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FORMULATION AND EVALUATION OF SULPHAMETHOXAZOLE SUSPENSION BY PH CHANGE METHODS

Ramya Krishna Seelam[1]* and Eliyas Kadi Abafita[1]

[1]Department of Pharmacy, College of Public Health and Medical Sciences, Jimma University, Ethiopia.

ABSTRACT

Dispersed phase preparation is an important step in the formulation of suspensions. One of the good criteria for suspension is fine (micron) sized dispersed phase particles. Fine size of the particles in a suspension is required for good physical stability and rapid dissolution rate. The particle size in a suspension can be reduced by techniques such as by micronisation using various size reduction machineries and also by pharmaceutical techniques such as co-precipitation and pH change method. The objective of this study was to prepare and evaluate sulphamethoxazole suspension by pH change method. The plots of sedimentation volume versus time indicated slow settling of dispersed particles in the case of suspensions prepared by pH change method when compared to control formulations. These results indicated that the dispersed phase particles remain suspended over a longer period of time in the case of suspensions prepared by pH change method. The better suspendability of the particles in the suspensions prepared by pH change method is due to reduction in particle size.

Keywords: Sulphamethoxazole, pH change method, Suspension, Sedimentation Volume, Micronisation, Physical stability.

INTRODUCTION

Dispersed phase preparation is an important step in the formulation of suspensions. One of the good criteria for suspension is fine (micron) sized dispersed phase particles. Fine size of the particles in a suspension is required for good physical stability and rapid dissolution rate. The particle size in a suspension can be reduced by techniques such as by micronisation using various size reduction machineries and also by pharmaceutical techniques such as co-precipitation and pH change method [1].

The objective of the present experiment was to prepare and evaluate sulphamethoxazole suspension by pH change method. In the pH change method, the drug was initially dissolved in the vehicle at an appropriate pH to get a clear solution. During the preparation of suspension,the pH is neutralized to result in precipitation of drug in fine micron sized particulate form. In the present experiment, the medicament sulphamethozaole was first dissolved in 0.1 N NaOH to get a solution. During the preparation of suspension, in the presence of suspending agent the alkaline pH is neutralized by the slow addition of 0.1 N HCl. This neutralization results in the precipitation of micron sized drug particles which are dispersed directly by the presence of suspending agent sod. CMC and methyl cellulose were used as suspending agents. In each case, one control formulation and another formulation by pH change method were prepared and subjected to evaluation of size of dispersed particles and for sedimentation characteristics [2].

EXPERIMENTAL

Materials

The materials used in this study were Sulphamethoxazole, 0.1 N NaOH, 0.1 N HCl, Methyl cellulose, sodium CMC, distilled water etc. All of the chemicals used were of analytical grades.

Method

Preparation of suspensions

Two sulphamethoxazole suspensions namely

a. Control formulation without polymer
b. Formulations with a change in pH were prepared

Corresponding Author:-Ramya Krishna Seelam Email:- ramya.krishna.seelam@gmail.com

as per the formulae given in the table.

Method of Preparation of Control formulation

Sulphamethoxazole was triturated in a dry mortar with tween 80 solution to wet the hydrophobic sulphamethoxazole particles. Suspending agents (sod. CMC/ MC) was added along with a part of the vehicle (water) and triturated thoroughly to form a smooth dispersion. More water was added gradually while triturating. The suspension formed is carefully transferred into a measuring cylinder and the volume were adjusted with water and mixed thoroughly [3].

Method for the preparation of suspension by pH change method

Sulphamethoxale was taken in a dry mortar; Tween 80 solution was added and mixed thoroughly. 0.1 N NaOH (3 ml) was added to the mortar and mixed to dissolve sulphamethoxazole and to obtain a clear solution. Suspending agent (sod. CMC/ MC) was added along with a part of the vehicle and mixed thoroughly to obtain a smooth dispersion. More water was added and mixed thoroughly. 0.1 N HCl was then added drop by drop to the mortar and mixed thoroughly. The addition of 0.1 N HCl results in the precipitation of sulphamethoxazole due to pH neutralization or change. The suspension was mixed thoroughly and transferred carefully into measuring cylinder and adjusted to volume with water. The suspensions were mixed thoroughly and stored [4].

Evaluation

Determination of Particle size: Particle sizes in the two suspensions mode were evaluated by Microscopy. Sedimentation study: the suspensions prepared were stored in graduated measuring cylinders and the volume of sediment formed was recorded at different time intervals. From the data of volume of sediment, the sedimentation volume in each case at each time interval was noted and calculated as follows [5].

$$\text{Sedimentation volume} = \frac{\text{Volume of sediment at time "t"}}{\text{Initial volume}}$$

The results are given in tables 1-3 and figure 1 and 2. Sedimentation volume was plotted against time as shown in the figures [6].

Table 1. Formula of Sulphamethoxazole Suspension Prepared By pH Change Method

Ingredients	Quantity for 30 ml
Sulphamethoxazole	600 mg
Tween 80 (0.01%)	3 mg
Sod CMC / MC	300 mg
0.1 N NaOH	3 ml
0.1 N HCL	3 ml
Water	Upto 30 ml

Table 2. Formula of Sulphamethoxazole Control Suspension

Ingredients	Quantity for 30 ml
Sulphamethoxazole	600 mg
Tween 80 (0.01 %)	3 mg
Sod CMC / MC	300 mg
Water	Upto 30 ml

Table 3. Sedimentation Data of Sulphamethoxazole Suspensions Prepared By pH Change Method

Time (hrs)	Sod CMC CONTROL	Sod CMC TEST	Methyl Cellulose CONTROL	MC TEST
0	1	1	1	1
0.5	0.96	1	0.86	0.8
1	0.9	0.93	0.56	0.52
1.5	0.86	0.9	0.5	0.36
2	0.83	0.86	0.36	0.32
2.5	0.76	0.83	0.26	0.32
3	0.7	0.8	0.2	0.28
3.5	0.6	0.76	0.2	0.28
4	0.5	0.66	0.16	0.26
5	0.43	0.6	0.16	0.25
7	0.43	0.6	0.13	0.24
9	0.43	0.52	0.13	0.22
11	0.3	0.46	0.13	0.22
13	0.23	0.4	0.13	0.22

14	0.16	0.34	0.13	0.18
15	0.13	0.2	0.13	0.18
16	0.13	0.2	0.13	0.18
17	0.13	0.2	0.13	0.18

Fig 1. Comparison of control and test formulations with MC

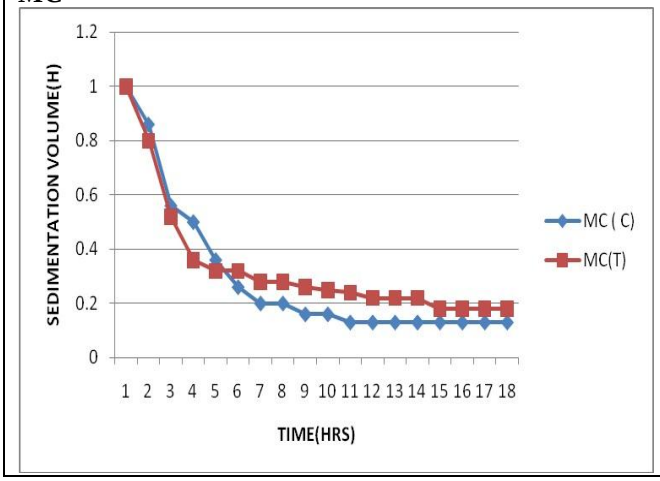
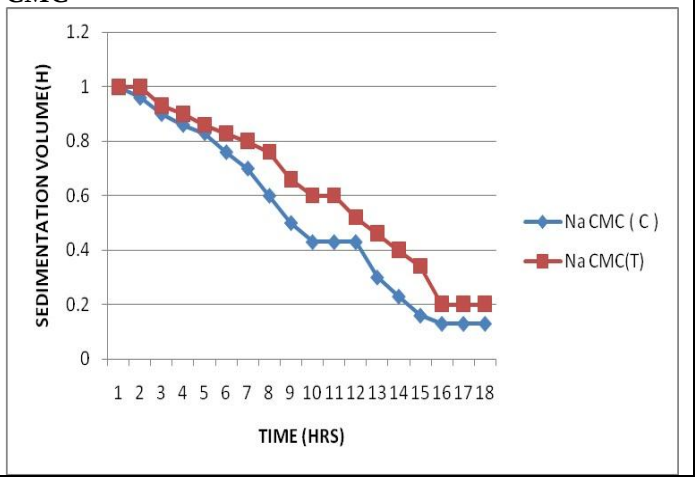


Fig 2. Comparison of control and test formulations with Na CMC



RESULTS AND DISCUSSIONS

Sulphamethoxazole suspensions were formulated employing pH change principle. A total of 4 sulphamethoxazole were made and subjected to evaluation [7]. All the suspensions prepared were found to be smooth and elegant in appearance without flocculation. The particle size of the suspensions was measured by microscopy. The results are given in table. The size of the particles in the control formulation prepared with sod. CMC as suspending agent was found to be 7.76µm whereas the size of the particles in the suspension made by pH change method was 6.9 µm [8].

Similarly the size of the particles in the control suspension prepared with Methyl cellulose was found to be 12.2 µm. The size of the particles in the suspension prepared by pH change method was found to be 7 µm. Thus, the size of the dispersed particles is greatly reduced in the suspensions prepared by pH change method with both sod. CMC and MC as suspending agents [9].

The results of sedimentation study are given in Tables and figures. The sedimentation of particles in the control suspensions was very rapid and sedimentation in the suspensions prepared by pH change method was very slow.

The plots of sedimentation volume vs. time indicated slow settling of dispersed particles in the case of suspensions prepared b pH change method when compared to control formulations. These results indicated that the dispersed phase particles remain suspended over a longer period of time in the case of suspensions prepared by pH change method. The better suspendability of the particles in the suspensions prepared by pH change method is due to reduction in particle size.

CONCLUSION

Sulphamethoxazole suspensions prepared by using pH change principle were found to be better than control formulations with regard to particle size and sedimentation characteristics. The particle size of the dispersed phase is greatly reduced in the suspensions prepared by pH- change method. The suspensions prepared by pH-change method were found to be more stable physically. The rate of settling in these suspensions is very slow and the particles remain suspended over a longer period of time in theses suspensions when compared to control formulations. Thus, pH-change method was found to be a better method for preparing suspensions.

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