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Research Article

STABILITY OF MARKETED ALBENDAZOLE SUSPENSIONS AND CORRELATION BETWEEN ZETA POTENTIAL AND SEDIMENTATION

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ABSTRACT
The study was aimed at evaluating the stability of marketed albendazole suspension through electrokinetic characterization of the particles. The marketed brands of Albendazole suspension that were studied include AVIZOLE®, BENTAL®, BENDEX®, NOWORM® and ZENTAL®.
Particle size, zeta potential, sedimentation volume, viscosity and pH of the suspension were the parameters determined and their correlation was established. ZENTAL® showed maximum sedimentation volume and its zeta potential was also found to be the highest. Rheological studies of the suspension displayed maximum viscosity with ZENTAL®. Particle size analysis showed that ZENTAL® had least size. From the study it is evident that particle size, zeta potential and sedimentation volume have an influence on the suspension stability.
KEYWORDS: Albendazole; Suspension; Stability; Sedimentation; Zeta Potential

INTRODUCTION

Albendazole (ABZ), methyl [5-(propylthio)-1-H-benzimidazol-2yl] carbamate, is a benzimidazole derivative with a broad spectrum of activity against human and animal helminthes parasites. ABZ is a poorly water-soluble drug (0.2 µg/ml in water at 25 °C) and consequently, it is poorly and erratically absorbed from the gastro-intestinal tract[1-3]. Commercially it is available in tablets and suspension. The choice for suspension instead of tablet or capsule is frequently governed by patient acceptance. Although tablets or capsules are usually given to adults, children are more easily treated with an adequately flavoured suspension[4].

A Pharmaceutical suspension is a coarse dispersion in which internal phase is dispersed uniformly throughout the external phase. The internal phase consisting of insoluble solid particles having a specific range of size which is maintained uniformly throughout the suspending vehicle with aid of single or combination of suspending agent. The external phase (suspending medium) is generally aqueous in some instance, may be an organic or oily liquid for non oral use. An acceptable suspension possesses certain desirable qualities such as the particles should not settle rapidly. The particles that do settle to the bottom of the container must not form a hard cake but should be readily redispersed and the suspension must not be too viscous to pour freely from the orifice of the bottle.

A useful parameter that can be derived from sedimentation studies is sedimentation volume. It is defined as the ratio of ultimate volume of the sediment V_u to the original volume of the suspension, V_0 before settling. Thus $F= V_u/V_0$.

One of the defining parameters of the quality of a suspension formulation is the stability of the suspension[5-7]. The stability of particles in suspension is controlled by the colloidal properties, e.g., the thickness of the double layer and the zeta potential of the fine particles. According to the Deryagin, Landau, Verwey, and Overbeek (DLVO) theory, the van der Waals attractive force and the electrostatic repulsive force are two important interaction forces dominating in an aqueous suspension system[8]. The need for methods of evaluating and predicting the stability of suspensions has been recognized. The factors of pH and viscosity do not enable the investigator to predict and evaluate a series of suspensions. Electrokinetic factors appear to be of value as these measurements seem to indicate the stability of a suspension.

The electro kinetic or zeta-potential is an important parameter of the electrical double layer and represents a characteristic of electrical properties of solid/liquid and liquid/gaseous interfaces. The magnitude of the zeta potential gives an indication of the potential stability of the colloidal system. The zeta potential indicates the degree of repulsion between adjacent, similarly charged

particles in dispersion. For molecules and particles that are small enough, high zeta potentials give raise to significant electrostatic repulsions between the particles and this situation should correlate with small sedimentation volumes, low settling rates, and difficult redispersion. The reverse will be true for low zeta potential. The general dividing line between stable and unstable suspensions is generally taken at either +30 or -30 mV. Particles with zeta potentials more positive than +30 mV or more negative than -30 mV are normally considered stable[9].

The success of a suspension over variety of brands available is attributed to its physical stability. The present work was designed to perform stability evaluation of marketed brands of albendazole suspension like AVIZOLE®, BENTAL®, BENDEX®, NOWORM® and ZENTAL® and its correlation with zeta potential.

MATERIALS AND METHODS

Various brands of albendazole suspension available were purchased from the pharmacy. AVIZOLE® was manufactured by Adley Formulation, Kotla, India. BENTAL® Lincoln Pharmaceuticals Ltd, Khatraj, India. BENDEX® Cipla Ltd, Sangli, India. NOWORM® Alkem Ltd, Mumbai, India, ZENTAL® from Glaxo Smith Kline, Mumbai, India.

Particle size and zeta potential

Particle size was determined by dynamic light scattering type particle size analyzer, Qudix Scatteroscope-I after suitable dilution of drug suspension with distilled water before each analysis[10].

Zeta potential of various brands of suspensions were determined by dynamic light scattering method (DLS), using a computerized inspection system Malvern Zetasizer Nano-ZS Series (Malvern Instruments, U.K.) at 25.0±0.5°C.

Sedimentation Volume

The sedimentation volume of all the five marketed suspensions (25 ml volume) were measured. For the study sediment volume Vu was measured after keeping the drug suspension in 100ml cylinder for 7 days at 35°C. Observations were made from 0 to7 hr and then for every 24 hr for 7 days. The sedimentation volume, F (%), was then calculated using the following equation:

$$F = 100Vu/Vo$$

Where Vu is the ultimate volume of the sediment and Vo is the original volume of the suspension[11].

Determination of the pH of the suspensions

The pH values of the suspensions were measured by a pH meter (Systronics Digital pH meter, μ pH system 361) at 27°C.

Rheological study

The viscosities of the samples was determined using the Brookfield programmable viscometer (LV3, Brookfield Inc., USA) equipped with the spindle no 40. The measurement was performed at 25°C.

RESULTS

Particle size and zeta potential

The different marketed brands of suspensions were evaluated based on their zeta potential, particle size, sedimentation volume, viscosity, and pH. Values of Zeta potential and particle size of suspensions are shown in Table No.1. Marketed brand ZENTAL® showing highest value of negative zeta potential (-64.3 mV) with smallest particle size (13.3μm) followed by than NOWORM® with lowest value of negative zeta potential (-38.0mV) and largest particle size (27.0 μm).

Sedimentation Volume

Percent sedimentation volume of suspension is shown in Table No. 2. Marketed brand ZENTAL® showed highest value of sedimentation volume (95%) followed by AVIZOLE® (88%), BENTAL® (88%), BENDEX® (80%) and then NOWORM® .

Determination of the pH of the suspensions

The pH values of all brands of suspension given in Table no.3, ZENTAL® showed somewhat higher value of pH (6.65) than other brands viz. BENTAL® (4.72), BENDEX® (5.70), AVIZOLE® (4.65) and NOWORM® (4.37).

Rheological study

The Viscosities of suspensions are shown in Table No.3. Maximum viscosity was found with ZENTAL® whereas NOWORM® displayed lowest viscosity .

DISCUSSION

From the results, it is evident that all brands of suspension found to be stable. The sediment volume was high and it decreased with time only after 7 days. ZENTAL® with high zeta potential and high percent of sedimentation volume (95%) was found to be more stable compared to other brands. NOWORM® showed low zeta potential and lower sedimentation volume and hence it is found to be less stable than ZENTAL®. In case of other brands like BENDEX®, BENTAL®, and AVIZOLE® all have almost nearest values of zeta potential and sedimentation volume, hence suspensions have better stability with consideration to its sedimentation volume.

The particles in a colloidal suspension or emulsion usually carry an electrical charge. The amount of charge on the particle surface is an important particle characteristic because it determines many of the properties of the suspension. It has long been recognised

that the zeta potential is a very good index of the magnitude of the interaction between colloidal particles and measurements of zeta potential are commonly used to assess the stability of colloidal systems. Particles with zeta potentials more positive than +30 mV or more negative than -30 mV are normally considered stable[9]. Among the suspensions evaluated, ZENTAL® exhibited maximum zeta potential and that justifies the reason for maximum sedimentation volume.

The stability of a suspension is also affected by pH. An increased pH of suspension imparts more negative charge in zeta potential as in case of ZENTAL®, it shows higher pH value and more negative zeta potential, hence found to be more stable. Also higher viscosity of ZENTAL® than other brands aid stability characteristics in suspension.

CONCLUSION

Different brands of Albendazole suspension were evaluated based on different parameters like Zeta potential, Particle size, sedimentation volume, viscosity and pH. The presented results have shown that the stability of suspension mainly controlled by the zeta potential of the particles and the thickness of their ionic double layers. The pH and viscosity also play an important role in stability of suspension.

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Table 1: Particle size and zeta potential of various brands of albendazole suspension

Suspensions	Particle Size (µm)	Zeta Potential
AVIZOLE®	19.9	-46.9
BENDEX®	24.8	-43.5
BENTAL®	18.1	-50.3
NOWORM®	27.0	-38.0
ZENTAL®	13.3	-64.3

Table 2: Sedimentation volume of various brands of albendazole suspension

Brands of suspension	Sedimentation Volume %														
	Time (Hours)								Time (Days)						
	0	1	2	3	4	5	6	7	1	2	3	4	5	6	7
AVIZONE®	100	100	100	100	100	100	100	100	98	96	93	93	92	92	88
BENDEX®	100	100	100	100	100	100	100	100	97	94	92	92	88	84	80
BENTAL®	100	100	100	100	100	100	100	100	98	96	92	92	90	88	88
NOWORM®	100	100	100	100	100	100	100	100	98	96	96	92	84	76	72
ZENTAL®	100	100	100	100	100	100	100	100	99	97	96	96	96	95	95

Table 3: pH and viscosity of various brands of albendazole suspension

Suspensions	pH	Viscosity (Poise)
AVIZOLE®	4.65	1.24
BENDEX®	5.70	0.92
BENTAL®	4.72	1.36
NOWORM®	4.37	0.78
ZENTAL®	6.65	1.65

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