduced to 74 presses per session.

Effects similar to those described in the foregoing example are observed when other compositions falling within the scope of the invention are administered to drug addicted animals. Although the exact mode of action of the compounds here resulting in the improvement in the condition of drug addicts is not known, it is apparent that they materially aid in reducing the insatiable craving so prevalent in the withdrawal of drugs upon which the addict has become dependent.

What is claimed is:

1. A method for the treatment of drug addiction which comprises administering to a drug addict at least an effective amount of a composition selected from the group consisting of (1) 2-imino-5-phenyl-4-oxazolidinone; (2) a pharmaceutically-acceptable salt thereof and (3) the combination comprising 2-imino-5-phenyl-4-oxazolidinone or a pharmaceutically-acceptable salt thereof and an additional agent comprising a base or salt selected from the group consisting of an aluminum base, aluminum salt, an alkaline earth metal salt, and an alkaline earth metal base.

2. The method of claim 1 wherein said composition comprises 2-imino-5-phenyl-4-oxazolidinone.

3. The method of claim 1 wherein said composition
comprises a pharmaceutically-acceptable salt of 2-imino-5-phenyl-4-oxazolidinone.

4. The method of claim 1 wherein said composition comprises the combination of 2-imino-5-phenyl-4-oxazolidinone and additional agent comprising a base or salt consisting of an aluminum base, an aluminum salt, an alkaline earth metal salt or an alkaline earth metal base.

5. The method of claim 4 wherein said base is magnesium hydroxide.

6. The method of claim 5 wherein said combined composition comprises magnesium hydroxide combined in a ratio of about one mole of magnesium hydroxide to about one mole of 2-imino-5-phenyl-4-oxazolidinone.

7. The method of claim 1 wherein said composition is administered orally.

8. The method of claim 1 wherein said drug addiction comprises dependence upon a stimulant-type addictive drug.

9. The method of claim 8 wherein said addictive drug is cocaine.

10. The method of claim 8 wherein said addictive drug is amphetamine or a derivative thereof.

11. The method of claim 1 wherein said composition is given to said drug addict in a daily dosage ranging from about 0.1 to about 10 mg./kg.

References Cited
UNITED STATES PATENTS
3,348,999 10/1967 Woroch et al. 424—272

STANLEY J. FRIEDMAN, Primary Examiner
U.S. Cl. X.R.
424—154, 272