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PROCESS OF PREPARING PENTONE ACIDS AND THEIR SALTS

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The subject matter of the present invention is a process for the preparation of pentone acids by transforming pentoses, such as arabinose, xylose, ribose and lyxose by means of oxidation into the corresponding I-carbonic acids and the salts of same with the aid of bacteria of the acetobacter, mucor or aspergillus families, and the further processing of the compounds thus prepared, in order to obtain under already known processes wholesome salts of the pentone acids for pharmaceutical purposes.

It is already known to electrochemically prepare the corresponding acids from sugars by way of their oxidation, availing oneself for this purpose of bromide of potassium and carbonate of calcium. The further processing of the substances thus obtained is, however, very difficult in view of the presence of bromide of potassium. It is also already known to transform glucose on bacterial methods by means of acetobacter, aspergillus bacteria or mucoraceae into gluconic acid, the salts of which then can be kept free of harmful admixtures. It is, however, not yet known to work pentoses in this manner. This will most probably be due to the fact that the biological characteristics of pentoses are perfectly different from those of hexoses. Whereas, for instance, hexoses are quickly and thoroughly fermented by baking yeast, such a fermentation does not take place in the case of pentoses.

It has now been found that pentoses upon intense aeration are attacked by hyphomycetes of the aspergillus, mucor and acetobacter types, and in particular by acetobacter suboxydans, in which cases concentrations of 20% are oxidised so as to furnish a 98% yield of the corresponding pentone acids which, after having been neutralised by an addition of metallic carbonates or basic metal salts, can be immediately used as liquids for injection in metal therapeutics.

As sufficient quantities of pentoses are at disposal in the wood saccharification industry, where they are produced as intermediary extracts from the wood of deciduous or coniferous trees, the new process possesses a particular technical importance.

The use of pentone acids in the place of hexone acids for pharmaceutical uses implies particular advantages. Already for a long period of time experiments have been made in order to render the non-readily soluble salts of the polyoxycarbonic acids, e. g. Ca-gluconate, suitable for injections as supersaturated aqueous solutions containing a high percentage of said salts, but not being inclined to crystallise. A great number of compounds has been suggested as stabilisers for this purpose, but an ideal solution of this problem has not been found in this manner.

The present invention is based on the discovery that the salts of the pentone acids are much more readily soluble in water, and that the salts of the earthy alkalines cannot be caused to take on a crystalline form, even at the highest possible rate of concentration. It is furthermore to be taken into consideration that in consequence of the lower molecular weight of the pentone acids the contents of metallic ions are comparatively higher than for instance in the case of the hexone-acid salts. Only small quantities are therefore used for injection, whereby a subcutaneous application, which always is aimed at, is rendered possible without thereby causing pains at the place of injection.

The aqueous salt solutions of the pentone acids prepared by the bacterial method under the process of the present invention, can be immediately used for injections, after they have been purified with active coal in a heated condition, and after a subsequent sterilization.

As a matter of course it is also possible to prepare solutions for purposes of injection, which show an even higher degree of purity. So, for instance, the pentone-acid salts can be isolated in a pure condition, by a precipitation from the thoroughly fermented sugar solutions with organic solvents, e. g. methylic alcohol, and by a reprecipitation, if necessary, whereupon they are dissolved in water at the desired rate of concentration.

Example

750 g. of crystallized xylose are dissolved in 5 litres of water with an admixture of 0.05% of a nutritive salt solution consisting of 33% of $(NH_4)_2SO_4$, 33% of KH_2PO_4, 12% of $Ca(NO_3)_2$, 12% of $MgSO_4$, 0.2% of $FeCl_3$, and the solution thus obtained is aerated in a suitable vessel by fritting. Thereupon a suspension of acetobacter suboxydans in water is admixed, and quantities of $CaCO_3$ added in the course of the testing period in accordance with the reduction of the sugar index figure. After the xylose concentration has been reduced to a lower percentage than 0.1%, the solution is filtered, and at a heated condition boiled for 30 minutes with 5% of active coal ("Norit"), filtered again and by dilution adjusted so as to show 20% of Ca-xylonate (Yield: 98%). This solution can after its sterilisation immediately be used in metal therapeutics for intramuscular, subcutaneous or intravenous injections.

A portion of the liquid which is clear like water, is fed into cold methylic alcohol, filtered in the cold condition, this operation being repeated after the residue has been dissolved in water. The residue which is now very fair, is dissolved in water so as to furnish a 50% Ca-xylonate solution, which continues to be perfectly limpid even after having been kept for a prolonged period of time, just as the residue not having been re-purified.

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