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Establishment of blending control for Hand operated Double Cone Blender

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ABSTRACT

In the current study, a fundamental approach is used to establish operation procedure, for a hand operated double cone blender. Initially, assuming for a potent drug, where in, the strength of the drug is very less in the final dosage form, a one percent concentration of potassium permanganate with respect to final one kilogram of blended powder using starch as diluent was planned. With a kind of geometric progression method, at a rate of 10 rotations per minute, the final outcome of the uniform distribution of the potassium permanganate was found to be for at least for fourteen hours of rotations, leading to concentration range of potassium permanganate 0.08 ± 0.025 mg per mg of final blended powder.

Keywords: Hand operated double cone blender, geometric method, blending controls.

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1. Introduction

A research was conducted on quality of marketed products and it was observed that a few products deviate from standards prescribed (1). A study was initiated with an objective of identifying the product quality attributes that are responsible for withdrawal or recall of the product from the market. To achieve the task, a few regulatory databases were reviewed and reasons for withdrawal were compiled. One of the reasons for product withdrawal or recall from the market is deviation from standard deviate (2). In a third study, a tablet dosage form was collected from market and in-house quality attributes were measured and the acceptable range was established, indicating the role of distribution curve and establishing acceptable limit from deviation with respect to quality attribute (3). A pilot survey was conducted earlier, to know the status of small scale pharmaceutical industry in terms of financial, scale of product, having manufacturing resources etc. It was observed that products available in the market from either small or large scale companies provide products complying to standards prescribed, with a few products deviating from standards irrespective of size of company (4). In one another study, health related quality of life of (HRQOL) of diabetic patients was studied by administering SF-36 questionnaire. It was observed that the scores of HRQOL being improved after counselling, regular administration of drug products (5).

Based on our past research conducted (2) and as per national or international drug regulatory guidelines, it is necessary that pharmaceutical manufacturing industry should fulfill installation, operational and performance qualification of the equipment. To ensure that, industry's research and development departments establishes procedures for various kinds of drug products which are using the same equipment? Even though, vendor of equipment for the manufacturing industry does provide the procedure, it is absolutely necessary that every company establish the various attributes in operation of the equipment so as to achieve the theoretical quality standard attributes fixed for the product. Several guidelines such as GMP, cGMP, WHOGMP, ICH, ISO insist on such protocols so as to ensure that the final products were ensured for quality, safety and efficacy. The current experimentation, even though well known, is aimed in disclosing as a fundamental approach to be known to the upcoming professionals in understanding the basic approaches of manufacturing. It is necessary to understand that several procedures established are not regularly seen by every professional in a manufacturing industry and the current article is aimed in disseminating

the fundamentals to the interested in the field in establishing blending controls (6).

2. Materials and Methods

2.1 Materials

All the chemicals were of analytical grade and the instruments and equipment used are well accepted by the fraternity from various vendors. Figure 1, illustrates the hand operated blender available and used for the current method development.

Figure 1 Double Cone Blender (hand operated)

2.2 Determination of λ_{max} of Potassium Permanganate Solution

Weighed accurately 0.1000 g (100 mg) of potassium permanganate and transferred in to a 100.0 ml volumetric flask. Dissolved in distilled water and made up the volume to produce 1 mg/ml (≡ 1000 µg/ml) solution (Stock solution A). From the stock solution A, pipetted 10.0 ml of the solution into a 100.0 ml volumetric flask and made up the volume to produce 100 µg/ml solution (stock Solution B). The resulting solution is subjected to various wavelengths at the visible range of a colourimeter for absorbance, Table 1, Figure 2, to find out the wavelength maximum and it was observed that potassium permanganate possess a λ_{max} of 540 nm.

Table 1 Determination of λ_{max} of Potassium permanganate

S. No	Wave Length (nm)	Absorbance
1	450	0.22
2	470	0.26
3	510	0.52
4	520	0.89
5	540	0.97
6	570	0.42
7	600	0.16
8	670	0.06

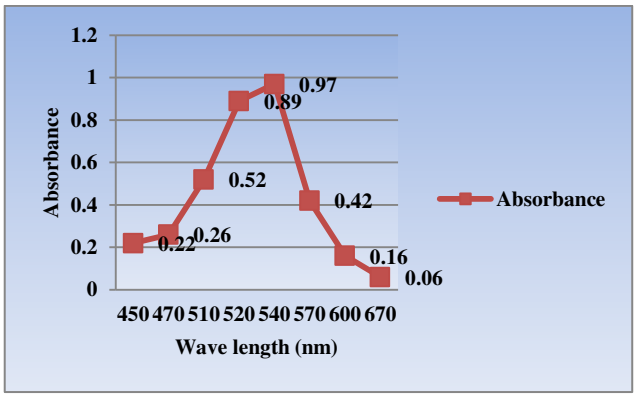

Figure 2. Determination of Lamda max of $KMnO_4$ Solution

2.3 Determination of standard plot of Absorbance vs. Concentration of Potassium Permanganate Solution (Triplicate sampling)

In triplicate, weighed accurately 0.1000 g (100 mg) of potassium permanganate and transferred in to a 100.0 ml volumetric flask. Dissolved in distilled water and made up the volume to produce 1 mg/ml (≡ 1000 µg/ml) solution (Stock solution A). From the stock solution A, pipetted 10.0 ml of the solution into a 100.0 ml volumetric flask and made up the volume to produce 100 µg/ml solution (Stock solution B). From stock solution B, various concentrations of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 µg/ml solutions were prepared and subjected to visible spectroscopy at λ_{max} = 540 nm for determining the corresponding absorbances. Table 2, Figure 3 illustrates the Mean Absorbance vs. Concentration of $KMnO_4$. Using MS Office Excel, a best fit line with respect to line passing through origin and line with respect to intercept were determined and it has been observed the equations of the best fit lines as y=0.099x with R^2 = 0.980 (r=0.9899) and as y=0.090x+0.062 with R^2 = 0.992 (r=0.9959) respectively. Among the best fit lines, a line passing through origin is preferred and hence calculations were made with respect to the experimental using y=0.099x.

Table 2: Determination of Absorbance vs. Concentration of $KMnO_4$ (at 540 nm)

Concentration (µg/ml)	Absorbance 1	Absorbance 2	Absorbance 3	Mean	Mean ± SD
10	0.12	0.12	0.12	0.12	0.12 ± 0
20	0.22	0.23	0.23	0.23	0.23 ± 0.006
30	0.33	0.34	0.33	0.33	0.33 ± 0.006
40	0.44	0.45	0.45	0.45	0.45 ± 0.006
50	0.53	0.55	0.53	0.54	0.54 ± 0.012

60	0.63	0.64	0.63	0.63	0.63 ± 0.006
70	0.71	0.73	0.72	0.72	0.72 ± 0.01
80	0.79	0.8	0.78	0.79	0.79 ± 0.01
90	0.86	0.88	0.86	0.87	0.87 ± 0.012
100	0.92	0.94	0.92	0.93	0.93 ± 0.012

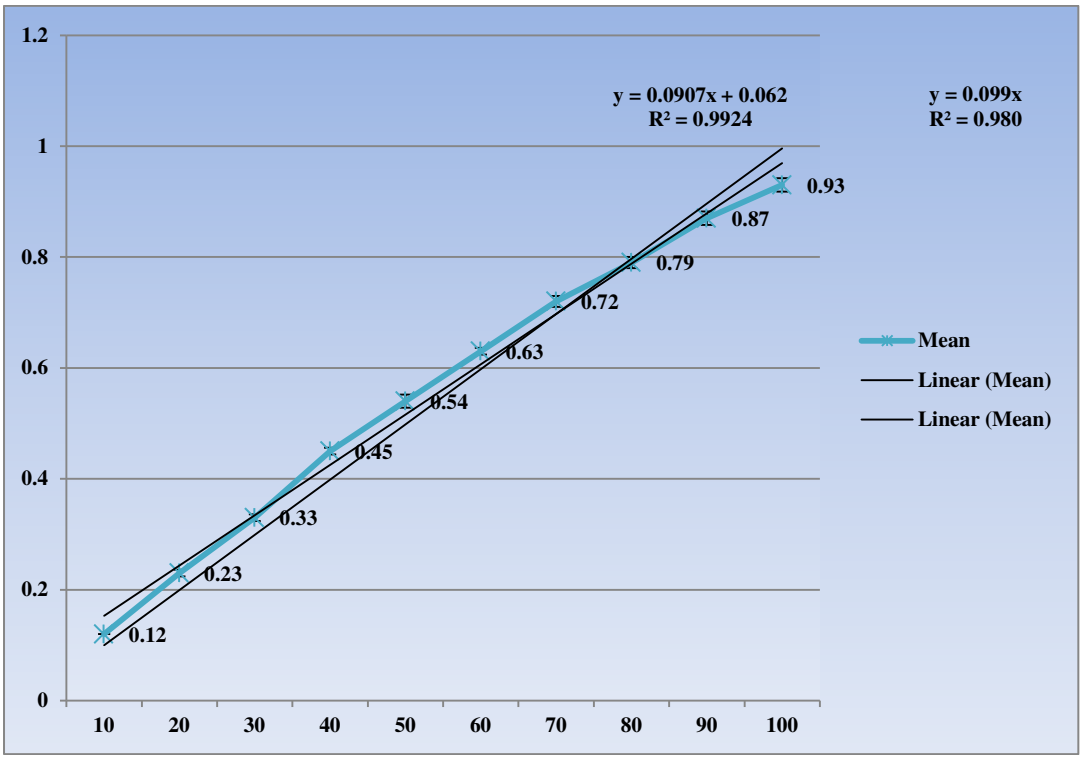

Figure 3. Standard Plot of $KMnO_4$ (at 540 nm)-Triplicate Study (Absorbance vs. Concentration-µg/ml)

2.4 Determination of Blending procedure

Weighed accurately 10 g of Potassium permanganate and blended in a double cone blender with 100 g of Starch at ten rotations per minute for one hour. To the resulting mixture, 100 g of Starch was added and blended for one hour. To the resulting mixture, 200 g of Starch was added and blended for one hour. To the resulting mixture, 400 g of Starch was added and blended for one hour. Finally, the left over 200 g of Starch was added and blended for one hour. Every resulting mixture was quantitatively analyzed at respective one hour intervals. After complete additions, the resulting mixture was further blended at one hour intervals for ensuring uniformity of blending. Table 3, Figure 4, illustrates the sampling drawn and the respective quantitative estimations. It has been observed that, Figure 4, a sudden drop in the concentration of $KMnO_4$, after 3 hours blending (from about 0.7 mg to about 0.08 mg of $KMnO_4$ per mg of blended powder). After the 11^{th}, 12^{th}, 13^{th} and 14^{th} hours of blending, the sample was drawn for six times each, for ensuring uniformity in the entire powder. It has been observed that deviations in dispersion of active ingredient, Table 3, indicating 0.08 ± 0.025 mg $KMnO_4$ per mg of final blended powder.

Table 3: Intervals of Samples drawn from Hand operated Double Cone Blender (At fixed rpm of 10 rotations per minute)

Time (hrs)	Quantity of $KMnO_4$ (g)	Quantity of Starch added (g)	Cumulative Quantity of Starch added (g)	Sample Drawn (Yes/No)	Sample Taken	Absorbance at 540 nm		Quantity of $KMnO_4$ (mg) per 50 mg powder	Quantity of $KMnO_4$ (mg) per mg	Mean	Standard Deviation
						For 50.0 mg powder in 10.0 ml water (after blending)	After dilution (1.0 ml to 10.0 ml with water)				
0	10.0 g	100 g	100 g	No	---	---	---	---	---	---	---
1 hrs	---	100 g	200 g	Yes	**After 1 hr**	1.46	0.35	35.35	0.71	---	---
2 hrs	---	200 g	400 g	Yes	**After 2 hrs**	1.39	0.29	29.29	0.59	---	---
3 hrs	---	400 g	800 g	Yes	**After 3 hrs**	0.65	---	6.57	0.13	---	---

4 hrs	---	200 g	1000 g	Yes	**After 4 hrs**	0.38	---	3.84	0.08	---	---
5 hrs	---	---	---	Yes	**After 5 hrs**	0.19	---	1.92	0.04	---	---
6 hrs	---	---	---	Yes	**After 6 hrs**	0.31	---	3.13	0.06	---	---
7 hrs	---	---	---	Yes	**After 7 hrs**	0.37	---	3.74	0.07	---	---
8 hrs	---	---	---	Yes	**After 8 hrs**	0.17	---	1.72	0.03	---	---
9 hrs	---	---	---	Yes	**After 9 hrs**	0.46	---	4.65	0.09	---	---
10hrs	---	---	---	Yes	**After 10 hrs**	0.62	---	6.26	0.13	---	---
11 hrs	---	---	---	Yes (six samples for ensuring uniform distribution of $KMnO_4$)	**After 11 hrs**	0.59,0.65, 0.59, 0.49, 0.37, 0.27	---	5.96, 6.57, 5.96, 4.95, 3.74, 2.73	0.12, 0.13, 0.12, 0.10, 0.07, 0.05	0.10	0.030
12 hrs	---	---	---	Yes (six samples for ensuring uniform distribution of $KMnO_4$)	**After 12 hrs**	0.37, 0.51, 0.33, 0.32, 0.33, 0.27	---	3.74, 5.15, 3.33, 3.23, 3.33, 2.73	0.07, 0.10, 0.07, 0.06, 0.07, 0.05	0.07	0.017
13 hrs	---	---	---	Yes (six samples for ensuring uniform distribution of $KMnO_4$)	**After 13 hrs**	0.45, 0.51, 0.56, 0.6, 0.45, 0.48	---	4.55, 5.15, 5.66, 6.06, 4.55, 4.85	0.09, 0.10, 0.11, 0.12, 0.09, 0.10	0.10	0.012
---	---	---	---	Yes (six samples for ensuring uniform distribution of $KMnO_4$)	**After 14 hrs**	0.34, 0.5, 0.44, 0.25, 0.6, 0.36	---	3.43, 5.05, 4.44, 2.53, 6.06, 3.64	0.07, 0.10, 0.09, 0.05, 0.12, 0.07	0.08	0.025

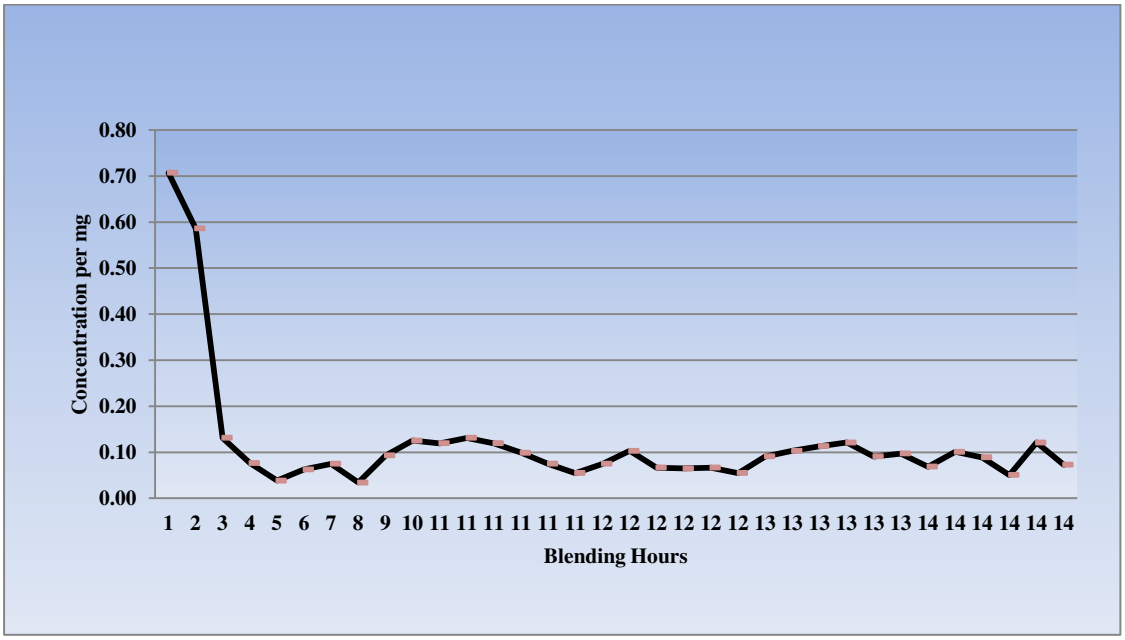

Figure 4. Trend in Dispersion of $KMnO_4$ (Concentration -per mg vs. Blending Hours)

3. Results and Discussion

When two coloured powder substances were blended, Figure 5, and ensured for visible uniformity, of the colour dispersion (purple colour of potassium permanganate-assumed active ingredient) with diluent (off-white colour of starch-diluent), it seems to be appearing that the active

ingredient dispersed uniformly with the diluent, Figure 6, 7. After geometric dilutions of Potassium permanganate with Starch (10g: 1000 g i.e., 1 percent), the end concentration of potassium permanganate is in the range of 0.08 ± 0.025 mg per mg of blended powder.

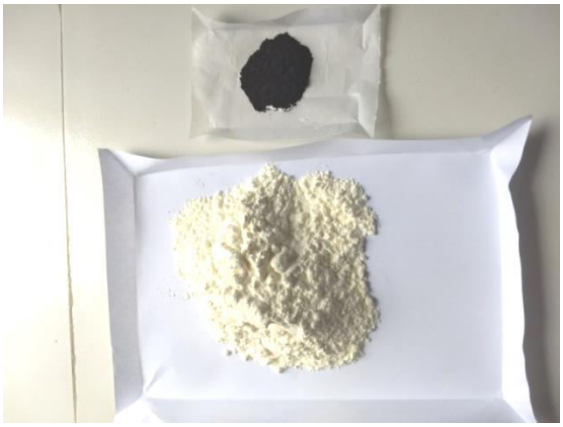

Figure 5. Potassium Permanganate and Starch Powders at Zero Time

Figure 6. Potassium Permanganate and Starch Powders Mixture after One hour Blending

Figure 7. Potassium Permanganate and Starch Powders Mixture after 14 hour Blending

4. Conclusion

Double cone blender is one of the types of blenders widely used in pharmaceutical industry. The available hand operated double cone blender is used for academic, awareness purpose, at the student level and the current procedure requires at least 14 hours of rotations for achieving uniformity of active ingredient distribution in the diluent. Yet, several experimentations are necessary to ensure only geometric progression method is the best choice for potent drugs for a hand operated double cone blender operations.

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Conflict of interest

The authors declare no conflicts of interest.

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