STABLE AQUEOUS PROCAINE PENICILLIN SUSPENSION

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The present invention relates to a stable aqueous suspension of procaine penicillin G and is more particularly concerned with a stable, aqueous suspension of procaine penicillin G which contains an excess of procaine ions, and to a method for the preparation thereof.

This application is a continuation-in-part of my prior, co-pending applications of Serial Numbers 130,592, 130,593, 130,595 and 130,596, all of which were filed December 1, 1949 and all of which are now abandoned.

The instability of penicillin compounds, including inorganic and organic salts, is well known in the pharmaceutical art. For this reason, aqueous suspensions of such salts, and, in particular, stable aqueous suspensions of procaine penicillin G have not been known, and have previously been considered an impossibility. As a consequence, the medical profession has been limited to the employment of procaine penicillin G as salt suspensions, and aluminum monostearate-procaine penicillin G suspensions, and such are not indicated for the particular case, have been faced with the necessity of preparing their own aqueous suspensions of procaine penicillin G by mixing sterile water or saline solution with dry preparations available from the pharmaceutical trade. This has, of course, been a great inconvenience to the medical profession, and, even when prepared in the office of the practising physician, such aqueous suspensions are of utility only for periods not exceeding ten days, according to recent Pure Food and Drug regulations. Although some aqueous suspensions of procaine penicillin G have been proposed previously, these have all had the expected disadvantage of an inferior shelf life. It is obvious that a stable suspensions of procaine penicillin G retaining its original therapeutic activity, and therefore having utility over prolonged periods, is highly desirable from a commercial standpoint, and much needed by the medical profession.

It is also well-known in the art that penicillin salts are unfortunately retained by the human body, after administration, for undesirably limited periods, necessitating repeated injections of the drug at intervals varying from several hours to one day, depending upon the blood levels of the drug desired to be maintained. This physiological phenomenon, the rapid absorption and excretion of penicillin drugs by the human body, is, of course, a limiting factor upon the effectiveness of any pharmaceutical preparation employed, and it has been a constant objective of researchers in the field to find a suitable penicillin composition, and in particular, an aqueous penicillin G composition which, upon human administration, would be productive of advantageous results, in one of two ways:

(1) Production of longer effective blood level, that is, retention of a therapeutically effective quantity of the drug in the blood stream over an extended period of time, say, forty-eight hours instead of twenty-four hours, which is the present maximum duration. This would allow administration of effective procaine penicillin G dosages only once every other day, instead of the requisite single day interval which is now customary.

(2) Production of a higher effective blood level of the drug at the end of any given period after administration, that is, retention of a higher percentage of the originally-administered activity. This, too, would be an important advance in the art, inasmuch as the therapeutic effectiveness of procaine penicillin G, within certain limits, appears to be directly proportional to the quantity which is present in the blood stream. Another theory, which has been advanced by way of explaining the significance of the quantity of procaine penicillin G in the blood, places the rate at which the quantity of drug in the blood stream diminishes, in an inverse proportion to the curative power of the composition.

It is obvious that attainment of either advantage would be of considerable importance, especially from the standpoint of the patient undergoing such treatment, and the medical profession administering the same.

It is an object of the present invention to provide a stable aqueous suspension of procaine penicillin G. It is a further object to provide such a stable, aqueous suspension of procaine penicillin G which contains an excess of procaine ions. It is a further object to provide such a stable, aqueous suspension of procaine penicillin G which contains an excess of procaine ions, a buffer, and a suspending agent. A further object of the invention is the provision of a sterile aqueous suspension of procaine penicillin G which, upon human administration, produces longer effective blood levels than previously known compositions; and is therefore of increased efficacy and importance. Other objects of the invention will become apparent hereinafter.

The objects of the present invention have been accomplished and a stable, aqueous suspension of procaine penicillin G which is productive of longer effective blood levels upon administration than known aqueous compositions, has been obtained, by providing an aqueous suspension containing procaine penicillin G, a suspending agent, an excess of procaine ions, and water.

The range for the procaine, which may be in the form of the free base, the, tetrathionate, the tetrahydrochloride, or another water-soluble, ionized, injectable procaine salt, is between about 0.5 and 5.0 percent by weight of the total composition, and preferably about 2.0 percent is employed.

If desired, a buffering agent may be added, such as 0.25 to 5.0 percent by weight, and preferably 0.5 percent, of sodium citrate or 1.0 to 7.5 percent sodium phosphates and preferably 2.6 percent sodium dihydrogen phosphate and 2.4 percent disodium hydrogen phosphate to make a total of five percent by weight of the total composition. When appropriate, as in the presence of excess added procaine free base, the suspension may be buffered by the addition of free acids, e.g. citric acid, phosphoric acid. The use of the buffering agent is not essential, however, to either the stability or the therapeutic effectiveness of the compositions of the present invention.

If desired, suspending or dispersing agents may be added to increase pharmaceutical elegance. As a suspending or dispersing agent, sodium carboxymethyl cellulose has been found highly satisfactory but carboxymethylcellulose, methylcellulose, polyvinyl alcohol, polyvinylpyrrolidone, gum tragacanth, gelatin, pectin, sodium alginate, dextran, gum Karaya, and the like, are also useful. The amount of suspending agent will vary to a certain extent, but usually from about 0.2 to 5.0 percent, preferably from 0.5 to 2.5 percent, is employed and variations within these ranges may be made by any experienced chemist or pharmacist with regard to the intended use of the composition. Thus the concentration of polyvinylpyrrolidone may vary from 0.1% to 2.5%,
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with about 10% preferred. The concentration of dextran may vary from 0.1% to 20%, with about 10% preferred. The concentration of pectin may vary from 0.1% to 0.5%, with about 0.2% preferred. The concentration of gum tragacanth may vary from 0.5% to 2%, with about 1% preferred; 5% sodium chloride may be added thereto.

It is to be understood that the words “suspending agent” and “dispersing agent” are used interchangeably to describe the additives such as sodium carboxymethylcellulose, lecithin, Spans and Tweens which improve the pharmaceutical elegance of these preparations, as by increasing ease of injection and ease of resuspension upon settling. Other suspending and dispersing agents include lecithin, Falba, cholesterol, Span 20, Span 40, Span 60, Span 80, the Tweens, Anechroms, sodium alginate, potassium alginate, ammonium alginate, calcium alginate, alginic acid, propylene glycol alginate, polyoxyxylene derivatives of sorbitol fatty acid esters, urea and sodium p-aminobenzoate.

The procaine penicillin G suspension may have a potency of anywhere from 10,000 to about 500,000 units per milliliter, preferably from about 100,000 to 400,000 units per milliliter. Ordinarily, a suspension of procaine penicillin G having a potency of about 300,000 units per milliliter is optimum, and found to be entirely satisfactory.

The potency of the procaine penicillin G is not to be construed as a limiting factor, and the various activities are merely mentioned to indicate that procaine penicillin G of various activities is suitable for incorporation into the composition of the present invention, again with regard for the intended application of the aqueous suspension.

The composition is not limited to the exact ingredients previously described and to the exclusion of all others, since various other ingredients, while not necessary, may be added, if desired. For instance, a small amount of preservative, such as Phenol U. S. P., Cresol U. S. P., Methyl Paraben (methyl ester of p-hydroxybenzoic acid), Ethyl Paraben (ethyl ester of p-hydroxybenzoic acid), Butyl Paraben (butyl ester of p-hydroxybenzoic acid) or Propyl Paraben (propyl ester of p-hydroxybenzoic acid) may be employed. A small quantity of a vasoconstrictor may also be considered as advantageous addition, and, whatever additional ingredients are employed, the total amount should ordinarily not exceed more than about ten percent by weight, and preferably not more than five percent by weight, of the total composition. Other ingredients which improve blood levels, handling properties and stability may be added. Examples of such ingredients are lecithin, Falba, cholesterol, Span 20, Span 40, Span 60, Span 80, Tween 20, Tween 40, Tween 60, Tween 80, Tween 85, Anechroms, urea, and sodium para-aminobenzoate.

The method of the present invention comprises dissolving the prescribed amount of procaine compound (from 0.5 to 5.0 percent, preferably about 2.0 percent of the total weight) and, if desired, a buffer (e.g. sodium citrate, from about 0.25 to 5.0 percent, preferably about 0.5 percent of the total weight) in sterile distilled water or physiological saline, adding suspending agent (0.2 to 5.0 percent, preferably 0.5 to 2.5 percent, of the total weight) thereto with stirring, and then mixing in the procaine penicillin G crystals. The volume is then adjusted by addition of the requisite amount of water to bring the concentration of ingredients within the required range. The pH of the final suspension is adjusted to 5.5 to 7.5 by adding citric acid or phosphoric acid. The admixture is, of course, conducted under sterile conditions, and all solids introduced are in a finely-divided or powdered form, preferably below about eighty microns in diameter and usually below about fifty microns in diameter, e.g. micronized.

The following examples are given for purposes of illustration only, and are not to be construed as limiting.

Example I

Under sterile conditions, 5.0 parts of procaine hydrochloride and 2.5 parts of sodium citrate are dissolved in sterile distilled water in a glass flask, and about 2.0 parts of sodium carboxymethylcellulose added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaken continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles, and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increasing effectiveness over known aqueous suspensions of procaine penicillin G.

Example II

Under sterile conditions, 0.5 part of procaine hydrochloride and 5.0 parts of sodium citrate are dissolved in sterile distilled water. About 2.5 parts of sodium carboxymethylcellulose is added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaken continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example III

Under sterile conditions, 2.0 parts of procaine hydrochloride and 0.5 parts of sodium citrate are dissolved in sterile distilled water in a glass flask, about 0.5 parts of sodium carboxymethylcellulose added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaken continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example IV

5.0 grams of anhydrous sodium citrate, 1 gram of procaine hydrochloride and 0.5 gram of sodium carboxymethylcellulose were added to 50 cc of water and stirred with a laboratory agitator until solution was complete. 25 cc of this solution were added to a 100 cc beaker and 16.5 grams of procaine penicillin G (potency about 1000 units/milligram—screened through a 200 mesh screen) added. The volume was adjusted to 50 cc with the citrate-CMC-procaine hydrochloride-water gel and the suspension thoroughly mixed. The pH of the suspension was adjusted to 6.5 with citric acid and the suspension thoroughly mixed. The suspension contains approximately 300,000 units of procaine penicillin G per cc, is stable for periods in excess of one year and gives blood levels of increasing effectiveness over known aqueous suspensions of procaine penicillin G.

Example V

0.25 gram of anhydrous sodium citrate, 1 gram of procaine hydrochloride and 0.25 gram of sodium carboxymethylcellulose were added to 50 cc of water and stirred with a laboratory stirrer until solution was complete. Twenty-five cc of this solution were added to a 100 cc beaker and 16.5 grams of procaine penicillin G (potency about 1000 units/milligram—screened through a 200 mesh screen) added. The volume was adjusted to 50 cc with the citrate-sodium carboxymethylcellulose-procaine hydrochloride-water gel and the suspension thoroughly mixed. The pH of the suspension was adjusted
Example VI

The following ingredients were added to a 15 cc. vial:

- 4.0 grams procaine penicillin G (potency about 1000 units per milligram—screened through a 250 mesh screen)
- 0.04 gram sodium carboxymethylcellulose
- 0.2 gram sodium citrate anhydrous
- 1.0 gram procaine carbonate
- 9.0 cc. distilled water

The vials were thoroughly shaken to give a homogenous suspension. Several of these were made. The suspension contains approximately 300,000 units of procaine penicillin G per cc., stable for periods in excess of one year and gives blood levels of increasing effectiveness over known aqueous suspensions of procaine penicillin G.

Example VII

Under sterile conditions, 2.0 parts of procaine hydrochloride is dissolved in sterile distilled water, and about 2.0 parts of sodium carboxymethylcellulose added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaken continued for a few minutes. Water is then added to make 100 parts, whereafter the suspension is bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of one year at temperatures below 30° C. and, upon administration, gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example VIII

Under sterile conditions, 5.0 parts of procaine hydrochloride is dissolved in sterile distilled water in a glass flask. About 2.5 parts of sodium carboxymethylcellulose are added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaken continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G upon administration.

Example IX

Under sterile conditions, 0.5 part of procaine hydrochloride is dissolved in sterile distilled water and about 0.5 part of sodium carboxymethylcellulose added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaken continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example X

One gram of procaine hydrochloride and 0.375 gram of sodium carboxymethylcellulose were dissolved in 50 cc. of distilled water using a laboratory stirrer. About 25 cc. of this gel were placed in a 100 cc. beaker and 16.5 grams of procaine penicillin G (potency about 1000 units per mg.—screened through a 250 mesh screen) added and mixed in with a laboratory stirrer. The volume was adjusted to 50 cc. with the aqueous carboxymethylcellulose procaine hydrochloride gel and the suspension thoroughly mixed with a laboratory stirrer. This suspension is vised and tested. The suspension contains approximately 300,000 units of procaine penicillin G per cc., is stable for periods in excess of one year at room temperature (73° F.) and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example XI

Under sterile conditions, 2.0 parts of procaine phosphate is dissolved in sterile distilled water, and about 2.0 parts of sodium carboxymethylcellulose added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaken continued for a few minutes. Water is then added to make 100 parts; whereafter the suspension is bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of one year at temperatures below 30° C., and, upon administration, gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example XII

0.375 gram of sodium carboxymethylcellulose was dissolved in 50 cc. of distilled water using a laboratory stirrer. To this solution was added one gram of procaine base—with which was suspended with a laboratory stirrer. About 25 cc. of this suspension were placed in a 100 cc. beaker and to it were added 16.5 grams of procaine penicillin G (potency about 1000 units per mg.). The procaine base-CMC suspension was added to make 50 cc. Phosphoric acid was added until the pH of the suspension was 6.5. The suspension was thoroughly mixed with a laboratory stirrer. The suspension contains approximately 300,000 units of procaine penicillin G per cc., is stable for periods in excess of one year at room temperature (about 73° F.) and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example XIII

Under sterile conditions, 2.0 parts of procaine hydrochloride, 0.5 part of sodium citrate, and 5.0 parts of disodium phosphate are dissolved in about 50 cc. of sterile distilled water, and about 2.0 parts of sodium carboxymethylcellulose added thereto with shaking, whereafter 30 parts of procaine penicillin G, having an activity of about 1,000,000 units per part, is added and shaking continued for a few minutes. Water is then added to make 100 parts. The pH of the suspension is adjusted to pH 6.5 with phosphoric acid, whereafter the suspension is bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per cc., is stable for periods in excess of one year and, upon administration, gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

Example XIV

Under sterile conditions, 5.0 parts of procaine hydrochloride, 5.0 parts of sodium citrate, and 0.25 part of disodium phosphate are dissolved in about 50 cc. of sterile distilled water in a glass flask. About 2.5 parts of sodium carboxymethylcellulose is added thereto with shaking, whereafter 30 parts of procaine penicillin G, having an activity of about 1,000,000 units per part, is added and shaking continued for a few minutes. Water is then added to make 100 parts. The pH of the suspension is adjusted to pH 6.5 with phosphoric acid, whereafter the
suspension is bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of one year, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G upon administration.

**Example XV**

Under sterile conditions, 0.5 part of procaine hydrochloride, 0.25 part of sodium citrate, and 7.5 parts of sodium phosphate, are dissolved in about 50 cc. of sterile distilled water and about 1.5 parts of sodium carboxymethylcellulose added thereto with shaking, whereafter 30 parts of procaine penicillin G, having an activity of about 1,000,000 units per part, is added and shaking continued for a few minutes. Water is then added to make 100 parts, the pH of the suspension is adjusted to pH 6.5 with phosphoric acid, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of one year and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XVI**

Under sterile conditions, 0.5 part of procaine hydrochloride and 7.5 parts of disodium phosphate are dissolved in sterile distilled water in a glass flask, and about 2.0 parts of sodium carboxymethylcellulose added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaking continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XVII**

Under sterile conditions, 5.0 parts of procaine hydrochloride and 0.25 part of disodium phosphate are dissolved in sterile distilled water. About 2.5 parts of sodium carboxymethylcellulose is added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaking continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XVIII**

Under sterile conditions, 2.0 parts of procaine hydrochloride and 5.0 parts of disodium phosphate are dissolved in sterile distilled water in a glass flask, about 1.5 part of sodium carboxymethylcellulose added thereto with shaking, whereafter five parts of procaine penicillin G, having an activity slightly in excess of 6,000,000 units per part, is added and shaking continued for a few minutes. Water is then added to make 100 parts, the suspension bottled in sterile bottles and stored. The suspension contains approximately 300,000 units of procaine penicillin G per milliliter, is stable for periods in excess of six months, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XIX**

The following ingredients were added to a 15 cc. vial:
- 4.0 grams procaine penicillin G (potency about 1000 units per mg)—screened through a 200 mesh screen
- 0.04 gram sodium carboxymethylcellulose

8.5 cc. of an aqueous solution containing 5% Na₂HPO₄ and 2% procaine hydrochloride.

The vials were shaken thoroughly to give a homogenous suspension. Several vials were made. The suspension contains approximately 300,000 units of procaine penicillin G per cc., is stable for periods in excess of one year and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XX**

The following ingredients were added to a 15 cc. vial:
- 4.0 grams procaine penicillin G (potency about 1000 units per mg)—screened through a 200 mesh screen
- 0.04 gram sodium carboxymethylcellulose
- 0.6 gram Na₂HPO₄ anhydrous
- 0.6 gram procaine carbonate
- 9.0 cc. distilled water

The vials were shaken thoroughly to give a homogenous suspension. Several vials were made. The suspension contains approximately 300,000 units of procaine penicillin G per cc., is stable for periods in excess of one year, and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XXI**

The following ingredients were added to a 15 cc. vial:
- 4.0 grams procaine penicillin G (potency about 1000 units per mg)—screened through a 200 mesh screen
- 0.13 gram procaine base
- 0.04 gram sodium carboxymethylcellulose
- 0.6 gram Na₂HPO₄
- 9.0 cc. distilled water

The vials were shaken thoroughly to give a homogenous suspension. Several vials were made. The suspension contains approximately 300,000 units of procaine penicillin G per cc., is stable for periods in excess of one year and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XXII**

The following ingredients were added to a 15 cc. vial:
- 4.0 grams procaine penicillin G (potency about 1000 units per mg)—screened through a 200 mesh screen
- 0.25 gram procaine phosphate
- 0.6 gram Na₂HPO₄ anhydrous
- 0.04 gram sodium carboxymethylcellulose (CMC)
- 9.0 cc. water

The vials were shaken thoroughly to give a homogenous suspension. Several vials were made. The suspension contains approximately 300,000 units of procaine penicillin G per cc., is stable for periods in excess of one year and gives blood levels of increased effectiveness over known aqueous suspensions of procaine penicillin G.

**Example XXIII**

Using sterile technique the following solution was made: In a 1 liter beaker was placed 400 cc. of distilled water, 25 grams of Na₂HPO₄ anhydrous, 2.5 grams phenol U. S. P. and 5.0 grams of sodium carboxymethylcellulose. This was mixed with a laboratory stirrer until solution was complete. Then 10 grams of procaine base were added and sufficient distilled water to bring the volume to 500 cc. The pH of this suspension was then adjusted to 6.5 with 12 cc. of 42.5% H₂PO₄. This suspension was thoroughly mixed and the autoclaved for 30 minutes at 15 lbs. pressure. About 100 cc. of the above suspension were placed in 0.5 cc. beaker and to it were added 66 grams of procaine penicillin G (potency about 1000 units per mg)—screened through a 200 mesh screen and the volume adjusted to 200 cc. with the above suspension. The finished suspension was thoroughly mixed and passed through the Eppenbach colloid mill. The suspension
contains approximately 300,000 units of procaine-penicillin G per cc., is stable for periods in excess of one year and gives blood levels of increasing effectiveness over known aqueous suspensions of procaine-penicillin G.

Example XXIV

The following are mixed in filtered, pyrogen-free distilled water (97.88 cc.): Lecithin (0.70 g.), Tween 40 (0.93 g.), Span 40 (0.33 g.), sodium citrate U. S. P. (0.57 g.), and Butyl Paraben (0.021 g.). There is thoroughly mixed into 69.40 cc. of this mixture under sterile conditions procaine hydrochloride U. S. P. (2.0 g.), micronized lecithin-coated procaine penicillin G (24.15 g.) and pulverized, 250 mesh, lecithin-coated procaine penicillin G (8.05 g.). The product contains approximately 300,000 units of procaine penicillin G per cc. and is stable for periods in excess of one year. The product is more stable and gives higher blood levels than previously known aqueous suspensions of procaine penicillin G which do not contain the added, excess procaine ion.

While the present invention has been described with particular reference to procaine penicillin G, it is to be understood that the procaine salts of other penicillins are also included within the scope of this invention. For instance, the penicillins G, F, X, O, dihydro F and K, and mixtures of two or more such penicillins, particularly mixtures containing at least 85% penicillin G, are included within the scope of this invention.

It is to be understood that the invention is not to be limited to the exact details of operation or exact compositions shown and described, as obvious modifications and equivalents will be apparent to one skilled in the art, and the invention is therefore to be limited only by the scope of the appended claims. For example, any injectable compound of procaine capable of yielding procaine ions, such as procaine hydrochloride, procaine base or procaine phosphate, may be employed.

I claim:

1. A sterile, aqueous suspension of procaine penicillin which is stable over long periods of time at room temperature and which is productive of highly effective blood levels upon administration, including procaine penicillin, a suspending agent, and a member selected from the group consisting of procaine base and water-soluble, ionized, injectable salts of procaine other than procaine penicillin.

2. A sterile, aqueous suspension of procaine penicillin which is stable over long periods of time at room temperature and which is productive of highly effective blood levels upon administration, including procaine penicillin, a suspending agent, and from 0.5 to 5.0 percent of a member selected from the group consisting of procaine base and water-soluble, ionized, injectable salts of procaine other than procaine penicillin.

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