Patented Dec. 5, 1950 2,533,066

UNITED STATES PATENT OFFICE

2,533,066

MICROPULVERIZED THERAPEUTIC COMPOSITIONS

George V. Taplin and Frederick A. Bryan,
Brighton, N. Y.

No Drawing. Application March 27, 1947,
Serial No. 737,724

4 Claims. (Cl. 167—65)

1

The present invention relates to therapeutic agents and to their administration. More specifically it relates to anti-biotics, such as penicillin and streptomycin and their administration by inhalation.

Penicillin, streptomycin and others of the recently discovered anti-biotics are wonder drugs. It has been found, however, that some patients, to whom these anti-biotics are administered, develop local reactions at the site of administration of the drug. The part may become inflamed and severe sores may develop. For instance, in the administration of penicillin by the aerosol method, that is, by inhalation of a penicillin solution in the form of a spray or vapor, it is known that the incidence of local sensitivity reactions to penicillin is roughly fifteen percent. The throat and mouth become red, swollen, and painful.

This local sensitivity reaction is not limited, however, to the anti-biotics. Other therapeutic agents, such as the sulphonamides, opiates, and iodine-containing radio opaques frequently cause severe local reactions, thus not only hampering the diagnosis and treatment of a disease but producing troubles with which the patient was not previously afflicted. The accepted theory about sensitivity reactions is that they are caused by release of histamine at the reacting organ or site.

Heretofore, when a patient has reacted to a therapeutic agent, such as penicillin or streptomycin, with local sensitivity, either the treatment with the drug has had to be discontinued and some other treatment prescribed, or the patient has had to be treated for the local sore or inflammation developed, and has had to put up with the inconvenience, discomfort, and oftentimes pain of the local sensitivity reaction until that reaction yields to treatment. This frequently takes more time than the illness or disease which in the first place caused the administration of the therapeutic agent.

In our copending application, Serial No. 733,280, filed March 8, 1947, there is disclosed a new method of administering penicillin, streptomycin and other therapeutic agents by inhalation of these agents in micro-pulverized powdered form, the agent being suspended in air. In both this method and in the aerosol method of administration, the therapeutic agent is supplied directly to the lungs. If the lung of the patient should be locally sensitive and react locally from the penicillin or streptomycin treatment, it would be serious and might even be fatal.

The primary object of the present invention is to provide a new method and a novel form, by

2

which penicillin, streptomycin, the sulphonamides, morphine and other opiates, iodine-containing radio opaques and other diagnostic agents, and similar therapeutics may be administered, that will inhibit local sensitivity reactions to these therapeutic agents.

Another form of the invention is to provide a new method and a novel form for administration of therapeutic agents of the character described which will allow the use of these agents to be extended.

Other objects of the invention will be apparent hereinafter from the specification and from the recital of the appended claims.

The present invention is predicated upon incorporation of a small amount of an anti-histamine substance, such as "Benadryl" or "Pyribenzamine," with penicillin, streptomycin, or other therapeutic agent, which might cause a local sensitivity reaction, and administering to the patient the mixture of anti-histamine substance and therapeutic agent. We have found that when this mixture is used there is a very low incidence of local sensitivity reaction to the therapeutic agent. The anti-histamine substance not only reduces the incidence of reactions to the therapeutic but permits extension of the use of the primary agent, for it allows the therapeutic to do its work without being hindered by any other reaction in the body of the patient. The anti-histamine substance acts as a prophylactic.

We prefer to administer the new mixture by incorporating the "Benadryl" or "Pyribenzamine" in a micronized therapeutic-glucose mixture such as disclosed in application Serial No. 733,280 above mentioned and causing the micro-pulverized new mixture to be suspended in air and inhaled in the manner disclosed in said application. The "Benadryl" or "Pyribenzamine" can be mixed, for instance, with penicillin and anhydrous glucose or other water-soluble sugar in the proportion of about one-part of "Benadryl" or "Pyribenzamine" to one hundred parts of the mixture of penicillin and glucose, and the whole is then ground to a powder whose particulate size is one micron or less For inhaling the mixture, the apparatus shown in application No. 733,280 may be employed. The penicillin and glucose may have the proportion of 1:5 to 1:20 as described in said application.

The invention is not restricted, however, to administration by suspension of a micro-pulverized agent in air. It is applicable also where the therapeutic agent is to be administered by the aerosol method. Thus a 2% solution of "Pyri-

benzamine" may be mixed with a penicillin solution and the mixture inhaled in the form of a spray or vapor. The invention may also be used where the penicillin, streptomycin, opiate, or other therapeutic is administered by other methods, as for instance by the hypodermic needle. Incorporation of an anti-histamine substance with the therapeutic agent will inhibit the production of the sores or painful lumps that so often occur at the point where the needle enters the body, when a therapeutic agent is administered hypodermically.

It will be obvious, too, that while the invention has been described in connection with particular embodiments and particular uses thereof, it is capable of various further modifications and uses, and that this application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure as come within known or customary practice in the art to which the invention pertains and as may be applied to the essential features hereinbefore set forth and as fall within the scope of the invention or the limits of the appended claims.

Having thus described our invention, what we claim is:

1. A therapeutic agent for direct administration to humans by inhalation comprising a dry, micropulverized, powdered mixture of an antihistaminic chemical blocker and a soluble antibiotic substance from the group consisting of penicillin and streptomycin, said mixture having a particulate size in the order of one micron.

2. A therapeutic agent for direct administration to humans by inhalation comprising a dry, micropulverized, powdered mixture of an antihistaminic chemical blocker and penicillin, said mixture having a particulate size in the order of one micron.

3. A therapeutic agent for direct administration to humans by inhalation comprising a dry, micropulverized, powdered mixture of an antihistaminic chemical blocker and streptomycin, said mixture having a particulate size in the order of one micron.

4. A therapeutic agent for direct administration to humans by inhalation comprising a dry, micropulverized, powdered mixture of an antihistaminic chemical blocker and a soluble antibiotic crystalline substance from the group consisting of penicillin and streptomycin, said mixture having a particulate size not exceeding one micron.

GEORGE V. TAPLIN.
FREDERICK A. BRYAN.

REFERENCES CITED

The following references are of record in the file of this patent:

UNITED STATES PATENTS

Number	Name	Date
2,421,714	Rieveschl	June 3, 1947

OTHER REFERENCES

Article by Harris et al. in Amer. J. Medical Sciences, vol. 205, pages 1 to 6.

Science, Nov. 29, 1946, pages 498 and 499.

Proc. Staff Meetings Mayo Clinic, Nov. 14, 1945, pages 417 to 429.

The Pharmaceutical Journal (London), Feb. 8, 1941, page 40.

J. A. M. A., Dec. 14, 1946, pages 915 to 919.

J. A. M. A., July 21, 1945, page 910.

J. A. Pharm. Assoc., Scientific Edition, Nov. 1946, pages 326 and 7.

California Medicine, Apr. 1947, pages 242 to 248.