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Particle Size Determination of Mirtazapine

KIRAN MANGAONKAR, PULKESHI DESAI and DHANAJI PATIL*
Department of Chemistry, Ramnarain Ruia College, Matunga, Mumbai-400 019, India

A simple, fast and accurate particle size determination method has been developed for the mirtazapine. Mirtazapine is an anti-depressant drug. The reproducible values of analysis results indicate high precision of the method. The average recovery and reproducibility of the method was found to be satisfactory.

Key Words: Particle size determination, Ro-tap sieve shaker, Mirtazapine, Silicon dioxide.

INTRODUCTION

Mirtazapine is an anti-depressant drug and not official in any of the pharmacopoeia. Sieving is one of the oldest methods of classifying powders by particle size distribution[1]. There was no reference listed for the determination of particle size of mirtazapine in the literature survey. The present work describes a simple, fast and an accurate particle size determination method using Ro-tap sieve shaker. Most appropriate weight for given drug was determined by testing accurately weighed mirtazapine of different weights such as 25 g and 50 g for same time period on a mechanical shaker.

Mirtazapine is prone to picking up significant amount of water with varying humidity; hence a test is carried out in an appropriately controlled environment with relative humidity not more than 40% RH.

Mirtazapine develops an electrostatic charge during analysis which results into pseudoretention on higher mesh size sieve; hence 0.5% of colloidal silicon dioxide added as an antistatic agent (sieving aid). Test results obtained with and without addition of sieving aid were compared in order to prove necessity of addition of sieving aid.

Principles of Analytical Sieving: The basic analytical method involves stacking the sieves on the top of one another in ascending degree of coarseness and placing the test powder on the top sieve.

The nest of sieves is subjected to a standardized period of agitation and then weight of material retained on each sieve is accurately determined. The test gives weight percentage of powder in each sieve size range.

EXPERIMENTAL

MIRTAZAPINE PSD WITHOUT SIEVING AID

Sieve No.	Mesh Size	Log of Sieve	Cumulative % retained
40	425	2.628	9.39
60	250	2.398	22.67
80	180	2.255	42.77
100	150	2.176	51.76
200	75	1.875	71.85

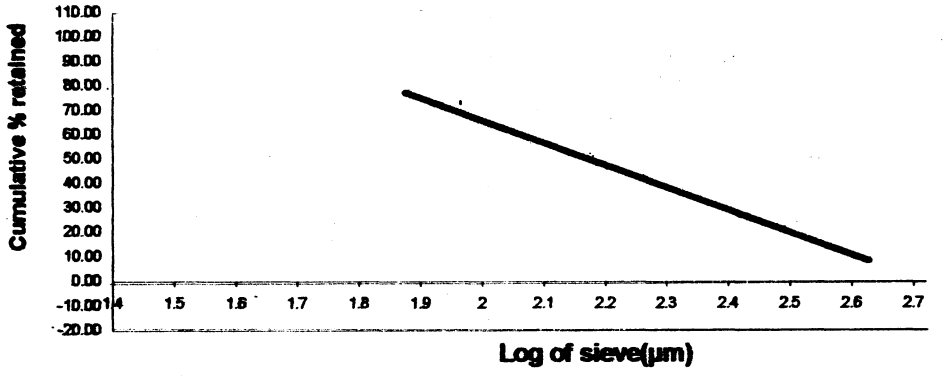

Fig. 1. Mirtazapine psd without sieving aid

MIRTAZAPINE PSD WITH SIEVING AID

Sieve No.	Mesh Size	Log of Sieve	Cumulative % retained
40	425	2.628	1.79
60	250	2.398	23.83
80	180	2.255	40.83
100	150	2.176	51.19
200	75	1.875	77.36

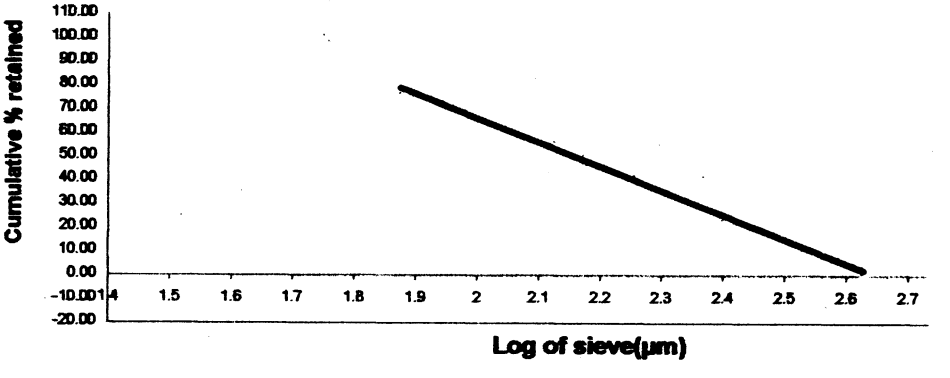

Fig. 2. Mirtazapine psd with sieving aid

Agitation Methods: A mechanical device called Ro-Tap sieve shaker was used that imparts 285 horizontal revolutions and 156 taps per minute.

End point determination: The test sieving analysis is complete when weight on any test sieve does not change by more than 5% of previous weight on that sieve. If less than 5% of total specimen weight is present on a given sieve, the end point for that sieve increases to a change of not more than 20% of the previous weight on that sieve.

Following are the steps involved during the analysis:

(1) Obtained the sieves of the following mesh size namely 40, 60, 80, 100, 200 #.
(2) Ensured sieves were intact and free from dirt.
(3) Weighed each sieve individually along with the fine collector pan and lid and recorded their weights to the nearest hundredth of a gram.
(4) Stacked the sieves in increasing mesh size order with the lowest mesh number being on top. Covered them with the lid.
(5) Placed fine collector pan at the bottom.
(6) Weighed accurately into tared beaker 25 g of mirtazapine.
(7) Weighed about 125 mg of colloidal silicon dioxide. De-lumped with the help of glass rod to ensure uniform mixing of mirtazapine and colloidal silicon dioxide.
(8) Poured the mixture on top sieve.
(9) Weighed empty beaker after transfer of the drug on to the sieve to determine the total sample weight.
(10) Placed a lid over the top sieve and placed the entire stack on the Ro-Tap sieve shaker.
(11) Turned on the shaker and operated for 5 min.
(12) After shaking for specified time period, removed stacked sieves and reweighed each sieve accurately, along with the lid and fine collector pan.
(13) Repeated the steps from 10 to 12 for total time interval of 10, 15, 20 and 25 min.
(14) Then determined the per cent retained on each sieve by using the following formula and recorded the results.
(15) Determined the cumulative per cent retained for each sieve by adding the per cent retained for the sieve of nearest with the per cent retained with all the sieves of smaller mesh number.

Calculation

$$\% \text{ Retained} = \frac{\text{Sieve weight after shaking} - \text{Sieve weight empty}}{\text{Total sample weight}} \times 100$$

$$\text{Cumulative \% retained} = \sum_{i=1}^{n} (\% \text{ retained})$$

Sieve No.	Mesh size (μm)	Cumulative % retained after 15 min shaking	
		Without sieving aid	With sieving aid
40	425	9.30	1.79
60	250	26.67	23.83
80	180	42.77	40.83
100	150	51.76	51.19
200	75	76.85	77.36

REPRODUCIBILITY OF THE METHOD

Sieve No.	Mesh size (μm)	Cumulative % retained after 15 min shaking						
		Test-1	Test-2	Test-3	Test-4	Test-5	Average	% RSD
40	425	1.79	1.83	1.79	1.76	1.82	1.80	1.54
60	250	23.83	24.05	24.12	23.77	23.85	23.92	0.64
80	180	40.83	41.00	40.52	40.68	41.08	40.82	0.56
100	150	51.19	50.63	51.33	51.50	50.98	51.13	0.66
200	75	77.36	77.80	78.10	78.35	76.99	77.72	0.71

TIME STUDY FOR OPTIMIZATION OF TAPPING TIME

Sieve No.	Mesh size (μm)	Cumulative % retained after tapping				
		5 min	10 min	15 min	20 min	30 min
40	425	7.55	3.48	1.79	1.70	1.69
60	250	33.83	27.05	23.83	23.17	23.10
80	180	45.23	43.65	40.83	40.68	40.08
100	150	53.19	52.90	51.19	50.95	50.80
200	75	82.36	79.10	77.36	77.04	76.95

RESULTS AND DISCUSSION

The proposed method is simple, fast, accurate and precise. Cumulative % retained on 40 mesh after 15 min shaking with sieving aid is approximately 1.8%. This value is negligible as compared to the same experiment carried out without sieving aid (*ca.* 10%). The experiment was found reproducible when the same study was conducted for five replicate analyses on different days by different analysts—time study conducted to determine minimum optimum time required to get constant values. The optinum time required was found 15 min.

Conclusion

From the above experiment it can be concluded that sieving aid is necessary for removing static charge of drug and hence for prevention of pseudo retention. Thus the proposed method can be used for the routine quality control analysis of mirtazapine.

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REFERENCE

1. United States Pharmacopea-25, 786, p. 2044.

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