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1

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MEDICINAL PREPARATION CONTAINING ACETYL SALICYLIC ACID AND A PYRIDOXINE COMPOUND

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The primary object of the invention is to provide a vehicle for administration of medicines via the oral and parenteral routes which will act to enhance the potentiation and synergistic effects of the medicine as well as increase rapidity of absorption of the medicament into the blood stream of the patient.

This is a continuation-in-part of my applications Serial No. 747,561 filed July 7, 1958 and Serial No. 742,981 filed June 19, 1958, both now abandoned.

It is a further object of my invention to provide such a vehicle which will increase the effect and rapidity of absorption of the following medicines among others: antibotics and antifungal agents, steroids, salicylates (analgesics and antipyretics), local anaesthetics (cocaine, procaine, etc.), parenteral anaesthetics and analgesics and hypnotics (morphone and opium alkaloids), barbiturates, bromides, mental action drugs including central nervous system stimulants or depressants, cardiovascular drugs, diuretics, metalloids and heavy metals, antacids and digestants, chemotherapeutic drugs including sulphur derivatives, hematinics, and endocrines.

It is well known that medicines for the treatment of human beings show their effect by the concentration of the medicine in the system of the patient and also by the rapidity in which the medicine is absorbed in the system of the patient. In the use of my invention, I can both increase the concentration of the effect of the drug as well as the rapidity of absorption of the drug in the system of the patient, while using smaller percentages of the basic drug than would ordinarily be required for an average dose.

I achieve the objects of my invention by combining a medicine such as aspirin (acid acetyl salicylic) or Bufferin (which contains acid acetyl salicylic combined with aluminum glycinate), with my vehicle. My vehicle may comprise any of the following members of the pyridoxine family: pyridoxine, pyridoxic acid, pyridoxine hydrochloride, pyridoxamine, pyridoxal, pyridoxine phosphate complex, pyridoxamine phosphate complex, pyridoxal phosphate complex, pyridoxine carbonate complex, pyridoxamine carbonate complex and pyridoxal carbonate complex. In another form of my invention, I add a quantity of sodium bicarbonate to my vehicle as will be described hereinbelow. I find that this increases the effectiveness of the vehicle for the purposes stated herein.

When my invention is to be used for oral administration, I combine the medicine such as aspirin with my vehicle such as pyridoxine, by compressing the powders together in tablet form. A capsule may also be made for oral administration by placing the combined powders of the mentioned chemicals in a gelatine capsule. The preparation may be made for oral administration by any other method known to the art.

I prepare my invention for parenteral administration, or administration by injection, by combining the powders of the ingredients in aqueous or oily solution suitable for injection in the usual manner.

2

In preparation of the composition of my invention for either oral or parenteral administration, I find that five milligrams of a member of the pyridoxine family combined with less than the average dose of any of the medicines listed hereinabove makes a satisfactory and useful medicine. Although I find that the use of my invention requires less than the average dose of a specific medicine since it increases the effect of the medicine it may also be used with a regular dose of the medicine for an enhanced effect.

Describing my invention further, I shall use the term "vehicle" to cover all members of the pyridoxine family mentioned hereinabove. Thus, I find that five milligrams of the vehicle in combination with a medicine such as mentioned hereinabove either in powder form compressed into a tablet for oral administration, or in a solution for parenteral administration (or oral administration) will make these drugs much more efficient in becoming rapidly absorbed and potentiating the action of the drugs to such an extent as to give as much as twofold the concentration in the bloodstream as normally would be obtained by the use of the drug alone without the vehicle.

I have found that patients respond to treatment more quickly and with less discomfort with less than an average dose of medicine when used in combination with my vehicle. For example, the average dose of aspirin has a particle size of 10 mesh. When aspirin is used in combination with my vehicle, the particle size may be reduced to 200 mesh and the results are more efficient.

My invention is especially useful in oral administration where the clinical effect of the drug is not achieved until it first enters the stomach of the patient and is thence absorbed into the bloodstream of the patient. The use of my vehicle in combination with a specific medicine results in dilatation of the blood vessels in the stomach producing a greater supply of blood to the area for absorption of the medicine.

While I find that a dose including five milligrams of the vehicle is satisfactory, I have also found that the dose may include vehicle as small as 1 milligram and as high as 1 gram per kilo of body weight of the patient. While higher ranges of doses will work as well as the five milligram dose of vehicle, additional dosage does not add to the effect desired, to warrant the use of more of the drug. However, since the drug works well within the entire range stated, I do not desire to be limited to any particular amount even though I state preferred form or amount.

I have made several clinical tests to prove the utility of my invention and I set forth specific examples as follows:

In Table I, in which the results of six different tests made on eighteen patients are tabulated, the results are shown as follows:

Table I shows the case number in the first column; the diagnoses of the patient in the second column; the treatment in the third column; the duration of the illness in the fourth column; the index of comfort experienced by the patient in the fifth column and, complications if any, in the sixth column. The index of comfort as shown in the fifth column, was made up as follows:

Comfort is defined as the subjective feeling of the patient in relation to his complaint. In other words, the maximum of comfort was experienced when the patient was free of any evidence of symptoms of his illness. The

minimum of comfort was experienced by the patient when he felt subjective symptoms of the infection to the maximum extent. I have graded these subjective experiences of comfort of the patient from one to five, one, being the maximum discomfort or the least comfort; and five, being the minimum discomfort or greatest comfort experiences by the patient.

TABLE I

Case No.	Diagnosis	Treatment	Duration	Comfort	Complications
1	Coryza	Aspirin & Anti Hist 2 q4h prn.	14 days	1	Sinus 2 weeks following cessation of treatment.[1]
2	Coryza	Aspirin & Anti Hist 2 q4h prn.	14 days	1	Sinus 2 weeks following cessation of treatment.[1]
3	Coryza	Aspirin & Anti Hist 2 q4h prn.	14 days	1	Sinus 2 weeks following cessation of treatment.[1]
4	Coryza	Aspirin 2 q4h prn	11 days	2	Subsequent sinus treatment.
5	Coryza	Aspirin 2 q4h prn	10 days	2	Subsequent sinus treatment.
6	Coryza	Aspirin 2 q4h prn	11 days	2	None.
7	Coryza-Rhinitis	Aspirin & X 2 q4h prn	5 days	4	Do.
8	Coryza-Rhinitis	Aspirin & X 2 q4h prn	6 days	4	Do.
9	Coryza-Rhinitis	Aspirin & X 2 q4h prn	6 days	4	Do.
10	Coryza	Bufferin 2 q4h prn	10 days	2	Do.
11	Coryza	Bufferin 2 q4h prn	9 days	2	Subsequently treated for pus retention.
12	Coryza	Bufferin 2 q4h prn	10 days	2	Subsequently treated for pus retention.
13	Coryza Acute Rhinitis.	Aspirin & X & Y 2 q4h prn.	3 days	5	None.
14	Coryza Acute Rhinitis.	Aspirin & X & Y 2 q4h prn.	3 days	5	Do.
15	Coryza Acute Rhinitis.	Aspirin & X & Y 2 q4h prn.	3 days	5	Do.
16	Coryza Rhinitis Acute.	Bufferin & X+Y 2 q4h prn.	1 day	5	Do.
17	Coryza Rhinitis Acute.	Bufferin & X+Y 2 q4h prn.	2 days	5	Do.
18	Coryza Rhinitis Acute.	Bufferin & X+Y 2 q4h prn.	1 day	5	Do.

[1] Observation: Course of treatment not shortened.

The higher the comfort figure the better the patient felt.

X=Pyridoxine Hydrochloride—5 mgm.
Y=Sodium Bicarbonate—2 gr.

All of the patients complained of a condition of coryza, an upper respiratory infection, known as the common cold. Cases 1, 2 and 3 were treated with the usual dosage of aspirin together with an antihistimine, 10 grains every four hours during the patient's waking hours. Cases 4, 5 and 6 were treated with aspirin alone, 10 grains every four hours during waking hours for the amount of time indicated in the fourth column of Table I. Cases 7, 8, and 9, which also complained of a condition of rhinitis, or running nose, in addition to the coryza were treated with aspirin, 10 grains, combined with five milligrams of pyridoxine every four hours during waking hours for the time shown in column 4 of Table I. Patients 10, 11 and 12 were treated with Bufferin, 10 grains every four hours, during waking hours, for the days shown in Table I. Patients 13, 14 and 15, who also complained of acute rhinitis, were treated with a combination of aspirin, 10 grains, pyridoxine, 5 milligrams, and sodium bicarbonate, 2 grains, for three days each during waking hours at four hour intervals, and patients 16, 17 and 18 who also complained of acute rhinitis, were treated with a combination of Bufferin, 10 grains, pyridoxine, 5 milligrams, and sodium bicarbonate, 2 grains, every four hours during waking hours, for the time shown in column 4, Table I.

From the table, it can be readily ascertained that patients 1, 2 and 3 who were merely treated with the usual dosages of aspirin combined with an antihistimine experienced illness of the longest duration and the least comfort. In addition, they all had sinus infection two weeks after apparent cure.

Patients 4, 5 and 6, who were treated with aspirin alone, did not recover until ten or eleven days after the beginning of the treatment. Their comfort experience was

little better than that of patients 1, 2 and 3 and two of them developed sinus complications following cessation of treatment.

Patients 7, 8 and 9 who were treated with a preparation in accordance with my invention, aspirin in combination with pyridoxine, had illnesses of only five or six days duration, high comfort index of four and had no after complications.

Patients 10, 11 and 12 were treated with Bufferin alone. The duration of their illnesses lasted nine or ten days and two of them were subsequently treated for pus pretection in the sinuses.

Patients 13, 14 and 15 were treated with another form of my invention, aspirin in combination with pyridoxine and sodium bicarbonate. The duration of their illnesses lasted three days and they had the maximum of comfort (grade of 5) and no after complications.

Patients 16, 17 and 18 were treated with Bufferin combined with pyridoxine and sodium bicarbonate, another form of my invention, and the duration of their illnesses lasted one or two days with maximum comfort (grade of 5) and no after complications.

The eighteen cases given in Table I are representative of over 100 cases tested. Thus, from the results of these tests, it is apparent that when the medicine is used in combination with pyridoxine, one feature of my invention, the illness is cured in less than half the time and there was no record of after complications. In addition, the comfort level of the patient was higher than without the use of my invention. I also found that in the form of my invention which comprises sodium bicarbonate, the cure is made quicker and the comfort level is higher as shown in the tests.

In another series of tests, the presence of salicylates in the blood was measured. The medicine used was Bufferin in all cases. Where Bufferin alone was used, at the end of ten minutes, the tests showed 12 milligrams percent, and at the end of twenty minutes, 26.2 milligrams percent. When a preparation in accordance with my invention, comprising Bufferin and pyridoxine was used in combination with sodium bicarbonate, at the end of ten minutes, the results showed 23.8 milligrams percent, and at the end of twenty minutes 38.9 milligrams percent.

The doses given to patients 7, 8 and 9 as set forth in Table I, were made by crushing 10 grains of aspirin and

combining with 5 milligrams of powdered pyridoxine. The mixture was placed in a capsule which was then administered orally as a dose to the patient. The doses for patients 13, 14 and 15 were made by crushing 10 grains of aspirin combining with 5 milligrams of powdered pyridoxine and 2 grains of powdered sodium bicarbonate. The mixture was placed in a capsule and administered to the patient orally, as a dose. The medicine for patients 16, 17 and 18 was prepared by crushing 10 grains of Bufferin combined with 5 milligrams of powdered pyridoxine and 2 grains of sodium bicarbonate. The mixture was placed in a capsule and administered to the patient orally, for each dose.

Although in the preferred forms of my invention, which used sodium bicarbonate, in the combination, I show the use of 2 grains, I do not wish to be limited to this exact amount, but state that my invention will work well with sodium bicarbonate in the range of ½ to 60 grains.

Example 1

I use a member of the pyridoxine family with a halogen preferably fluorine such as sodium fluoride and sodium acid fluoride. Also I use a member of the pyridoxine family with bromine notably sodium bromide and potassium bromide as well as chlorines and iodines, as recited above. That is, the pyridoxine is used with sodium chloride, potassium chloride, sodium iodide, potassium iodide, sodium bromide, potassium bromide, sodium chlorates, potassium chlorates, sodium fluoride and sodium acid fluoride, in the proportions recited in the foregoing specification.

Example 2

I prepare a mixture of pyridoxine with sodium fluoride in the amount of five milligrams pyridoxine in a 2% aqueous solution of sodium fluoride (NaF). The sodium fluoride is used in from .1 to 2% solution and the pyridoxine is used in the amount of 5 milligrams to 30 milligrams per ounce of the sodium fluoride solution. This product is useful in preventing dental caries and is incorporated in any of the numerous conventional toothpaste formulations and mouth washes.

Example 2a

In this example five milligrams of pyridoxine powder and 20 milligrams of sodium fluoride were mixed and pressed into a tablet. The powder was also incorporated in a gelatin capsule. 0.5 milligram of pyridoxine powder was also used successfully. The products of Example 2*a* were likewise useful in connection with toothpaste and mouth wash formulations.

Example 3

This example was like Example 2 except that sodium bifluoride (NaHF2) was used.

Example 4

This was the same as Example 2 except that potassium chlorate was used instead of sodium fluoride.

Example 5

I prepared a mixture of pyridoxine carbonate as mentioned above and aspirin in the proportions recited namely 5 milligrams of the pyridoxine carbonate with 0.333 gram of aspirin. The proportions may be modified as recited above and in addition, sodium bicarbonate was added in some cases but frequently is not required.

Example 6

This example was like Example 2 and Example 3 except that pyridoxine carbonate was employed in each instance and in a further pair of examples pyridoxine hydrochloride was employed in each instance.

Example 7

This example was like Examples 2 and 5 in that in the several products prepared, pyridoxine carbonate was employed as the member of the pyridoxine family.

Toothpastes and mouth washes embodying the compounds described above have a wide utility and effectiveness and as stated, are incorporated with formulations which are well known and conventional. In the toothpaste and mouth wash pharmocopei and of themselves form no part of this invention.

While I have described my invention in its preferred forms, I do not wish to be limited by the specific embodiment as set forth herein but desire to be protected within the limits of the claims hereinbelow, wherefore, I claim:

1. A medicinal preparation comprising in combination (1) a material selected from the group consisting of acetyl salicylic acid and acetyl salicylic acid combined with aluminum glycinate, (2) a non-toxic pyridoxine compound and (3) sodium bicarbonate.

2. A medicinal preparation comprising in combination (1) acetyl salicylic acid, (2) a non-toxic pyridoxine compound and (3) sodium bicarbonate.

3. A medicinal preparation comprising in combination (1) acetyl salicylic acid, (2) aluminum glycinate, (3) a non-toxic pyridoxine compound and (4) sodium bicarbonate.

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