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INJECTABLE MEDICINAL COMPOSITION

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My invention relates to an injectable medicinal composition in which an antibiotic is combined with a vehicle material, to act as a repository for the antibiotic, to accomplish certain results as set forth in the objects hereinbelow.

In the treatment of various disease processes for which antibiotics have been found to be effective specifics, it has usually been found that the antibiotics are most effective when injected. The administration of injectable antibiotics has, however, many drawbacks and disadvantages. For example, the wide spectrum antibiotics, such as chloramphenicol; and the tetracyclines comprising tetracycline hydrochloride, chlortetracycline hydrochloride, oxytetracycline hydrochloride, tetracycline citrate or phosphate, and other chloride, phosphate, or citrate salts of tetracycline; sodium or potassium salts of penicillin; and streptomycin may not usually be administered parenterally without the accompaniment of excruciating pain. Another disadvantage is found specifically in the treatment of tuberculosis. In such a case it has been found desirable to administer an antibiotic such as streptomycin in a dosage of approximately one to four grams per day in order to effect the desired therapeutic value. This dosage may, however, affect the auditory nerve of the patient adversely resulting in a substantial loss of hearing. On the other hand, if the amonut of streptomycin is reduced to a point which will insure no harm to the auditory nerve, there may be an insufficient amount to effect a therapeutic result.

Certain other antibiotics, such as neomycin and bacitracin are relatively toxic and either should not be used at all or, if used, can be tolerated by the patient in such small dosages as to be largely ineffective as medicines. Penicillin, which is universally believed to be non-toxic, has also been found to have some bad effects when large dosages are administered especially over a considerable period of time.

Another disadvantage of administering injectable medicines is the ordinary factor of pain and discomfort to the patient associated with the use of the hypodermic needle. It has also been found that the tetracyclines have side effects in that there is possibility of favoring the development of fungi and bacteria which are harmful to the host when administered orally.

It is, therefore, an object of my invention to provide a vehicle for incorporation with an antibiotic to diminish the pain factor resulting from the parenteral administration of drugs. Another object of my invention is to provide for such a vehicle to permit parenteral rather than oral administration of drugs especially where it is desirable to keep the particular drug out of the intestinal tract of the patient.

Another object of my invention is to provide such a vehicle for an antibiotic which will act as a repository for the antibiotic and will hold the bacteriostatic effect in suspension and permit its release over a prolonged period into the blood stream for the purpose of reducing the number of injections required in a course of treatment.

Still another object of my invention is to provide a vehicle for an antibiotic which acts as an anti-infective agent increasing the resistance of the patient to infection and which will act to reduce the toxicity of the specific medicine so that larger dosages may be given on a non-toxic level to the end that the beneficial action of the antibiotic may be fully utilized. Other and further objects and advantages of my invention will appear in this specification hereinbelow.

In my Patent No. 2,381,830, I have described and claimed an anti-infective agent which is a special composition composed of vitamin A, guaiacol and eucalyptol in the form of an injectable oil preparation, preferably in olive oil, with which may be optionally associated camphor, mixed tocopherols and thiamin chloride.

My present invention is a combination of the anti-infective agent, such as the material which I have claimed in my Patent No. 2,381,830 and a bacteriocidal agent, such as an antibiotic, all being incorporated in an injectable preparation. This is the first time that both an anti-infective agent and a bacteriostatic agent have been combined and incorporated in an injectable preparation as described herein.

This invention has, for example proved to have unexpected utility in that the toxicity of the antibiotic is rendered minimal or completely negative, thus making it possible to employ antibiotics which have been found to have specific utility for given disease conditions but which have been too toxic and far too painful for use at optimum dosage levels. For example, injections of tetracycline with procaine and tetracycline with lidocaine hydrochloride are associated with most painfully excruciating pain. However, when the mentioned drugs are injected in association with my vehicle of vitamin A, guaiacol and eucalyptol in an injectable oil there is, in most cases, relative freedom from pain.

In addition, my new composition is characterized by the fact that the rate of absorption or assimilation of the antibiotic is reduced or retarded without loss of the antibiotic function, and the rates of excretion and detoxification are increased. Moreover, fewer injections are required and each injection is effective for a greater period of time.

Any antibiotic may be employed in combination with my anti-infective vehicle and in each case the antibiotic selected can be the one of choice for the treatment of a given disease condition or process. In the treatment of pneumonia, for example, the antibiotic of choice may be a wide spectrum antibiotic. Prior to my invention, the excruciating pain associated with its parenteral administration made it impossible to employ such a drug in most cases. In any case where a wide spectrum antibiotic such as chloramphenicol or tetracycline is indicated, my invention may be incorporated. By combining the wide spectrum antibiotic with my vitamin A oil vehicle, herein described, the use of the drug can be realized.

The desired dosage of the antibiotic is incorporated by known procedures in the minimum amount of the vitamin A oil vehicle into which it is possible to get it. When combined with the vitamin A oil vehicle, the wide spectrum antibiotic is relatively slowly released from the site of the injection for absorption and assimilation and for effecting its action.

Thus, doses of antibiotics can be administered parenterally through the combination therewith of the vitamin A oil vehicle and, also, the number of injections can be reduced and the effects of each injection prolonged. The cost of treatment is markedly reduced and pain is substantially eliminated.

The vitamin A vehicle is preferably composed of vitamin A in olive oil (the first extract) together with mixed terpins which act as anti-spasmodic analgesic agents. The mixed terpins are eucalyptol and camphor. The combination also includes guaiacol which acts as an analgesic and antiseptic agent. I prefer to use the following proportions: Vitamin A usually present in the amount of at least 50,000 to 500,000 units per injection, together with .05 to .1 gram of guaiacol, .05 to .1 gram of cam-

phor and .05 to .1 gram of eucalyptol. The individual dosage is usually one to two cubic centimeters, but may be any dosage which is effective or tolerated having due regard to the particular antibiotic involved and the total amount thereof which it is desired to administer. The vitamin A vehicle may optionally contain a stabilizing and anti-oxidant substance such as mixed tocopherols (vitamin E), which also has the effect of prolonging the useful life of the vitamin A thus increasing the shelf life of the product. The vehicle may also contain a substance which has a beneficial effect upon the nervous system, such as thiamin chloride.

An alternative and antiseptic substance, such as iodoform, may also be included. I prefer to use .01 to .05 gram of iodoform per injection. Other oils such as sesame oil and peanut oil may optionally be employed in place of olive oil but I have found that olive oil is best tolerated by the body and, therefore, the other oils are somewhat less desirable although still effective. I have found that my anti-infective agent, described herein, in combination with any of the bacteriostatic agents, mentioned herein, provides repository action in an injectable preparation. The oil carrier holds the bacteriostatic agent in suspension and permits release over a prolonged period of time with increased concentration into the blood stream and also acts as a barrier to the immediate absorption of the bacteriostatic agent.

In addition, by virtue of the vitamin A content, the carrier acts as an anti-infective agent thereby reducing the incidence of infection. It also diminishes the pain factor resulting from the parenteral administration of the drugs. Another beneficial effect is that the resistance to disease of the patient is increased.

While the invention has been more particularly described in connection with certain antibiotics, such is not to be deemed a limitation of the invention since injectable preparations for the treatment of other diseases for which other antibiotics or drugs are useful are also included within the purview hereof.

In this connection, I wish to point out that effective antibiotic dosages of chlortetracycline hydrochloride, oxytetracycline hydrochloride and tetracycline hydrochloride of 1 to 3 grams daily and of neomycin of 1 to 4 grams daily, as well as antibiotic penicillin, used in the form of one of its salts such as sodium or potassium penicillin, within the range of at least 300,000 units daily and preferably within the range of 500,000 to 1,500,000 units daily are possible when combined with the special vitamin A vehicle as explained above. The use of my combination above eliminates the necessity of using potentially harmful cocaine or any of its derivatives, such as procaine.

The vitamin A vehicle and the antibiotic coact to give the new and useful results herein set forth which results cannot be secured in any other way, so far as I am aware, and, in particular, cannot be attained by separate or uncombined administration of the antibiotic and the vitamin A vehicle.

While I have described the preferred forms and applications of my invention, there may be other combinations and applications falling within the scope of the claims set forth hereinbelow and I desire to be protected for all such combinations and applications.

Wherefore, I claim:

1. An anhydrous injectable parenteral preparation which is liquid at room temperature consisting essentially of a non-gelled physiologically compatible vegetable oil selected from the group consisting of olive oil, sesame oil, peanut oil, vitamin A, guaiacol, eucalyptol, and an antibiotic selected from the group consisting of chloramphenicol, tetracycline, penicillin, neomycin and bacitracin.

2. A preparation according to claim 1 also containing a compound selected from the group consisting of camphor, mixed tocopherols, thiamin chloride and iodoform.

3. A preparation according to claim 1 wherein the antibiotic is a tetracycline.

4. A preparation according to claim 3 containing mixed tocopherols.

5. A preparation according to claim 3 further containing an anaesthetic selected from the group consisting of procaine and lidocaine hydrochloride.

References Cited in the file of this patent

UNITED STATES PATENTS

2,055,083	Klein et al.	Sept. 22, 1936
2,081,934	Jacobson	June 1, 1937
2,381,830	Lobel	Aug. 7, 1945
2,443,778	Romansky	June 22, 1948
2,507,193	Buckwalter	May 9, 1950
2,518,510	Welch	Aug. 15, 1950
2,529,461	Schneiderwirth	Nov. 7, 1950
2,592,149	Jacobson	Apr. 8, 1952
2,661,315	Jurist et al.	Dec. 1, 1953
2,733,184	Ziegler	Jan. 31, 1956
2,768,112	Buckwalter	Oct. 23, 1956
2,791,609	Kaplan	May 7, 1957
2,792,329	Woodward	May 14, 1957
2,795,528	Buckwalter et al.	June 11, 1957
2,796,381	Borst	June 18, 1957
2,812,283	Geschickter et al.	Nov. 5, 1957
2,951,014	Garman	Aug. 30, 1960
2,961,374	Lieb et al.	Nov. 22, 1960
3,016,330	Jacobson	Jan. 9, 1962
3,049,473	Beatson et al.	Aug. 14, 1962

FOREIGN PATENTS

507,692	Belgium	June 9, 1952

OTHER REFERENCES

Grant: "Hackh's Chemical Dictionary," 3rd Ed., 1944, p. 446.

U.S. Dispensatory, 25th Ed., part I, J. B. Lippincott Co., Phila., 1955, pp. 366–7, Corn Oil; pp. 397–8, Cottonseed Oil; pp. 921–2, Olive Oil; p. 978, Peanut Oil; p. 1232, Sesame Oil.