Drying as a Unit Operation in the Pharmaceutical Industry I

Drying of Tablet Granulations in Fluidized Beds

By M. W. SCOTT, H. A. LIEBERMAN, A. S. RANKELL, F. S. CHOW, and G. W. JOHNSTON

The results of drying tests in a fluidized bed and a tray dryer are reported for typical tablet granulations. The data are analyzed to give estimates of total drying times, rates of drying, and overall heat transfer coefficients in each unit. It is concluded that fluidized bed drying of tablet granulations is at least 15 times faster than tray drying procedures. Additional factors, such as capacities per unit floor space, operating costs and thermal efficiencies are reviewed and illustrate other advantages of the fluidization technique.

DRYING procedures, like other important unit operations in pharmacy, such as size reduction, solids blending and liquid agitation, have received little attention in pharmaceutical literature. Within recent years, however, growing interest in these pharmaceutical engineering areas has become apparent. This report on fluidized bed drying is one in a series by the authors in this new investigative field of pharmacy.

Fluidization operations, although relatively unexplored in pharmacy, have been firmly established on a broad scale in other industries. Textbooks and other extensive references on fluidization have been published during the past 20 years (1–5). However, relatively few reports have appeared on the applications of fluidized beds to materials of pharmaceutical interest (6–10).

Fluidized bed drying of coal, sand, plastics, and numerous other materials have been discussed in technical literature (11–14). These studies show that high heat transfer, mass transfer and drying rates are obtainable in fluidization systems. As a result of turbulence and excellent interphase contact, uniform bed temperatures are readily achieved. Product temperatures also are controllable over narrow limits within the fluidized bed. These reported advantages would appear to have particular importance in processing pharmaceuticals. It is surprising to note, therefore, that no studies on fluidized bed drying have appeared in pharmaceutical literature.

The object of the work conducted in the present report was to investigate the applications, advantages, and limitations of fluidization techniques in drying pharmaceutical tablet granulations. A representative, commercially available, fluidized bed dryer was used for these studies. Comparative data were obtained from drying tests with a conventional tray dryer.

EXPERIMENTAL

Materials.—Two tablet granulations were used in this study. The first was a lactose placebo made with a solution of methylcellulose as the binding agent. This granulation was prepared also with added color (FD&C No. 1 Red). The second test granulation was an antacid consisting primarily of magnesium trisilicate with syrup as the binding agent. These granulations were prepared by conventional techniques and screened through a standard No. 4 sieve before drying.

Equipment.—The fluidized bed dryer used in this work was the Glatt dryer, laboratory model TR-5.[1] Figure 1 gives an illustration of the equipment, which consists of a fan, a drying chamber fitted with a wire mesh support for the granulation, a bag dust collector, an air filter, and electrical heating elements. Controls are provided for adjustment of air flow (by damper settings) and inlet air temperatures.

The instrument operates by forcing, by induced draft, heated air through the drying chamber at

Received March 5, 1962, from the Department of Pharmaceutical Technology, Warner-Lambert Research Institute, Warner-Lambert Pharmaceutical Co., Morris Plains, N. J.
Accepted for publication June 15, 1962.
Presented to Section Np, National meeting of A.A.A.S., Denver, Colo., December 1961.

[1] The authors express their appreciation to the Chemical and Pharmaceutical Industry Co., Inc., New York, N. Y., for loan of the Glatt dryer, manufactured by Werner Glatt, Inc., West Germany.

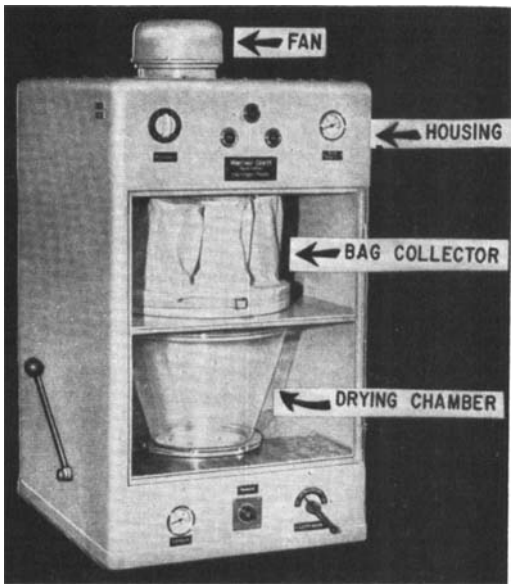

Fig. 1.—Glatt TR-5 dryer.

velocities which are sufficient to fluidize the granulation charged in the chamber. The air escapes through the bag collectors and is vented through an exit port. Granulation is quickly charged and discharged from the drying chamber by dumping. The Glatt dryer was modified for this study by attaching auxiliary thermometers within the drying chamber and immediately outside the dust collector bag.

The tray dryer used in these experiments was a Stokes dryer, model 38A, fitted with 16 shelves and automatic thermostat controls. Damper positions for air recirculation were set in accordance with the manufacturer's recommended operating directions. Air temperatures were measured with auxiliary thermometers installed within the inlet and outlet air ducts. Bed temperatures were obtained from thermometers inserted into the granulation on the bottom, middle, and top trays.

Drying Methods.—All experiments were performed in an air conditioned, temperature-controlled area. Readings of relative humidity were taken throughout each run and found to be relatively constant at 40 to 45%.

Equilibrium inlet air conditions were established at the start of each fluidized bed run. All experiments were conducted with a 5-Kg. charge of wet granulation except where the load was the variable. In these latter experiments, loads of 1, 3, 5, and 7 Kg. were employed. Inlet air temperatures (3 levels) and air velocities (2 levels) were the other experimental variables studied.

Tray dryer experiments were run, using 40 Kg. of placebo granulation (full dryer capacity) as the charge. This was equally distributed by weight over each tray to give a uniform bed thickness of approximately one inch. Inlet air temperatures were varied (5 levels) in these experiments. In one drying experiment the same colored placebo test granulation was used that had been studied by the fluidized bed technique.

Product Evaluation Techniques.—Aliquots of granulation were obtained by combining at least 10 random spot samples from representative locations within each drying unit. Samples and instrument measurements were taken at 5- or 10-minute intervals in fluidized bed experiments and at hourly intervals in the tray dryer studies. Moisture analyses were performed on each sample, using a Cenco moisture balance set at 90 volts for 6 minutes. Replicate determinations established the levels of reproducibility at ±0.2%. Screen analyses were performed on 100-Gm. coned and quartered aliquots of the total dried product collected in each run. Portions of the dry granulations then were mixed with lubricant and compressed into tablets. Compression characteristics were noted for each test granulation. Tablets made from the colored placebo granulations were inspected further for mottling and overall color uniformity.

DISCUSSION OF RESULTS

Engineering Analysis of Fluidized Bed Drying.—Figure 2 presents typical data for drying the placebo and antacid granulations in the fluidized bed. Moisture contents are expressed here on a wet basis in terms of the weight loss on drying or L.O.D. values. This method of expressing moisture has been employed in the pharmaceutical industry and is defined by Eq. 1

$$\% \text{ L.O.D.} = (100)\ \frac{x}{y + x} \qquad \text{(Eq. 1)}$$

where x = weight of water, y = weight of dry solid.

L.O.D. values were obtained directly by analysis with the Cenco moisture balance. Equilibrium L.O.D. values for each drying run were obtained by inspection of the plots of L.O.D. *vs.* time. In Fig. 2, for example, the equilibrium L.O.D. for the dried placebo and antacid granulation were found to be 0.9 and 3.0%, respectively. Over the range of inlet air conditions studied, equilibrium values were found to fall in the range of 1.1 ± 0.2% for all

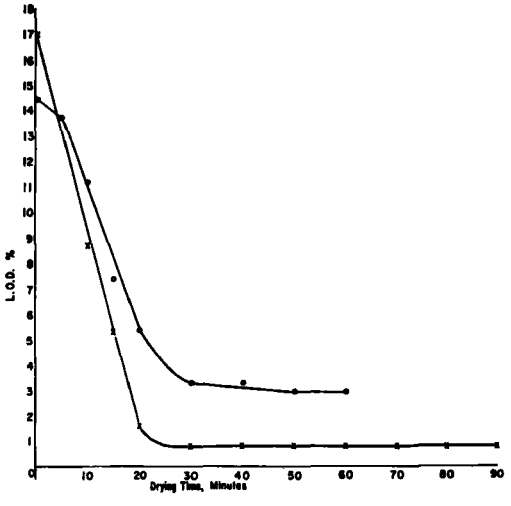

Fig. 2.—Loss on drying *versus* time for placebo and antacid granulation in fluidized beds. ×— Placebo, run 2; O— antacid, run 13.

placebo runs and 3.2 ± 0.2% for all antacid tests. These moisture levels were consistent with those desired for good compression characteristics of each granulation.

The total processing time required to dry the test granulations to their equilibrium L.O.D. values also were obtained from drying curves of the type illustrated in Fig. 2. The drying times for runs 2 and 13 were 24 and 30 minutes, respectively. For other runs in the fluidized bed, total drying times ranged from approximately 10 to 62 minutes. Table I reviews the conditions employed in these experiments and summarizes the data for fluidized bed drying. The rapidity of the fluidized bed drying technique is demonstrated by drying time results shown in Table I.

Inspection of drying data on the basis of L.O.D. values serves as a convenient starting point for comparison of drying operations. For a more detailed analysis, however, it is generally preferable to express moisture contents on a dry basis, *i.e.*, % M.C., defined by Eq. 2

$$\% \text{ M.C.} = (100)\,\frac{x}{y} \qquad \text{(Eq. 2)}$$

where x = weight of water, y = weight of dry solid.

The conversion of % L.O.D. to % M.C. is expressed by Eq. 3

$$\% \text{ M.C.} = \frac{\% \text{ L.O.D.}}{100\% - \% \text{ L.O.D.}} \qquad \text{(Eq. 3)}$$

Figure 3 gives the moisture content (% M.C.) histories for runs 2 and 13 and is representative of the other fluidized bed experiments. Estimates of drying rates were obtained from these curves by graphic determinations of slope values. Next, rates of drying were plotted as a function of drying time, as illustrated in Fig. 4. A semilogarithmic graph was employed here for better visualization of the slower drying rates. In passing, it should be noted that L.O.D. values as such cannot be used for calculation of drying rates. The basis for these values (wet basis) changes continuously as drying proceeds, thereby introducing significant errors into the rate determinations.

Data presented in Fig. 4 for run 13 (antacid) exhibit the typical rate patterns observed in drying studies (15, 16). Three major drying rate periods are apparent. The first is a period of initial rate adjustment which lasts approximately 5 minutes. This is followed by a constant drying rate period of about 15 minutes duration. Continued drying then occurs at falling rates. This last interval is referred to as the falling rate period. Similar constant and falling rate periods are seen with the placebo granulation (run 2). In this case, however, experimental demonstration of an initial rate adjustment period was not obtained.

Rate data were also examined as a function of granulation moisture content, as illustrated in Fig. 5. The various rate periods and the critical moisture content values (defined as the moisture content which terminates the constant rate period) are readily identified. For experiments 2 and 13,

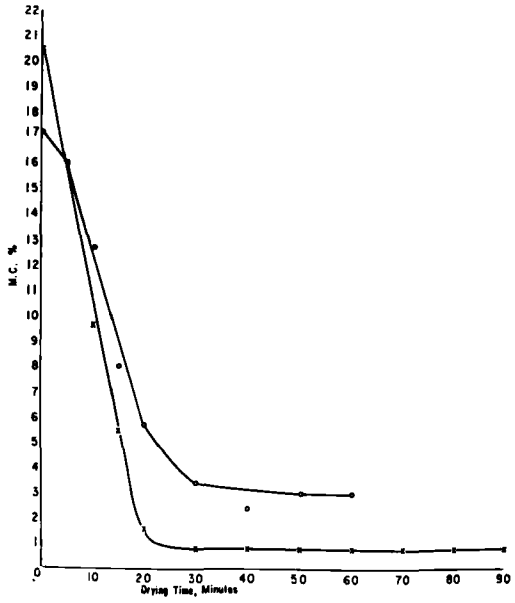

Fig. 3.—Moisture content *versus* time for placebo and antacid granulation in fluidized beds. ×— Placebo, run 2; O— antacid, run 13.

TABLE I.—DATA FOR FLUIDIZED BED DRYING

Run[a]	Bed Load on Wet Basis, Kg.	Inlet Air, °F.	Damper Setting	Time to Reach Equilibrium L.O.D.,[b] min.	Duration of Constant Rate Period, min.	Critical Moisture Content, Per Cent	Rate of Drying[c] Kg. (H_2O)/min./ Kg. (Dry Product)
1P	5	125	2	35	20	2.0	8.2×10^{-3}
2P	5	128	2	24	20	1.7	9.4×10^{-3}
3P	5	126	6	25	15	3.0	12×10^{-3}
4P	5	108	2	62	55	2.4	3.4×10^{-3}
5P	5	113	6	57	15[d]	4.0	10×10^{-3}
6P	5	139	2	25	8	7.6	14×10^{-3}
7P	5	150	6	16	13	1.4	13×10^{-3}
8P	7	129	6	38	20	3.1	7.6×10^{-3}
9P	3	129	6	18	10	2.7	16×10^{-3}
10P	1	131	6	10	5	2.0	31×10^{-3}
11A	5	115	2	60	35[d]	5.5	3.9×10^{-3}
12A	5	129	2	60	30	6.8	4.5×10^{-3}
13A	5	145	2	30	15[d]	4.9	7.4×10^{-3}
14A	5	147	2	40	22[d]	4.8	6.2×10^{-3}

[a] P = Placebo; A = Antacid. [b] Equilibrium L.O.D. values for all runs were found to be 1.1 ± 0.2% for the placebo granulation and 3.2 ± 0.2% for the antacid granulation. [c] Constant rate period. [d] Duration of initial rate adjustment period was less than 10 min. In all other runs duration was less than 5 min.

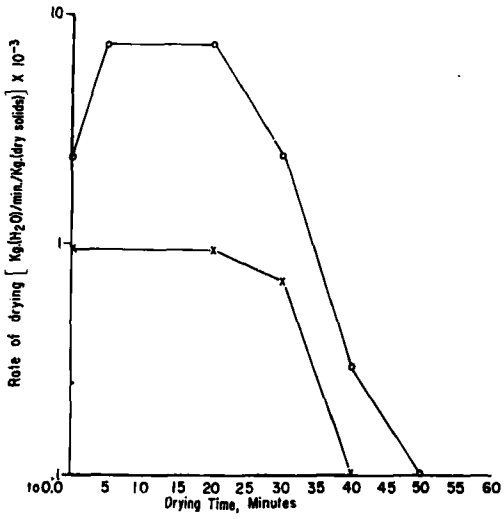

Fig. 4.—Rate of drying *versus* drying time for placebo and antacid granulation in fluidized beds. ×— Placebo, run 2; O— antacid, run 13.

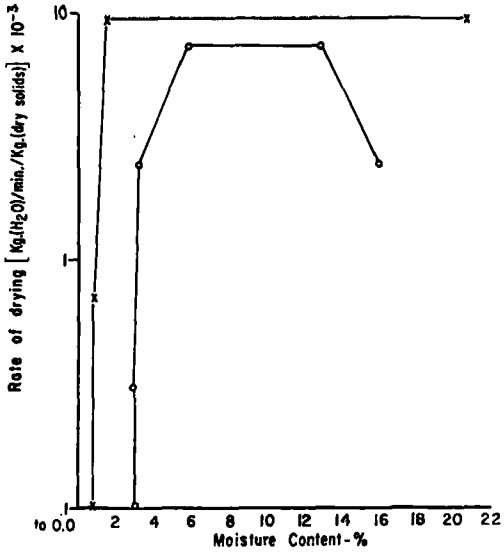

Fig. 5.—Rate of drying *versus* moisture content for placebo and antacid granulation in fluidized beds. ×— Placebo, run 2; O— antacid, run 13.

critical moisture contents were estimated at 1.7 and 4.9%, respectively. Critical moisture content values for other drying runs are listed in Table I.[2]

Theoretical mechanisms for moisture movement during each rate-of-drying period have been reviewed elsewhere (15, 16). In general, constant drying rates occur during the period when the surface of the solid is completely wet with a thin film of unbound moisture. Water that is evaporated from the surface during this interval is immediately replaced by moisture diffusing out from within the solid. Constant rates of drying are maintained so long as the rate of internal moisture diffusion equals the rate of surface evaporation. As drying proceeds, a condition eventually is reached at which the surface film of moisture can no longer be replenished completely by internal moisture diffusion. At this point (critical moisture content), the surface of the solid becomes partially dry and the rate of drying decreases. This initiates the period of falling drying rate. During the falling rate period, mass transfer (diffusion) effects within the solid control the course of drying. During the constant rate periods, external factors which influence heat transfer to the surface and mass transfer from the surface govern the operation.

Each drying period may be analyzed separately to simplify mathematical treatments and correlations of the drying variables. If the bulk of the moisture is evaporated during constant rate periods, analysis of this period alone will be sufficient for definition of the drying operation. For the experiments reported in this study, inspection of the curves of the rate of drying *vs.* moisture content, as illustrated in Fig. 5, indicated that evaporation occurred predominantly under constant rate conditions. Major emphasis, therefore, was placed on analysis of this drying period.

Data for the constant rate periods of drying are given in Table I for all fluidization runs. Rate of drying is defined by Eq. 4.

$$R = \frac{\text{M.C.}_s - \text{M.C.}_e}{\theta} \qquad \text{(Eq. 4)}$$

where R = rate of drying—Kg. (H_2O)/min./Kg. (dry solid); M.C.$_e$ = moisture content at end of constant rate period (critical moisture content)—Kg. (H_2O)/Kg. (dry solid); M.C.$_s$ = moisture content at the start of constant rate period—Kg. (H_2O)/Kg. (dry solid); θ = duration of constant rate period (minutes). All values in Eq. 4 are obtainable directly from the plots of rates of drying *vs.* drying time (Fig. 4) and rates of drying *vs.* moisture content (Fig. 5).

Constant rate values for fluidized bed drying of the placebo granulation using 5-Kg. loads ranged between 3.4 and 14 × 10^{-3} Kg. of water evaporated per minute per Kg. of dry product, as shown in Table I. Drying rates for the antacid were of the same order of magnitude. Comparison of rates of drying at approximately equal inlet air temperatures shows, however, that the placebo generally was easier to dry than the antacid granulation. This conclusion is supported further by the data for drying times listed in Table I.

As expected, increasing the bed load in the fluidization runs was found to have an adverse effect on the drying rate. This is shown in Fig. 6. The derivation of the semilogarithmic correlation obtained here is not fully understood at present. It is believed to result in part from the influence of the conical geometry of the Glatt drying chamber on the height of the bed at different charge weights.

Although drying rates decreased with increased loads, overall processing rates were shown to be highest when 5 and 7 Kg. of granulation was used as charge. In the present experiments, loading and emptying of the fluidized bed was accomplished in less than 2 minutes. This handling time was added to the drying time data listed in Table I to give

[2] Critical moisture contents are not constants, but vary from material to material and with the drying conditions employed. In general, the values are expected to be higher at increasing drying rates (15). No correlations in this direction could be established, however, in the present study.

estimates of the total cycle times. Processing rates per unit weight of product (throughput) were obtained from these values and found to reach a maximum with 5 Kg. of charge. This is in line with the manufacturer's statement of optimum load for the model TR-5 dryer.

Figure 7 shows the relationship between the duration of the constant rate period and bed load. Extrapolation of the data to 0 Kg. was used to give an estimate of the duration of the initial rate adjustment period, *i.e.*, the time when constant rate begins. An intercept value of 2.5 minutes was obtained under the inlet air conditions employed for these load experiments. The duration of this period was expected (15) and observed to change with varying inlet air temperatures.

During constant rate periods, rates of drying can be based on heat transfer relationships as shown in Eq. 5

$$R = \frac{h_t(\Delta T)}{DL\lambda} = K(\Delta T) \qquad \text{(Eq. 5)}$$

where R = rate of drying—Kg. (H_2O)/min./Kg. (dry solid); D = density of dry solid—Kg./meter^3; L = thicknes of drying solid—meter; λ = latent heat of vaporizaton—B.t.u./Kg.; h_t = total heat transfer coefficient—B.t.u./min./meter^2/° F.; K = overall transfer coefficient—Kg. (H_2O)/min./Kg. dry solid/° F; ΔT = temperature gradient between drying air and product—° F. Plots of rates of drying *vs.* ΔT are expected to give linear relationships which pass through the origin as indicated by Eq. 5. The slope of the line is numerically equal to K, the overall transfer coefficient.

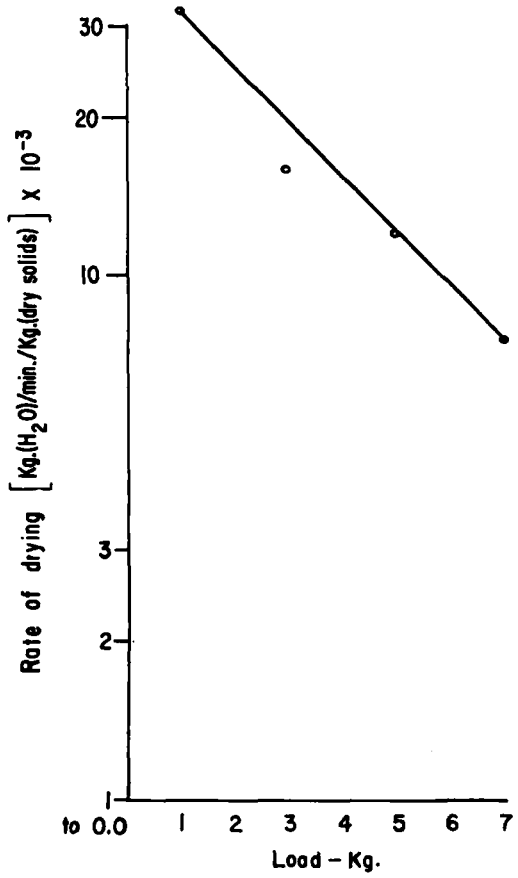

Fig. 6.—Plot of rate of fluidized bed drying *versus* bed load.

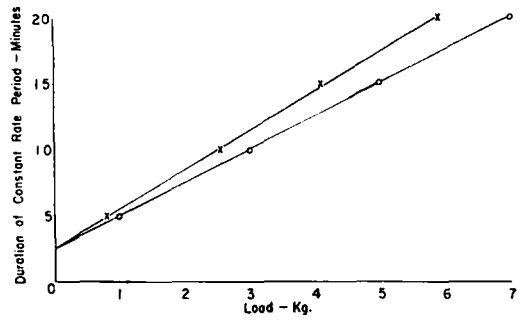

Fig. 7.—Plot of duration of constant drying rate *versus* bed load. X— Bed load expressed on dry basis; O— bed load expressed on wet basis.

Rate data for fluidized bed drying under two different inlet air velocity settings are plotted in Fig. 8. The temperature gradients used here were calculated from averaged inlet air temperatures and bed temperatures which existed during the constant rate period of drying. The linear relationship in Fig. 8 is considered satisfactory, particularly in view of the averaging procedures used in obtaining ΔT values. Results obtained for the two air velocity settings appear to follow identical relationships. This suggests that the transfer coefficient, K, is independent of air velocity settings over the range studied. Therefore, little or no increase in drying rates can be expected at the higher setting, setting 6.

The numerical value of the overall transfer coefficient obtained from the slope of the line in Fig. 8 is 2.8 × 10^{-4} Kg. of water evaporated per minute per Kg. of dry solid per ° F. This value does not compare favorably with published transfer coefficients for fluidized bed drying when all are expressed in common units (17, 18). Undoubtedly, the low Glatt value arises because the bed did not fluidize completely during all of the drying cycle. Efficient fluidization of the granulation occurred only after considerable drying had taken place. This lack of complete fluidization throughout the

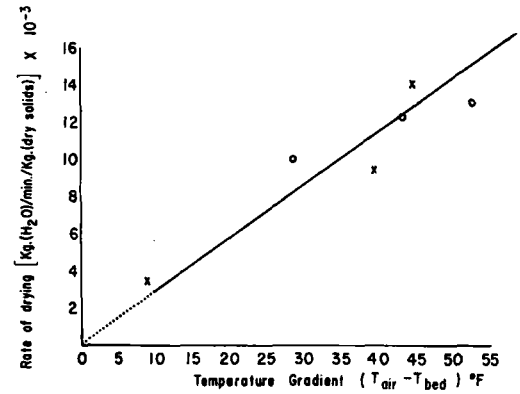

Fig. 8.—Rate of fluidized bed drying *versus* thermal gradient. O— Fan setting 6; X— fan setting 2.

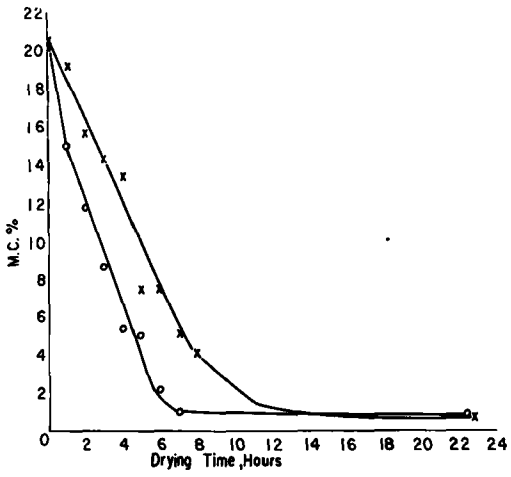

Fig. 9.—Moisture content *versus* drying time for two placebo granulations in tray dryer. X— Placebo, run 15; O— placebo, run 16.

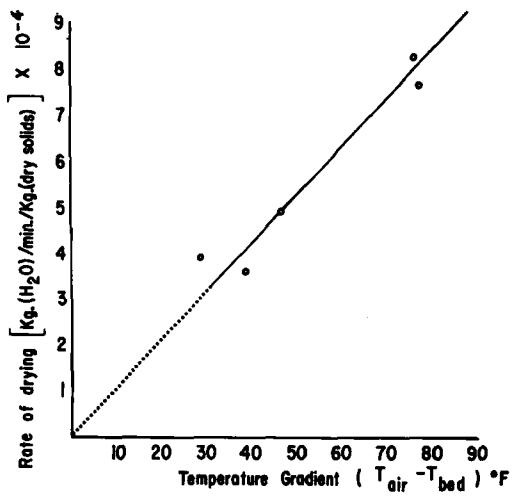

Fig. 10.—Rate of drying *versus* thermal gradient in tray dryer.

entire drying cycle represents an area for needed improvement in the Glatt equipment.

Comparison of Tray Drying and Fluidized Bed Drying.—Data collected for drying the placebo granulation in tray dryers was subjected to the same analysis techniques used above. Figure 9 illustrates moisture content histories for two typical runs. Pertinent operating and performance data for all tray experiments are summarized in Table II. Results of the present study show that drying times ranging from about 330 to 720 minutes are required in tray drying operations. These values are significantly higher (by a factor of about 20) than those observed in fluidized bed drying. Direct comparisons of the two operations on the basis of drying times alone are not completely valid, however, because different loads are handled in each unit.

Meaningful comparisons of tray and fluidized bed drying can be obtained using rate data which have been expressed on a common weight basis as listed in Tables I and II. Rates of tray drying during the constant rate period were found to be in the range of 3.6–8.2 $\times 10^{-4}$ Kg. of water evaporated per minute per Kg. of dry solid (Table II). These rates are approximately 15 times lower than those obtained in the fluidized bed drying and again indicate the comparative rapidity of the fluidization technique.

Rates of tray drying noted above are equal to 0.02–0.05 when expressed in units of lb. of water evaporated per hour per lb. of dry solid. These constant rate values fall toward the lower side of the range (0.1–2.0 lb. per hour per lb.) previously reported for tray drying (19). Overall rates of tray drying have been reported also (15), and fall between 0.03–0.30 lb. of water evaporated per hour per ft.^{2} of tray surface. When calculated on this basis, the present data indicate a rate of approximately 0.02 lb. per hour per ft.^{2} which is slightly lower than expected. These results suggest, therefore, that areas for improved performance also may exist with the particular tray drying unit used here.

Figure 10 presents the plot of rate of drying *vs.* temperature gradient for the tray dryer studies. The agreement of the experimental data with the relationship expressed by Eq. 5 is satisfactory. The overall transfer coefficient determined from the slope of the line in Fig. 10 is equal to 1×10^{-5} Kg. of water evaporated per minute per Kg. dry solid per ° F. This value has the correct order of magnitude. It is lower, however, by at least a factor of 2 to 5 than the values previously reported in the literature for transfer coefficients (15).

It will be recognized that K values are independent of temperature gradient and weight of feed charge. Therefore, these coefficients also are useful indices for comparative evaluation of different drying procedures. Comparison of the transfer coefficients for the two drying operations studied in the present report shows that heat transfer is at least 28 times more effective in the fluidized bed than in the tray dryer. This is fully in accord with theoretical considerations and results from the very favorable interphase contact obtainable in fluidized beds. Relative thermal efficiencies between fluidized bed and tray drying pointed to other advantages of the fluidization technique in this study.

TABLE II.—ANALYSIS OF DATA FOR TRAY DRYING OF PLACEBO GRANULATION[a]

Run	Average Inlet Air Temperature, ° F.	Drying Time to Reach Equilibrium L.O.D., min.	Duration of Constant Rate Period, min.	Critical Moisture Content, Per Cent	Rate of Drying During Constant Rate Period Kg. (H_2O)/min./Kg. Dry Solid
15	131	720	420	5.3	3.6×10^{-4}
16	140	420	270[c]	3.3	4.5×10^{-4}
17	160	480	240[c]	3.2	4.9×10^{-4}
18	177	430	180	6.8	7.6×10^{-4}
19	191	330	216	3.2	8.2×10^{-4}

[a] Data for 40 Kg. charge to dryer. [b] Equilibrium L.O.D. values for all runs were found equal to 1.1 ± 0.2%. [c] Constant rate period began after 60-minute interval initial of rate adjustment.

Thermal efficiency was defined as the ratio of the minimum thermal energy theoretically required to dry the solid to the actual thermal energy used in the drying unit.[3] For the present experiments, a 2–6 fold advantage in thermal efficiency was determined for the fluidized bed operation. This can be related directly to potential fuel cost savings obtainable with the fluid bed.

Other Considerations.—Several additional advantages of fluidization techniques which have direct importance in the drying of tablet granulations were apparent in this study. Firstly, fluidized beds are turbulent systems which give rise to good mixing effects. As a consequence, uniform bed temperatures (product temperatures) are readily achieved and easily controlled. With a properly designed unit, local areas of overheating can be completely eliminated. In tray drying procedures, however, nonuniform tray and product temperatures are the rule rather than the exception. For example, in the present study it was observed that tray temperatures varied as much as ±7° from location to location within the dryer. The close control of product temperature in fluidized bed drying suggests that the operation will be particularly suited for processing heat-sensitive materials and granulations which tend to case harden.

Tablets made from granulations dried in the fluidized bed compared favorably in all respects to those made from tray dried granulations. Visual inspection of tablets made from the colored granulations showed further that improved color uniformity is obtained with the fluidized bed granulation.

Agitation and product turnover are inherent in fluidization. As a consequence, opportunities appeared to exist for blending lubricants and other materials with the dry granulation within the fluidized bed itself. The use of the fluidized bed for the blending of solids has been reported previously (20, 21), and this aspect was not explored further in the present study.

For tray drying procedures, it is generally agreed that the labor involved in loading and unloading represents about one-third of the total operating costs (15). About one man-hour was required for these steps in the present experiments. In comparison charging and emptying the fluidized bed dryer was completed in less than two minutes. On this basis, therefore, fluidized bed drying offers significant opportunities for reductions in labor costs.

Caking of the granulation was observed at the start of several of the fluidization runs. In one experiment (not reported in Table I), severe caking was noted when using a slightly overwet granulation. This decreased drying rates significantly and led to the development of many oversized granules. The results of this single experiment suggest, therefore, that tacky granulations may pose special difficulties in fluidized bed drying. Friable and dusty granulations also may be troublesome because of their tendency to clog the bag collectors.

In the majority of the fluidization experiments reported here, only small amounts of oversize granules (larger than 10 mesh) were present in the final dried product. The bulk of the granulation was suitably sized for compression without additional grinding operations. The elimination of this post-drying grinding step represents an important advantage of the fluidized bed technique.

The present experiments indicate that fluidized drying of tablet granulations may require special control of drying times. Turbulence in the fluidized bed was found to give varying degrees of particle attrition. These attrition effects became particularly significant when fluidization was continued for extended time intervals with dry granulations. The degree of attrition also was found to increase at the higher air velocity, damper setting 6. For example, in run 1 at damper setting 2, the final dry granulation contained 9.3% fines (less than 60 mesh) with 15% of the granulation larger than 10 mesh. At damper setting 6 (run 3), no particles larger than 10 mesh were present while fines increased to 15%. Under usual operating conditions, however, good reproducibility of granulation size distribution was readily obtainable.

A Glatt fluidized bed dryer of about 30 Kg. wet load capacity occupies slightly less floor space than the 40 Kg. tray dryer. It is reasonable to assume that with proper scale-up, drying times in the larger fluidized bed can be maintained at one-half hour. Production rates per unit floor space will be expected, therefore, to be at least 15 times higher than those obtainable by tray dryers.

CONCLUSIONS

The results of this study show that the fluidized bed dryer offers significant advantages over the conventional tray dryer commonly used in the pharmaceutical industry. These advantages are not limited to the particular commercial unit tested in this report but rather arise from the inherent qualities and characteristics of the fluidization process itself. These advantages include:

1. Increased rates of drying and product throughput, accompanied by significant improvements in thermal efficiency.
2. Increased drying capacities per unit floor space.
3. Increased ability to control product tem-

---

[3] Thermal efficiency $= (100)\dfrac{E_T}{E_A}$ (Eq. 6)

E_T = minimum energy input theoretically required to dry the solid in B.t.u./min., while E_A = actual energy input used by the unit in drying the solid in B.t.u./min. E_T values for Eq. 6 were obtained from Eq. 7

$$E_T = (W)(\lambda) \quad \text{(Eq. 7)}$$

where W = water evaporated per minute in drying solid to equilibrium M.C.—Kg./min., λ = latent heat of vaporization for water—B.t.u./Kg. The values of E_A required for Eq. 6 were calculated from Eq. 8.

$$E_A = (C_p)V\rho\Delta T \quad \text{(Eq. 8)}$$

where C_p = heat capacity of air—$\dfrac{\text{B.t.u.}}{\text{lb.}\,^\circ\text{F.}}$,

V = air velocity through dryer—C.F.M. $\dfrac{(\text{ft.}^3)}{(\text{minute})}$ (air velocities can be approximated from the manufacturer's stated operating values); ρ = density of air—$\dfrac{\text{lb.}}{\text{ft.}^3}$; ΔT = temperature gradient between ambient air temperature and averaged temperature of heated air at inlet to drying compartment—°F.

perature during drying, thereby reducing color bleeding and case hardening effects, and facilitating the handling of heat sensitive materials.

4. Decreased handling costs resulting from simplified loading and unloading operations.

5. Simplification of tablet manufacturing procedures by the possible elimination of grinding steps. Opportunities may also exist for blending lubricants and other materials into dry granulations directly in the fluidized bed.

Fluidized drying beds of small capacity appear to have further significant usefulness in research operations for routine testing of new tablet formulas on a rapid basis.

Because of the extensive application in other industries of the fluidized bed drying technique, it is reasonable to assume that the conclusions of this report are not limited to the prototype granulations actually tested. The Glatt dryer used in this study represents a significant improvement over conventional tray dryers. The present data suggest, however, that the drying performance of this unit is not as high as that which can be expected from fluidized bed dryers.

REFERENCES

(1) Zenz, F. A., and Othmer, D. F., "Fluidization and Fluid Particle Systems," Reinhold Publishing Co., New York, N. Y., 1960.
(2) Othmer, D. F., "Fluidization in Practice," Reinhold Publishing Co., New York, N. Y., 1956.
(3) McCabe, W. L., and Smith, J. C., "Unit Operations of Chemical Engineering," McGraw-Hill Book Co., New York, N. Y., 1956, pp. 262–270.
(4) McAdams, W. H., "Heat Transmission," McGraw-Hill Book Co., New York, N. Y., 1954, pp. 299–307.
(5) Perry, J. H., "Chemical Engineers' Handbook," 3rd ed., McGraw-Hill Book Co., New York, N. Y., 1950, pp. 1618–1619.
(6) Wurster, D. E. (to Wisconsin Alumni Research Foundation), U. S. pat. 2,648,609 (1953).
(7) Wurster, D. E. (to Wisconsin Alumni Research Foundation), U. S. pat. 2,799,241 (1957).
(8) Mesnard, H. W., Rosen, E., and Scott, M. W. (to Smith Kline and French Laboratories), U. S. pat. 2,986, 475 (1958).
(9) Wurster, D. E., THIS JOURNAL, 48, 451(1959).
(10) Singiser, R. E., and Lowenthal, W., *ibid.*, 50, 168 (1961).
(11) Wall, C. J., and Ash, W. J., *Ind. Eng. Chem.*, 41, 1247 (1949).
(12) Beeken, D. W., *Ind. Chemist*, 34, 329(1958).
(13) Beeken, D. W., *Brit. Chem. Eng.*, 5, 484(1960).
(14) Wender, L., and Cooper, G. T., *A.I.Ch.E. J.*, 4, 15 (1958).
(15) Perry, J. H., *op. cit.*, pp. 800–875.
(16) Badger, W. L. and Banchero, J. T., "Introduction to Chemical Engineering," McGraw-Hill Book Co., New York, N. Y., 1955, pp. 491–501.
(17) Mickley, H. S., and Trilling, C. A., *Ind. Eng. Chem.*, 41, 1135(1949).
(18) Heertjes, P. M., and McKibbins, S. W., *Chem. Eng. Sci.*, 5, 161(1956).
(19) Marshall, W. P., *Chem. Can.*, 7, 37(1955).
(20) Tailby, S. R., and Cocguerel, M. A. T., *Trans. Inst. Chem. Engrs. (London)*, 3, 195(1961).
(21) Sutherland, K. S., *ibid.*, 3, 188(1961).

Psychophysical Concept of Color

By ALLAN M. RAFF

Color has been defined as a psychophysical concept by the Committee on Colorimetry of the Optical Society of America. The concept of the Commission Internationale de l'Eclairage (C.I.E.) standard human observer is discussed, which illustrates the color sensitivity curves on which the C.I.E. color triangle is based. Examples are given which show the variance in results that occur in color stability studies when a "standard observer" is used as opposed to an evaluation made solely on the basis of spectrophotometric data. Several standard techniques for evaluating small color differences are reviewed.

WITHIN the last several years the stability studies of pharmaceutical products have become increasingly more sophisticated. The use of kinetics, cyclization of temperatures, and more advanced forms of instrumentation are just a few of the things that have brought the study of the chemical stability of pharmaceutical products to a very high level.

This same high level has yet to be reached in the matter of color stability studies. This deficiency may be due to two causes. The first cause has been a lack of the need for such studies until recent times. Until the FDA decertified some dyes and indicated a prospect for the decertification of several more, the pharmaceutical formulator had a relatively easy task. He had only to choose the most stable dye from a long list of dyes and color his product. Today he has the task of determining which of several very photosensitive dyes is the most stable. He must also make matches of colors heretofore achieved with one dye (perhaps now decertified), now with different colorants. The second cause of the deficiency noted is due in a very large part to a complete misunderstanding of the concept of color as it should be used in pharmaceutical stability studies.

Received March 29, 1962, from the Manufacturing Division of Smith Kline & French Laboratories, Philadelphia, Pa.
Accepted for publication June 7, 1962.
Presented to the Scientific Section, A.PH.A., Las Vegas meeting, March 1962.