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Analytical Method Development and Validation to Assess the Particle Size Distribution in Azithromycin Oral Suspension 200mg/5ml

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Abstract

Given that it influences the therapeutic product's dissolving profile and bioavailability, particle size is a crucial component of contemporary medication quality. Particle size analysis aids in improving drug quality and improving the pharma product development process. In this research, the particle size distribution of Azithromycin oral suspension is determined using an innovative and accurate approach that was established for the purpose of determining the particle size of the suspension. This approach has produced good, repeatable outcomes. The International Conference on Harmonization's Q2 (R1) guidelines were followed in the development and validation of the wet method, which used water as the dispersant. The results showed that the method was robust and reproducible, with the percentage RSD values found within acceptance limit. The approach presented here in is a precise, verified, and efficacious technique for ascertaining the particle size distribution of oral azithromycin suspension. In-depth discussion of the particle size approach is provided to guarantee comprehension of the particle size distribution and the performance of the method across the product's lifetime.

Keywords: ICH Q2R1, Method development, Method validation, Particle size distribution, Azithromycin oral suspension.

INTRODUCTION

An oral azalide antibiotic, such as azithromycin, belongs to the subclass of macrolide antibiotics. Azithromycin is a medication that can be used to treat pathogens, mainly respiratory infections caused by Gram-positive and Gram-negative bacteria [1]. Azithromycin, an antibiotic, inhibits bacteria from producing a number of proteins that are essential to their survival. The body rapidly absorbs and distributes azithromycin, which finally concentrates in cells [2]. With a molecular weight of 785.0 g/mol and a formula of $C_{38}H_{72}N_2O_{12}$•2H2O, azithromycin, in its dihydrate form, is a white and crystalline powder that is basically insoluble in water but easily solvable in ethanol and methylene chloride [3]. In chemical terms, azithromycin is [9-deoxo-9a-aza-9a-methyl-9a-homoerythromycin], a 15-membered ring containing nitrogen that has been substituted with methyl at the 9a position on the aglycone ring in place of a carbonyl group to inhibit metabolism [4]. Reducing particle size shows a essential role in enhancing the dissolution rate by increasing surface area, which in turn increases the possibility of oral medications that are poorly soluble [5]. The particle size of azithromycin affects its relative bioavailability, immediate release, and extended-release combined with bio equivalency [6]. According to literature survey several studies were reported in UV spectrometric and clinical trials [7-9]. A review of the literature on the particle size distribution method for azithromycin oral suspension revealed that there is no accessible method for determining the particle size. As a outcome, potential research was done to create a technique designed for using a particle size analyser to measure the azithromycin oral suspension's particle size distribution, and more research was done to validate the method.

MATERIALS AND METHODS

Drugs and Chemicals

Azithromycin oral suspension 200mg/ 5 ml oral suspension, Milli-Q Water.

Instrumentation

The Malvern particle size analyzer system, Model 3000, includes accessories for both wet and dry Aero S and Hydro MV. Mastersizer Software (Version 3.88) was used for data processing and evaluation.

Analytical Method Development

Malvern Mastersizer 3000, equipped with Wet Dispersion Unit (Hydro MV). The dispersant identified as Water. The Dispersant RI and Sample RI were 1.330, 1536 respectively. Following instrument parameters were Sample absorption - 0.1, Sample measurement time - 14 seconds, and. Background Measurement time - 14 seconds, Range of obscuration range was 10-20%, Configured stirrer speed 2000 rpm and number of measurement cycle 3. The acquired outcomes of d(0.1), d(0.5), and d(0.9) readings of analysis and obscuration was achieved satisfactory.

Sample Preparation

Shake the sample well for about 1 minute. Transferred the sample directly into the sampling unit dropwise until the obscuration reaches in between 10%-20%. Added enough dispersant solution to fill the Sampling Unit to the brim. Choose Configure: Accessories from the toolbar. Turned up the Stirrer/Pump gradually until it reached 2200 RPM by hand. Refilling the Sampling unit to the brim with dispersant solution will cause some of the dispersant solution within to be displaced. Verified that the Malvern Mesmerizer 3000's wet analysis mode instrument settings are in accordance with SOP. Verified that the sampling unit is free of air bubbles. Select the Start SOP option from the toolbar and then select the pre-existing SOP. To begin the background measurement, click Open. Empty the Sampling unit and repeat the cleaning process if the background measurement's laser intensity is less than 50%. Using a transfer pipette, add sample dispersion to the sampling device until the obscuration reaches between 10% and 20% (oscillating blue bar on green field). logged the findings and printed the average.

RESULTS AND DISCUSSION

Method Validation

Method precision

By inserting six distinct sample preparations into the sampling machine and recorded the particle size distribution, the precision of the particle size method was ascertained. Particle size at d (0.1), d (0.9) should have %RSD s no more than 15% and d (0.5) 10%, respectively (Table 1).

Table 1: Method Precision Results

S. No	d(0.1) µm	d(0.5) µm	d(0.9) µm
1	15.261	62.112	136.738
2	13.463	64.353	142.321
3	15.773	62.817	147.875
4	14.473	60.383	149.343
5	15.937	62.876	142.321
6	15.837	67.352	152.362
Average	15.124	63.316	145.160
%RSD	6.47	3.73	3.94

Robustness

By adjusting instrument parameters like stirring speed (±200 RPM) and obscuration (10%-20% and 20%-30%), one may ascertain how robust the process is. PSD was noted for the sample, and d(0.1), d(0.5), and d(0.9) %RSD were computed. Particle size at d(0.1), d(0.9), and d(0.5) should have %RSDs of no more than 15% d(0.1), d(0.9) and 10% d(0.5), respectively (Table 2 & 3).

Table 2: Robustness Results – (Stirring speed)

Measurement No	Stirring speed (RPM)	d(0.1) µm	d(0.5) µm	d(0.9) µm
1	1800	15.143	66.745	139.446
2		16.371	65.768	149.736
3		15.261	63.564	145.244
Average		15.592	65.359	144.809
%RSD		4.35	2.49	3.56
1	2200	14.146	68.637	142.853
2		16.373	65.234	147.112
3		15.443	63.123	148.432
Average		15.321	65.664	146.132
%RSD		7.30	4.24	2.00

Table 3: Robustness Results – (Obscuration)

Measurement No	Obscuration	d(0.1) µm	d(0.5) µm	d(0.9) µm
1	10-20%	13.455	60.846	148.911
2		15.654	62.446	145.434
3		15.261	63.564	139.958
Average		14.790	62.285	144.768
%RSD		7.93	2.19	3.12
1	20-30%	14.145	60.212	141.643
2		13.948	62.059	145.544
3		15.443	63.567	146.654
Average		14.512	61.946	144.6137
%RSD		5.60	2.71	1.82

Intermediate precision

Six separate sample preparations were transferred into the sampling unit by Analyst-2 on a different day, and the particle size distribution was noted. To evaluate the reliability of the particle size method. Particle size at d (0.1), d (0.9), and d(0.5) should have %RSD not more than 15% for d (0.1), d (0.9) and 10% for d (0.5) respectively (Table 4).

Table 4: Intermediate Precision Results

Sample No	Analyst-1			Analyst-2		
	d(0.1) µm	d(0.5) µm	d(0.9) µm	d(0.1) µm	d(0.5) µm	d(0.9) µm
1	15.261	62.112	136.738	13.123	61.312	144.310
2	13.463	64.353	142.321	14.422	60.123	152.455
3	15.773	62.817	147.875	16.294	66.657	141.098
4	14.473	60.383	149.343	15.533	68.848	155.435
5	15.937	62.876	142.321	14.357	67.023	150.365
6	15.837	67.352	152.362	15.234	63.456	140.123
Average	15.124	63.316	145.16	14.827	64.570	147.298
%RSD	6.47	3.73	3.94	7.45	5.38	4.31

CONCLUSION

Using the laser diffraction technique, a technique for determining the particle size distribution of Azithromycin oral suspension has been developed and validated. The approach was found to be precise in the validation process, with percentage RSDs of 6.47% for d(0.1), 3.73% for d(0.5), and 3.94% for d (0.9). The percentage RSDs obtained in the intermediate precision range were 7.45% for d(0.5), 5.38% for d(0.9), and 4.31% for d(0.1). Thus, the approach is seen as rugged. Specific parameters were found within the accepted range. It demonstrated how robust the method. The findings produced were in compliance with the requirements for acceptance and the percentage RSD ranges from 4.35% to 7.93% for d(0.1), 2.19% to 4.24 ford (0.5), and 1.82 to 3.56 ford (0.9). After compilation, all of the analytical data for development and validation was determined to be satisfactory. Therefore, the technique created for the particle size approach is appropriate for analysing the azithromycin oral suspension.

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Conflict of Interest: The authors declare that there is no conflict of interest.

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