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SELF-SPRAYING ANESTHETIC PREPARATION

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5 Claims. (Cl. 167—52)

The present invention relates to anesthetics and it particularly relates to local spray anesthetics.

In my prior application Serial No. 154,189, filed July 17, 1937, I have disclosed certain aromatic amino compounds which in solution in a relatively large proportion of ethyl chloride and a relatively small proportion of benzyl alcohol to form non-precipitating, non-narcotic, non-alkaloidal, self-spraying liquid synthetic local anesthetics which are capable of being sprayed through a fine capillary orifice of a spray nozzle without deposition of anesthetic and without clogging.

It is among the objects of the present invention to provide improved self-spraying local anesthetics of the character above described which will be capable of promptly inducing effective and profound local anesthesia of prolonged effect, when sprayed, and which will have high penetrating powers so as thoroughly to anesthesize the area to which it is applied.

Still further objects and advantages will appear from the more detailed description set forth below, is being understood, however, that this more detailed description is given by way of illustration, since various changes therein may be made by those skilled in the art without departing from the scope and spirit of the invention.

It has been found that the above objects may be most readily accomplished by dissolving or combining relatively small quantities of certain aminobenzoyl, aminoalkyl hydrochloride compounds in or with a greater proportion of a high boiling solvent, the preferred solvent being hydroxy-aromatic compounds, especially benzyl alcohol.

This combination then of a minor proportion of the active anesthetic principle or compound and a major portion of the hydroxy-aromatic compound is then dissolved in or combined with a relatively volatile solvent, the preferred solvents being readily vaporizable alkyl halide esters, especially methyl or ethyl chloride.

I have now found that certain aminobenzoyl aminoalkyl hydrochloride compounds are particularly effective in solution with ethyl chloride and benzyl alcohol and may be compounded and used under widely varying climatic conditions without difficulty.

Among the preferred anesthetic materials or compounds which may be utilized, either by themselves or in combination with each other or in combination with other anesthetics, are the following:

Amylcaine

$NH_2.C_6H_4.CO.OCH_2.CH_2.NH(HCl).C_5H_{11}$

Monocaine

$NH_2.C_6H_4.CO.OCH_2.CH_2.NH(HCl).CH_2.CH(CH_3)_2$

These anesthetics have the general formula

$$NH_2.C_6H_4.CO.O(CH_2)_n.NH(HCl).R$$

where n preferably 2 and R is preferably a saturated alkyl group containing 5 carbon atoms.

Less preferably other compounds of the following general formula may be used

$$NR_2R_3.C_6H_4.CO.O(CR_4R_5)_n.NR_6(HCl).R_1$$

n preferably 2 may vary from 1 to 5 and R_1, R_2, R_3, R_4, R_5 and R_6 may be hydrogen or a saturated alkyl or unsaturated alkyl group having from 1 to 8 carbon atoms or more desirably from 4 to 6 carbon atoms. Less desirably the aryl group—C_6H_4—may be replaced by other aryl groups, such as pyridyl, naphthyl, quinolyl, furfuryl and piperidyl.

Although the hydrochlorides, the borates sulphates and other salts may be employed, but the bases are most satisfactory.

These active anesthetic compounds just mentioned then will dissolve preferably at least in equal proportion and preferably in twice or three times the proportions of benzyl alcohol. It has been determined that ethyl alcohol and other alcohols of similar low boiling point are not satisfactory and cannot be utilized for a spray anesthetic of the character described.

Benzyl alcohol cannot be readily substituted by thymol, eugenol, camphor or eucalyptol and like compounds.

Although many different proportions and compounds of ingredients may be utilized, the following have been found to be typical formulae which are most suitable and may be widely employed:

Formula 1

	Percent
Amylcaine	5
Benzyl alcohol	10
Ethyl chloride	85

(All parts are by weight.)

Other local anesthetics may also be combined with the amylcaine or monocaine, in amounts varying from 1 to 5 parts of the amylcaine or monocaine to 5 to 1 parts of the other anesthetics, such other anesthetics being for example alypin, aposthesine, butyn, diothane, larocaine, metycaine, nupercaine-ciba, orthoform, phenacaine, procaine, tutocain, benzocaine, and butesin and their borates, hydrochlorides and other salts.

Formula 2

	Per cent
Monocaine	2.5
Amylcaine	2.5
Benzyl alcohol	10
Ethyl chloride	85

(All parts are by weight.)

In preparing the liquid spray anesthetic of Formula 1, 5 grams of amylcaine are dissolved in 10 grams of benzyl alcohol and this solution added to 85 grams of U. S. P. ethyl chloride and the mixture stirred or rapidly agitated and immediately measured and filled into dispensing containers. Though amylcaine is somewhat soluble in ethyl chloride, it is preferable to dissolve it first in the benzyl alcohol, which increases the solubility of the principal active ingredients and at the same time prevents clogging of the spray nozzle.

The anesthetic mixture so produced may be widely used as a liquid spray anesthetic for topical and infiltration anesthesia and it will produce prompt, diffusible and profound anesthesia upon various mucous surfaces.

When sprayed, it will produce anesthesia by rapid evaporation and diffusion of the solvent with the increase of pressure in the areas of application, causing penetration of the active anesthetic agent.

The anesthetic prepared according to the above procedures is uniform, is clear in solution and does not decompose or become turbid.

The carrier or stabilizer greatly increases the solubility of the active anesthetic ingredient and will act as a preventative for clogging of the spray nozzle.

The characteristic feature of the present invention resides in the provision of ethyl chloride as a carrier for an anesthetic, which ethyl chloride will produce a spray and also sufficient pressure at the point of application to assure penetration of the anesthetic. The ethyl chloride is not primarily used as an anesthetic in itself but solely as a carrier or solvent for the active anesthetic agent. Obviously other similar readily vaporizable organic solvents or carriers, such as ethyl chloride, may be employed.

In respect to the benzyl alcohol, this ingredient is less volatile or vaporizable than the active anesthetic agent and it prevents crystallization or deposition of the active anesthetic agent, particularly when the active anesthetic agent is forced through a thin capillary passage in the form of a spray by the pressure created by the ethyl chloride vapors inside of an ethyl chloride tube. These ethyl chloride tubes usually consist of sealed, elongated, glass vessels containing the ethyl chloride, which vessels at one end are provided with thin capillary orifices through which orifices the ethyl chloride will be ejected in the form of a spray by the vapor pressure of the ethyl chloride within the vessel.

Many other changes could be effected in the particular features of process treatment disclosed, and in specific details thereof, without substantially departing from the invention intended to be defined in the claims, the specific description herein merely serving to illustrate certain elements by which, in one embodiment, the spirit of the invention may be effectuated.

I claim:

1. A non-precipitating, self-spraying liquid, synthetic local anesthetic preparation, capable of being sprayed through a fine capillary orifice of a spray nozzle without deposition of anesthetic and without clogging, said preparation comprising a synthetic local anesthetic, dissolved in a mixture of a relatively small amount of benzyl alcohol and a relatively large amount of ethyl chloride, said local anesthetic being an organic compound having the formula

$$NH_2.C_6H_4.CO.O(CH_2)_2.NH(HCl).R$$

where R is a saturated low molecular weight alkyl group selected from the group consisting of butyl and amyl.

2. A non-precipitating, self-spraying liquid, synthetic local anesthetic preparation, capable of being sprayed through a fine capillary orifice of a spray nozzle without deposition of anesthetic and without clogging, said preparation comprising a synthetic local anesthetic, dissolved in a mixture of a relatively small amount of benzyl alcohol and a relatively large amount of ethyl chloride, said local anesthetic being an organic compound having the formula

$$NH_2.C_6H_4.CO.OCH_2.CH_2.NH(HCl).C_5H_{11}$$

3. A non-precipitating, self-spraying liquid, synthetic local anesthetic preparation, capable of being sprayed through a fine capillary orifice of a spray nozzle without deposition of anesthetic and without clogging, said preparation comprising a synthetic local anesthetic, dissolved in a mixture of a relatively small amount of benzyl alcohol and a relatively large amount of ethyl chloride, said local anesthetic being an organic compound having the formula

$$NH_2.C_6H_4.CO.OCH_2.CH_2.NH(HCl).CH_2.CH(CH_3)_2$$

4. A self spraying local anesthetic preparation comprising about 5% of monocaine, about 10% of benzyl alcohol, and about 85% of ethyl chloride

5. A self spraying local anesthetic preparation comprising about 5% of amylcaine, about 10% of benzyl alcohol, and about 85% of ethyl chloride.

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