

ALIEN PROPERTY CUSTODIAN

PROCESS FOR THE PREPARATION OF DURABLE AQUEOUS SOLUTIONS PARTICULARLY OF PHARMACEUTICAL NATURE

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It is known that many substances in aqueous solution are highly subject to oxidations; so, for instance, solutions of sodium salicylate are soon reddish coloured, and, when in presence of bicarbonate of sodium, even in some days violet.

Solutions of ascorbic acid, adrenaline, apomorphine, and many other substances are also readily oxidated in aqueous medium; under these circumstances solutions of adrenaline become red coloured, solutions of apomorphine become green coloured. Mixtures of adrenaline and p-aminobenzoyldiethylamino-ethanol become, when stored, yellow. All the oxidations mentioned take already place at common temperature; by heating these oxidations are considerably accelerated.

As further examples of these phenomena of oxidation, which are particularly extremely detrimental for the pharmacy, may be mentioned the following.

Solutions of ferrocchloride are, when stored, soon oxidated under forming of basic ferrisalts, which are not only undesired for their etching properties, but also worthless as therapeuticum by secondary anaemia and chlorosis. Also many alkaloides in dissolved state endure similar oxidations (quinine, morphine, emetine). Known is, for instance, the green colouring of a mixture of quinine-hydrochloride and ethylurethane after having been stored for some time.

In literature several means have been indicated to avoid such undesired oxidations. Partly these means are not inconceivable, seen from a medical point of view, such as, for instance, the addition of small quantities of sulphurous acid or potassium metabisulphite, partly they have appeared to be insufficient. The best means known up till now is the addition of small quantities of ascorbic acid. The objection thereof, however, is that the same itself is readily oxidated and loses its protecting working. It is true that it is possible to take measures to avoid this, such as the choice of the right pH and the use of double distilled water; a solution of the above mentioned objections satisfactory in all respects, however, has up till now not been obtained yet.

It has been found now that durable aqueous solutions of more or less oxidable substances can be prepared by taking care for the presence of hydrocyanic acid, resp. of a substance splitting off hydrocyanic acid, or of a mixture of such substances. For this purpose cherry-laurel-water, which is often used in medicine and which can split off 0.1% of HCN, is very suitable. The quantity of these substances required for the protection again oxidations, is so small, that the substances in themselves have not an pharmaco-

logical effect and in consequence thereof no objections can be raised against the addition of these substances. With good result also water of bitter almonds may be used.

Further it has appeared, that in many cases it is possible to increase the effect of the protecting working of ascorbic acid by addition of small quantities of a liquid containing HCN.

A further advantage of the present invention is, that the pH of the solutions can be increased and in this way for instance neutral durable solutions can be prepared as injection liquids. It appears that the protecting effect does not only consist in vitro, but also in vivo, so that in this way it is possible to bring substances, such as hormones, ferments, etc. into the organism in enterale way, which substances, would they be applied in this way, would be decomposed before they would have reached their place of action.

At hand of some examples the invention may be further explained.

Example I

1 cm³ Aqua Laurocerasi Ph. Neerl. V. cherry-laurel-water is added to a solution containing 50 g. quininehydrochloride and 25 g. ethylurethane pro 100 cm³. The liquid is brought into ampullae and after that sterilized in the usual way. While it appears, that without addition of cherry-laurel-water, such a liquid, brought into ampullae, has a green colour, after having been stored for a month, which colour is gradually darkening, the injection liquid, obtained according to the invention, was even after one year still entirely colourless.

Example II

A solution of 20% of potassium salicylate, to which solution 1% of cherry-laurel-water is added, is heated at 100° C. for one hour in a closed vessel. After three months the liquid is still entirely colourless, while a solution, prepared at the same time, but without addition of cherry-laurel-water and also heated at 100° C. for one hour, is clearly red coloured after the said time.

Example III

It is possible to protect solutions of apomorphine against oxidation by addition of 2 mg of ascorbic acid pro cm³, if the usual precautions are taken. However, is one vol % of cherry-laurel-water added, then it is possible to sterilize the solution at 100° C. without obtaining a green coloured solution. It has appeared that the solution prepared in this way, is pharmacologically as much active as a freshly prepared and non-sterilized solution.

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