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COMPOSITION FOR THE ALLEVIATION OF PAIN IN TUMOR GROWTH

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The present invention relates to a composition for the alleviation of pain in tumor growth and it is particularly useful in relieving pain and stress at the site of carcinomas and in some instances regression of tumor growth has been noted.

It is among the primary objects of the present invention to provide a composition which will have the effect of relieving pain at the site of tumor growth without the use of narcotics and without causing general anesthesia or somnifacient effects.

Another object is to provide a novel composition for the relief of pain in carcinoma without the use of analgesics, narcotics or combinations thereof, to which the body may become accustomed and which might have undesirable side effects and further lose their efficacy as the body becomes accustomed thereto.

A further object is to provide a novel composition which may be readily utilized by parenteral administration or by injection directly into the tumor mass and which will be selective in its pain relieving effects to the site of the carcinoma without otherwise causing a general anesthesia and which will have substantially no toxic effects.

Still further objects and advantages will appear in the more detailed description set forth below, it being understood, however, that this more detailed description is given by way of illustration and explanation only and not by way of limitation, since various changes therein may be made by those skilled in the art without departing from the scope and spirit of the present invention.

The above objects of the present invention may be most satisfactorily accomplished by means of a stabilized aqueous solution of polyvinylpyrrolidone and sodium formaldehyde sulfoxylate in relatively dilute aqueous solution with a pH of about 8.0 to 10.0.

It has been found most important to control the molecular weight of the polyvinylpyrrolidone, which apparently acts as a carrier to adsorb or take up the sodium formaldehyde sulfoxylate and carry it through the body to the site of the tumor or carcinoma without producing toxic effects in the host.

It has been found that if the molecular weight of the polyvinylpyrolidone is controlled, it will lodge and be retained within the tumor or carcinogenic growth and not be subject to retention by normal cell growth.

At the same time if the polyvinylpyrrolidone molecular weight is too small, it will not effectively adsorb or take up the sodium formaldehyde sulfoxylate and furthermore it will readily by-pass both the abnormal tumor cells as well as the normal cell structures without being particularly effective. Furthermore, a polyvinylpyrrolidone of lower molecular weight will not adsorb as efficiently and will be readily excreted by the kidneys.

On the other hand if the polyvinylpyrrolidone molecular weight is too large, the rate of release of the sodium formaldehyde sulfoxylate is too slow and there is a very high rate of adsorption with a very slow rate of release, which greatly reduces the efficacy and furthermore there is a tendency for retention in the reticulo-endothelial system and other phagocyte cells in the body.

The preferred molecular weight apparently is above 10,000 and below 50,000 molecular weight, and the preferred molecular weight averages around 15,000 to 35,000, with optimums of about 20,000 to 30,000.

It has been found that when the molecular weight is so regulated the polyvinylpyrrolidone will effectively adsorb and take up a relatively large amount of the sodium formaldehyde sulfoxylate, which then is fairly quickly released at the site of the stoppage, which release will be controlled at the tumor or cancerous cell growth site without the normal cell life being particularly affected.

Furthermore, this molecular weight is apparently quite effectively retained by the cancerous cell growth and will not lodge or accumulate in the kidney, and when released by the cancerous cell will readily pass out of the system.

The combination does not appear to have any toxic or general anesthetic effect, nor does it cause malfunction of the other body organs.

It may be readily administered by injection over a long period of time in small amounts, or it may be given in fairly massive doses at spaced intervals.

In making up the solution, it has been found that more rapid action and efficacy is achieved with the addition of sodium bicarbonate. The sodium bicarbonate enhances the efficacy of the polyvinylpyrrolidone-sodium formaldehyde sulfoxylate combination and hastens the release of the sodium formaldehyde sulfoxylate at the site. The reducing power of formaldehyde is greatly enhanced in the presence of sodium bicarbonate.

To give the preferred composition for about each 40,000 parts by weight, the following proportions have been found to be most satisfactory:

Active Ingredient	Preferred	Range
polyvinylpyrrolidone	1,400	1,000 to 5,000
sodium formaldehyde sulfoxylate	2,400	1,000 to 4,000
sodium bicarbonate	90	50 to 150

All of the above parts are by weight.

Parenteral water or physiological saline solution is used to make the above up to 40,000 parts by weight.

The latter will result in there being present about 340 parts by weight of sodium chloride.

Percentage-wise, by volume, there will be about 3.5% of polyvinylpyrrolidone, 6% of sodium formaldehyde sulfoxylate and 0.225% of sodium bicarbonate in parenteral water or physiological saline solution.

Generally there will be 3.5 grams of polyvinylpyrrolidone and 6 grams of sodium formaldehyde sulfoxylate and 0.225 grams of sodium bicarobnate in each 100 cc. of parenteral water or physiological saline solution.

All of the above constituents are desirable first dissolved in about twice to 10 times their weight of water so that they will be in solution in about between 2,000 to 8,000 cubic centimeters of water, and then the solutions are mixed together, using the polyvinylpyrrolidone solution as a base, followed by the addition of the sodium chloride solution and then the sodium bicarbonate solution with agitation with air.

After these three solutions are mixed together, the pH will be about 7.5.

Finally, the sodium formaldehyde sulfoxylate is added and the solution is brought up to 40,000 parts by weight, with the pH being checked at 8.0 to 10.0.

At each stage, or before and after the addition of the sodium formaldehyde sulfoxylate, the solution may be filtered through a porcelain candle or through charcoal.

It will be noted that the final solution will contain about 2½ parts of sodium formaldehyde sulfoxylate for every 40 parts of the aqueous solution and about 1.4 parts of polyvinylpyrrolidone for every 40 parts of the final solution and the sodium chloride should be about 2 to 4 times the amount of the sodium bicarbonate to achieve the most effective pain alleviation.

In respect to the dosage, desirably not more than 500

cc. can be administered intravenously in any six hour period.

Although the exact combination between the polyvinylpyrrolidone and the sodium formaldehyde sulfoxylate is not certain, apparently an addition or adsorption product is formed at least in part.

Desirably a dosage of about 500 cc. may be used at any one time over a period of four to eight hours. The manner of action of the preparation is not too clear, but it does appear that it causes a necrosis and regression of the tumor or carcinoma in addition to relief of pain. The formaldehyde, as well as the sulfoxylate part of the compound, tends to insolubilize and precipitate proteins in the tumor tissue.

To give a detailed procedure for preparing the final solution of the present preparation, 2400 grams of sodium formaldehyde sulfoxylate are dissolved in sufficient distilled water to make 8,000 cc. of the first solution.

Then 1,400 grams of polyvinylpyrrolidone of molecular weight 20,000 are dissolved in sufficient distilled water to make 8,000 cc. of the second solution.

Then 340 grams of sodium chloride are dissolved in sufficient distilled water to make 4,000 cc. of the third solution.

Finally, 90 grams of sodium bicarbonate are dissolved in sufficient water to make 2,000 cc. of the fourth solution.

Each of these solutions may be filtered through charcoal or through porcelain candles and then the second and third and fourth solutions are mixed together with air agitation and with sufficient additional distilled water to make up to 20,000 cc. and the pH is checked at 7.5.

Then the sodium formaldehyde sulfoxylate solution or the first solution is added and sufficient distilled water is added to make up to 40,000 cc.

When administered intranvenously, there apparently is quick alleviation of the pain and a necrosis and regression in the tumor mass, which appears to lose its attachment and affinity for adjacent normal tissue.

The formaldehyde portion of the sodium formaldehyde sulfoxylate as well as the keto group of the polyvinylpyrrolidone, appear to have an alleviating effect and it is this combination, in conjunction with the specific molecular weight of the polyvinylpyrrolidone, that is most effective in the presence of the cancerous cell.

As many changes could be made in the above composition for the alleviation of pain in tumor growth, and many widely different embodiments of this invention could be made without departure from the scope of the claims, it is intended that all matter contained in the above description shall be interpreted as illustrative and not in a limiting sense.

Having now particularly described and ascertained the nature of the invention, and in what manner the same is to be performed, what is claimed is:

1. A solution for parenteral administration having a pH of from 8.0 to 10.0 consisting essentially of

Active ingredients:	Parts by weight
Polyvinylpyrrolidone having a molecular weigh of from about 10,000 to about 50,000	2,400
Sodium formaldehyde sulfoxylate	1,400
Sodium bicarbonate	90

made up to 40,000 parts by weight with physiological saline solution.

2. A solution for parenteral administration having a pH of from 8.0 to 10.0 consisting essentially of

Active ingredients:	Parts by weight
Polyvinylpyrrolidone having a molecular weight of from about 10,000 to about 50,000	1,000 to 5,000
Sodium formaldehyde sulfoxylate	1,000 to 4,000
Sodium bicarbonate	50 to 150

made up to 40,000 parts by weight with physiological saline solution.

3. An isotonic solution for intravenous infusion consisting essentially of 3 grams of polyvinylpyrrolidone having a molecular weight of from about 10,000 to about 50,000, 6 grams of sodium formaldehyde sulfoxylate and 0.225 grams of sodium bicarbonate in each 100 cc. of solution, said isotonic solution having a pH of about 8.0 to 10.0.

4. An isotonic solution for intravenous infusion consisting essentially of 3 grams of polyvinylpyrrolidone having a molecular weight of from about 10,000 to about 50,000, 6 grams of sodium formaldehyde sulfoxylate and 0.225 gram of sodium bicarbonate in each 100 cc. of physiological saline solution, said isotonic solution having a pH of about 8.0 to 10.0.

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