Patented Apr. 25, 1939 2,155,658

UNITED STATES PATENT OFFICE

2,155,658

SURGICAL AND MEDICAL PREPARATIONS

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No Drawing. Application December 29, 1936, Serial No. 118,088. In Germany January 8, 1936

3 Claims. (Cl. 167—58)

This invention relates to surgical and medical preparations and has for its object the production of improved materials for insertion, infusion or injection into the human or animal system for their desirable therapeutic or cosmetic effects, or for use as plastic fillings, joint lubricants and other surgical purposes.

By means of our preparations, for example, medical deposits may be introduced into the tissues as a substitute for the usual method of making frequent injections of dissolved medicines. Similar deposits may be made for the purpose of introducing disinfectants, cosmetics, contrast media and anaesthetics into the body. An important advantage of the invention is that the effect of such deposits, whether for surgical or medical purposes, may be localized in any given region of the body; for example, by the infusion of a suitable deposit in lumbar anaesthesia, a localized effect of the anaesthetic contained in the deposit may be obtained.

Plastic fillings made according to our invention may be used wherever cavities are to be filled in the body. For example, lumbar fillings may be introduced after the resection or pathological destruction of parts of the lungs. Likewise, bone fillings may be inserted, paste-like joint greases introduced and the like. Not only does our invention provide improved materials for these and other surgical and medical purposes, but it furthermore extends the field of application of such materials to a wide variety of purposes not contemplated in the prior art.

Fillings and deposits for some of the purposes mentioned above have been manufactured from paraffine, stearic acids, waxes and the like, but they have met with only indifferent success. One disadvantage of such materials is that they have an irritating effect upon the environment and are treated as foreign bodies. Another disadvantage is that they can be sterilized only by means of additions which have a bactericidal effect, but which thereby aggravate the irritation and are furthermore not resorptive. Moreover, previously known materials of this type are very difficult to apply, and it is impossible accurately to adjust their viscosity, plasticity and other colloidal properties to medical and surgical requirements.

We have discovered certain novel preparations which can be adapted to the above surgical and medical purposes with the greatest accuracy and which, furthermore, are entirely free from the disadvantages of other deposit and filling materials. These novel preparations are polymerized vinyl alcohols of various viscosities, and their esters, acetals and ethers as well as ester-acetals and mixtures of such compounds, in so far as they have an appreciable solubility in water, which requirement is met in certain cases if the preparations are capable of swelling in water. These polymerized vinyl compounds are particularly well suited for the above purpose because they do not exercise any irritating effect upon living tissues but are tolerated in any quantity without any reaction; they can be made absolutely sterile without the addition of bactericidal substances because they can stand heating up to 130–140° C. without injury to their properties; and by means of suitable additions, preferably electrolytes and particularly organic acids such as lactic acid, acetic acid and the like, they can be made reabsorbable to any desired degree. Moreover, they are distinguished by an extraordinary compatibility with the most varied medicaments, for instance alkaloids, cardiacs, gland preparations, etc., anaesthetics, disinfectants, contrast media and cosmetics. Their excellent suitability as vehicles for iodine, iodoform and other iodine preparations is particularly important. In addition, these polymerized vinyl compounds may be treated to form solutions, jellies, pastes or powders adapted merely to swell up with solvents, or kneadable masses, with surprising deftness and with such exactness in their qualities as to meet the requirements of medicine and surgery from the standpoint of the patient as well as the physician, with the result that the desired final condition is attained with precision and entirely new fields of application are made possible.

The foregoing desirable results are obtained by treating the said solutions, jellies, pastes, swollen masses, etc., with solvents such as, for example, glycols, glycerine, formamid, and particularly water, which alter the colloidal properties of these more or less homogeneous mixtures in a manner dictated by the purposes to which the products are to be applied. The most important characteristic of this change is an alteration of the viscosity of the product. For example it causes more or less free flowing solutions to thicken, gelatinize or become more solid; it causes a further thickening or solidification of jellies; an increase of solidity of pastes; a rigidifying or toughening of plastic masses. In general the purpose is to effect an accurately graded conversion of flowable materials into thinner or thicker

solutions, jellies and pastes and, finally, into solid, rigid masses with a higher or lower softening point, of lower or higher fusibility; or to render paste-like masses more gelatinous to flowable, or even to liquefy them. This modification may be effected by means of physical or chemical (or colloidal chemical) reactions or a combination of the two. By the action of physical agencies, for instance irradiation, but particularly by means of thermal treatment, the complexion of the colloidal properties of the solutions, pastes, etc., may be changed in the direction which is characterized by an increase of viscosity in the sense indicated above.

If the solutions, pastes, etc., are subjected to the reaction of substances which tend to solidify them, a modification of the colloidal properties in the same direction is effected. Substances which operate to produce a solidifying effect are, for example, metal compounds such as chromium, iron and aluminum salts, which have a tanning effect; also soluble salts of organic acids such as acetates, particularly sodium acetate; and metalloid compounds which have a tanning effect, such as boric acid and borates, are also effective. A specific effect in this direction is had by the univalent and polyvalent alcohols, such, for instance, as ethyl alcohol and glycerine; their capacity to absorb water effects or promotes in a special manner the solidification of the colloids discussed here. Organic dyestuffs of the Congo red and benzo purpurin class as well as other dyestuffs having an equivalent reaction upon colloids are particularly active in this connection. As a general rule they act in very small concentrations which depend upon the particular dyestuff employed.

In this connection we have observed a special effect which is noteworthy, namely: the greater the quantity of a given dyestuff contained in a mass composed of polymerized vinyl alcohol and water which solidifies at body temperature, the smaller is the capacity of the mass to adhere to serous glands or membranes or other body parts. By way of example, Congo red is much more effective than benzo purpurin; accordingly, by using a suitable quantity of benzo purpurin instead of Congo red, in a mass which is non-adhesive and which solidifies at body temperature, it is possible to obtain a strongly adhesive substance. There are many situations in which this possibility of modification is important: for example in filling cavities in the upper part of the lung it enables us to make the inserted filling adhere strongly to the surface of the cavity so that it will not drop down during breathing; likewise, for segmentary localized lumbar anaesthesia we can produce a deposit material with suitable adhesive capacity together with other specific properties such as light weight and the capacity to become solid in the body. In other cases it is desirable to make the fillings lie, as far as possible without adhesion in a pocket-like cavity, and fillings for this purpose can also be produced in accordance with our invention.

By means of appropriate physical or colloidal-chemical solidifying methods or combinations of such methods, low concentrated solutions, jellies, pastes or plastic masses may be given the solidity characteristics of highly concentrated, relatively insoluble substances. In this way, for example, deposits, fillings, etc., which are made solid for some definite purpose, can be introduced into the body with the incorporation of a disproportionately small quantity of a substance foreign to the body. In certain cases, on the other hand, it is desirable to obtain highly concentrated fillings and the like which are as compact as possible, and in such cases concentrated solutions, jellies, pastes or plastic masses may be used and the consistency required for the simplest and best method of incorporation into the body may be effected by reducing the viscosity. This may also be accomplished according to our invention by influencing the colloidal properties of the mixtures of the above-mentioned polymerized vinyl compounds with solvents, particularly water. For this purpose organic acids, for example lactic acids, tartaric acid, acetic acid and the like may be incorporated in the solutions, pastes, etc. By appropriate selection and proportioning of the ingredients and suitable treatment of the mixture highly concentrated materials can be introduced into the body in abnormally thin and free flowing condition, these materials only gradually assuming the desired final consistency in the body as a result of the extraction by lixiviation of the lactic acid and the like.

An important advantage of our invention, as illustrated by the examples hereinafter given, is that it enables infusion masses, deposits of medicaments, plastic fillings, stiffening means and the like to be produced with great exactness; it makes it possible to produce materials of this type which can be readily injected into the body at moderate temperatures, for instance 40–44° C. in liquid form, and which solidify in the body in accordance with the intended purpose at its temperature range of 36–42° C. and thus localized themselves or permit themselves to be distributed more or less diffused as desired. In this way rib resections, for example in the filling of lung cavities, become unnecessary and are replaced by a simple injection. Our invention also results in a revolutionary improvement in the case of lung operations which heretofore have had to be performed at low or high pressure. As a result of our invention it is no longer necessary in opening the thorax to prevent the dangerous bending over of the mediastinum by artificially influencing pressure relations or conditions, because polymerized vinyl compounds produced according to our invention may be so adjusted that they can be injected into the mediastinum in liquid form and there solidify and thus act as stiffeners so that bending over during the operation is prevented. This surprisingly advantageous application of these compounds as stiffeners in surgical and medical cases is considered to be a particularly valuable feature of the invention.

The following examples are given for the purpose of illustrating the invention without limiting it in any way to the specific conditions, concentrations, etc., which are used:

Example 1

A solution of the consistency of honey, composed of 30 parts by weight of medium viscous polymerized vinyl alcohol and 120 parts by weight of water, is converted into a homogeneous jelly by heating for 48 hours to a temperature of 120° C. in a closed glass jar. The resulting product is exceptionally well suited, for example, for filling up cavities in the body or as a joint lubricant. In case reabsorbability is required, it may be effected by the addition of resorption promoting substances, particularly organic acids such as lactic acid or acetic acid.

Example 2

A gum-dry non-homogeneous mixture produced from 60 parts by weight of highly polymerized vinyl alcohol and 90 parts by weight of water is converted by heating for a period of 8 days to 100° C. in a closed bell jar into a homogeneous elastic mass which is gum-like when cold and which becomes soft under heat. This mass also produces good plastic fillings.

Example 3

1000 parts by weight of a readily flowable aqueous solution of 10% strength of medium viscous polymerized vinyl alcohol are mixed with 2 parts of sodium acetate. This produces a clear, homogeneous, thin jelly, which serves as a plastic filling, a vehicle for deposits of medicaments, and as infusion masses.

Example 4

An aqueous solution of polymerized vinyl alcohol of 5% strength, which is mixed with 5% of a suitable contrast medium containing 25% of thorium oxide (ThO_2), is readily flowable. By the addition of 2–10 parts by weight of Congo red to 1000 parts by weight of this solution of contrast media there are obtained masses with gradually increasing points of solidification up to 45° C., which may be sprinkled or poured when heated and they maintain this condition in the neighborhood of the solidifying point for a certain length of time.

Example 5

1000 parts by weight of a solution of highly viscous polymerized vinyl alcohol in water, of 6% strength, which is a readily flowable liquid, are mixed with 2 parts by weight of Congo red. As a result jellification occurs in the course of a few hours and the point of softening is increased to about 35° C. This mass is suitable as a base for deposits of all kinds and as plastic filling.

Example 6

If the procedure of Example 5 is followed, with the substitution of benzo purpurin for the Congo red, a jelly of lower consistency is obtained.

Example 7

1000 parts by weight of an aqueous solution of highly polymerized vinyl alcohol of 6% strength are hardened, by the addition of 3 parts by weight of benzo purpurin, to a jelly with a jellification point of 27–28° C.

Example 8

If, in carrying out the process of Example 7, the benzo purpurin is replaced by the same quantity of Congo red, the viscous solution solidifies to a rigid mass with a solidification point of 42° C. This mass may be liquefied by heating. It maintains this condition on cooling until it can be injected into the body with an injection syringe, for instance as solidification means into the mediastinum.

Example 9

1000 parts by weight of an aqueous solution of polymerized vinyl alcohol of 7% strength are mixed with 4.2 parts by weight of benzo purpurin. The resulting product is a jelly with a jellification point of 39.5° C., which adheres to serous glands or membranes and other body parts in the form of plastic fillings or deposits for therapeutically effective substances.

Example 10

If in the process of Example 9 the 4.2 parts by weight of benzo purpurin are replaced by 3.5 parts by weight of Congo red, there is obtained a rigid mass with a solidification point of 43–44° C., which does not adhere to serous glands or membranes or other body parts. It is suited, for example, for plastic fillings which are to rest in a body pocket in a manner capable of moving.

Example 11

A solution of polymerized vinyl alcohol in water, of 8.75% strength, is solidified with the addition of 4.4 parts by weight of Congo red to 1000 parts by weight of said solution, to a mass with a solidification point of 44° C. A quantity of 4 cu. cm. of this mass is mixed, after sterilization by heating to 120° C. for one-half hour, with 1 cu. cm. of sterile hydrochloric acid of 1% normal strength with a common salt content of 7 parts in 1000 parts and 200 guinea pig units of thyreotropic hormone. This mixture has a solidification point of 42–43° C., can be injected into the body upon heating to 44–45° C. by means of a standard injection syringe, and solidifies in the body.

It will be evident that many changes may be made in the processes and products described above without departing from the scope and spirit of the invention as defined in the appended claims.

The invention claimed is:

1. A surgical and medical preparation for injection into body cavities in the human and animal system comprising a mixture containing at least one material selected from the group consisting of polymerized vinyl alcohols and their water soluble derivatives, and a solvent for such material, said preparation being capable of being rendered flowable for ready injection into the body at temperatures above body temperature and which is not injurious to the body and becoming solid at body temperature after injection.

2. A surgical and medical preparation for injection into body cavities in the human and animal system comprising a mixture containing at least one material selected from the group consisting of polymerized vinyl alcohols and their water soluble derivatives, and a solvent for such material, said preparation containing an organic dyestuff selected from the group consisting of Congo red and benzo purpurin in a quantity sufficient to make said preparation capable of being rendered flowable for ready injection into the body at temperatures above body temperature and which is not injurious to the body and becoming solid at body temperature after injection.

3. A process of manufacturing surgical and medical preparations for injection into body cavities in the human and animal system comprising mixing at least one material selected from the group consisting of polymerized vinyl alcohols and their water soluble derivatives with a solvent for such material and adding an organic dyestuff selected from the group consisting of Congo red and benzo purpurin in a quantity sufficient to make said mixture capable of being rendered flowable for ready injection into the body at temperatures above body temperature and which is not injurious to the body and becoming solid at body temperature after injection.

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