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RECORDING POWDER FLOW METERS and THEIR USE IN PHARMACEUTICAL TECHNOLOGY

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ABSTRACT

Recording Powder Flowmeters (RPF) have received relatively little attention in the literature. This paper reports on a modified RPF which utilizes a Mettler PR-1200 electronic balance rather than the traditional specifically fabricated flowmeter. The versatility of this modification is discussed as a cost effective modification. This modification provides for the use of RPF's in many areas of pharmaceutical technology. The reproducibility of RPF data with its sensitivity to processing and formulation variables has been investigated. Suggestions for the application of RPF data in quality control, preformulation and other research areas of pharmaceutical manufacturing are discussed.

INTRODUCTION

The evaluation of powder properties has become increasingly important in many industries. Manufacturing operations for food, pigments, fertilizers, building materials, and many other major products involve powders. (1) The pharmaceutical industry has for many years recognized the importance of powder properties. Numerous investigators have examined these properties and various methods have been developed to quantitate the fundamental properties of particles and collections of particles. (2) Derived properties of powders, i.e., those concerned with the practical use of powders, are diverse and complex. (2)

Through the use of derived powder properties, it is possible to study powder rheology which involves the evaluation of how fundamental particle properties affect the flow and deformation of the assemblies of discrete particles contained in a powder. Pharmaceutical formulators have long sought to establish simple predictive tests of powder flow. The necessity of these tests has been stated numerous times in the literature. It is obvious now that, in many pharmaceutical manufacturing operations, the ability to predict possible problems due to powder flow will aid in the production of a more effective, safer, and less expensive medicinal product.

Hence, various methods have been developed to predict powder flow. The repose angles of powders, determined crudely by heaping on spatulas (3) or by more complex methods (4-10) have been commonly used to study flow. These angular measurements have been critically assessed by many authors (11-13) and it has been shown that the results of such tests are highly method dependent. Other procedures utilized to quantitate flow include timed delivery of a specified weight or volume through an orifice (8, 9, 12, 14-17), actual tabletting weight variation (12, 18-20), compressibility on tamping (3, 12, 21), and tensile strength measurements. (7, 12, 22, 24)

Recently, use of shear cells has become increasingly popular in the study of powder flow. (1, 12, 13, 22, 24-29) By the use of Jenike or annular type shear cells, investigators have made predictions concerning the flow of powders by calculating such factors as the "flow factor", cohesiveness, and effective angle of friction, from shear cell measurements.

More than a decade ago, Gold and coworkers, in a series of articles (11, 20, 30, 31) described a recording powder flowmeter (RPF), useful in measuring flow. Since then their work has often been erroneously grouped with other orifice flow techniques although it is distinctly different.

The purpose of this communication is to describe the successful use of a modified RPF and to reemphasize the value of this type of equipment in many phases of pharmaceutical manufacturing. The value of the RPF as a simple and reproducible predictor of powder flow is discussed.

EXPERIMENTAL

Materials

The powders used in this work, their manufacturers, and some relevant properties are listed in Table I. The size distribution of the powders determined by sieve analysis are listed in Table II.

Methods

Recording Powder Flowmeter Studies

Initial work was carried out on Dr. Garnet Peck's flowmeter at Purdue University. This apparatus is similar to that described by Gold. (11)

Work in our laboratory was carried out on an RPF which utilized a Mettler PR-1200 electronic top loading balance. The analog signal output from the balance was reduced with the aid of a linear potentiometer to a level suitable for input into a Perkin Elmer strip chart recorder. A number of glass funnels with various capacities and orifice sizes were utilized as hoppers. These funnels (actually designed for use in making infusions of whole leaf drugs) were supported by a ring stand over the balance and a glass plate was used to close the orifice until the flow of powder was desired. The plots obtained from the equipment are of mass flow per unit time.

Mixing

Mixing of powders was carried out in either a twinshell blender (with or without impeller bar) or an Erweka, Lotequi type Rapid Laboratory Mixer. Powders were initially mixed by blocking and dividing on a flat surface, then shaken briefly in a plastic bag before charging to the mixer for the specified period of mixing.

TABLE I
Materials and Properties

	Tapped Bulk Density	% Wt. Loss On Drying	Std. Timed Delivery Flow Rate Gm./Min.	Repose Angle
(1) Dicalcium Phosphate Dihydrate EMCOMPRESS (E. Mendell, Inc.)	1.1(7.3×10^{-3})	15.6(1.163)*	572(8.13)	35^{o}(0.8)
(2) Lactose, USP Spray Dried (Foremost McKesson)	0.8(2.5×10^{-3})	2.5(0.435)	315(3.06)	32^{o}(1.2)
(3) Mannitol, USP Granular (Atlas Chemical Co.)	0.8(8.5×10^{-3})	0.0(0.000)	802(11.61)	40^{o}(1.7)
(4) Drug (Investigational Substance)	0.5(2.8×10^{-3})	-------	NO FLOW	--------

*Material has lost water of hydration

TABLE II
Particle Size by Sieve Analysis

CUMULATIVE % RETAINED

ASTM Specified Opening	Material Number (1)	(2)	(3)	(4)
840 μ	0.0	0.0	19.3	0.0
420 μ	0.0	0.3	73.9	0.0
250 μ	12.7	4.4	93.0	4.0
177 μ	38.3	14.6	94.2	6.0
149 μ	73.5	37.5	96.6	9.5
106 μ	92.0	66.0	98.6	32.0
90 μ	99.1	88.6	99.0	59.0
75 μ	99.8	98.5	99.2	86.8

Tabletting Studies

The mixed powders were compressed on a Stokes B-2 Rotary press, with 7/16 inch punches, operating at a speed of 500 tablets per minute. Constant die volume was maintained for all materials. Samples of 100 tablets were randomly removed and weighed to obtain the coefficient of weight variation.

Sieve Analysis

A Fischer-Wheeler sieve shaker operating at an intensity of 500 cps was used to shake the sieve nests. The sieves were W.S. Tyler Co., U.S. Standard Sieves. A sample of 100 grams was charged and the nest was placed on the shaker for 20 minutes in all cases.

Loss on Drying

Moisture contents of the powders were determined by following the USP loss on drying procedure. (33) Five samples were subjected to the test.

Standard Timed Delivery Flow Studies

Orifice flow rates were determined by volume loading the same funnels used in the RPF studies. The delivery of a specified weight of material onto a glass plate mounted on a top loading balance was timed. Mass flow rates were determined for three runs of each powder The repose angles were also determined during the test. The height of the heap was measured and the base diameter determined by use of a grid mounted under the glass plate,

RESULTS AND DISCUSSION

Recording powder flowmeters (RPF's) do not seem to appear to have received much attention in the literature. Since Gold first described his flowmeter in 1966 (11) a number of commercial flowmeters have been marketed, but it is not apparent that they are in widespread use within the industry.

One criticism of RPF's may be the expense involved in buying the components necessary for building an RPF. Gold's initial RPF was manufactured for use as a flowmeter only, and the most expensive component which needed to be individually crafted was the cantilever balance. This balance converted mass to an electronic signal, directly proportional to the weight applied and linear over the range desired. This is basically the type of weighing apparatus used in the commercial flowmeters now available.

Following the advent of new technology in balance production, Cole et. al., while working on further RPF refinements for detecting variations in flow rate, reported what would be the single most important reduction of costs, in creating an RPF. (32) They utilized a commercially available Mettler electronic balance identical to the instrument we have exploited in the present work. The Mettler electronic balance fulfills the necessary sensitivity criteria and provides easily accessible linear analog signal output for connection to a suitable strip chart recorder. The only remaining part needed to begin dynamic flow studies is a suitable hopper from which the powder may flow.

Because it is possible to use commercially available electronic balances with only minor modification, it is no longer necessary to make a large capital investment in equipment dedicated solely to flow studies. It is probable that suitable electronic balances may already be available within a facility. Regardless of whether equipment exists, the investment may well be cost effective as in addition to the specialized use as flowmeters, these balances would be generally available for other routine purposes.

A further advantage the Mettler component provides is that the RPF system can now be modified to meet the needs peculiar to any given user. It would be possible to use existing production scale hoppers with the various capacities available in the electronic balances or to use scale models of actual equipment to individualize the flow studies for particular users. This hopper design versatility provides for study of powder flow in many different types of equipment. These specifically tailored designs will likely yield a greater amount of valuable information on powder flow to the user. Many will be able to determine more closely how powder flow may affect various operations and their products.

In his initial articles, Gold pointed out the value of actually recording orifice flow characteristics of powders. Because flow may be affected by many fundamental properties of powders such as: moisture content, particle size, shape, density, distribution, surface charge, etc., it is likely that graphical records of powders in dynamic motion will yield more information involved with the total interaction of these many factors.

Gold used flow studies to determine optimum formulations, and to study the effects of moisture, charge, and size distribution, on powder flow. His work was begun because "Powder flow problems encountered in this laboratory could not be satisfactorily resolved.." with other methods popular at that time. Similarly, in our work, the investment in shear cells and the complicated nature of their use, along with unsatisfactory results from other popular methods, lead us to RPF studies.

The reproducibility of RPF data for a number of systems was tested. Table III shows examples of reproducible flow rates in both a pure and a mixed binary powder. Because the flow profile of a powder is dependent on fundamental particle properties, it is characteristic and reproducible for a given system. This makes RPF data useful in numerous quality control and in-process testing situations. For instance, the supportive evidence of reproducible flow following a granulation operation would be extremely useful in process validation to prove control of that process.

The RPF is sensitive to processing variables as shown in Figure I. As the time of mixing increased, flow decreased. This phenomena may be due to a number of factors such as particle attrition, charge buildup, or more particulate coverage by the magnesium stearate which acts as a good lubricant but a poor glidant. Other processes likely to alter fundamental powder properties will also affect flow and alter RPF flow profiles.

Formulation variables were also detected by the RPF as shown in Figure II. Pharmaceutical formulators would undoubtably be aided by RPF data in their attempts to optimize formulations. This approach has been used successfully in troubleshooting a flow problem. (11)

TABLE III

REPRODUCIBILITY OF FLOW RATES

(A) PURE POWDER*

TRIAL #	FLOW RATE GM/MIN	VARIATION	
1	372.1	MEAN FLOW RATE	= 372.1
2	375.0	STANDARD DEVIATION	= 2.9
3	369.2	COEFFICIENT OF VARIATION	= 0.78%

*EMCOMPRESS (Edward Mendell Co., Inc.)

(B) MIXED POWDER SYSTEM**

TRIAL #	FLOW RATE GM/MIN	VARIATION	
1	252.6	MEAN FLOW RATE	= 247.3
2	246.1	STANDARD DEVIATION	= 7.1
3	252.6	COEFFICIENT OF VARIATION	= 2.88%

**EMCOMPRESS + 2% MAGNESIUM STEARATE
MIXING TIME = 15 min. (Erweka Laboratory Rapid Mixer SW-1)

In development stages for many products, this approach would be useful, as well as in the purchasing and quality control of incoming raw materials to be used in existing products.

Many workers have tried to correlate orifice flow rates with the weight uniformity of tablets. (12, 15) The most important factor affecting this problem is not the rate of powder flow, but the variations in flow rate that occur. This was reported by Gold and also by Cole et al when they further refined their RPF's to detect and analyze variations in flow rates. (20, 32) Cole attempted to explain a problem noted by other workers. These workers had found that in their standard timed orifice flow studies, the formulation with the fastest flow rate also exhibited the highest tablet weight variation. (15) Cole was able to show that flow rate was not correlated with the amount of variation in rate and concluded that this would explain variations noted in weight uniformity. Further work in this area is needed before any definitive conclusions can be reached.

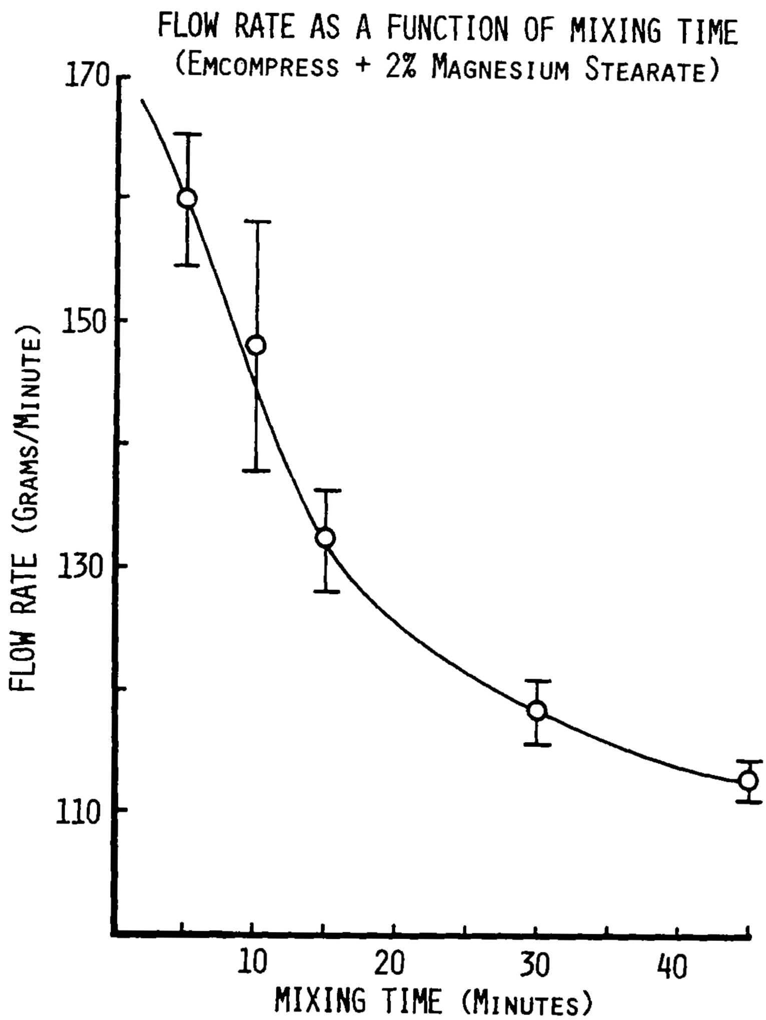


FIGURE I

We can show that flow rate is related to mean tablet weight as shown in Table IV. It might seem obvious that the fastest flow rate would yield the greatest weight tablet. Although this is true in part (A) of the table, it is not the case in part (B) where other fundamental powder properties were affected by the mixing process. Again, because orifice flow is dependent on many fundamental powder

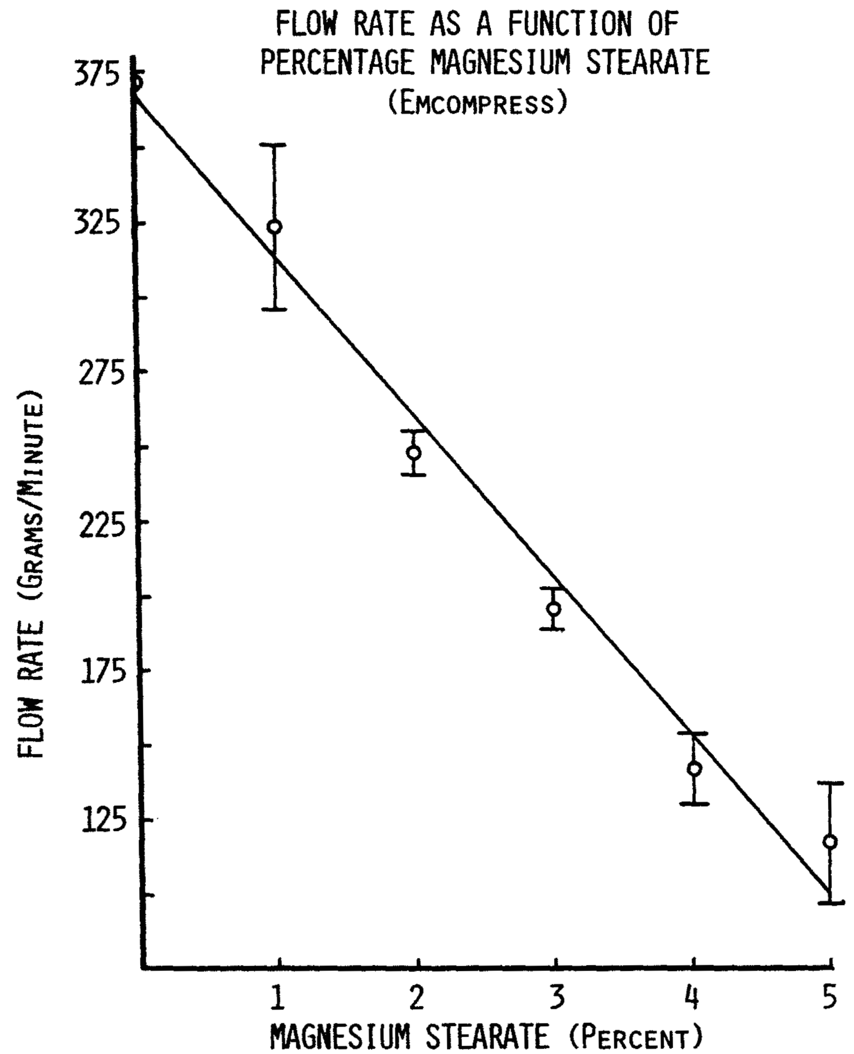


FIGURE II

properties, it is unlikely that any simple rules applicable to all systems will be developed. It can be shown that the trends noted in Table IV are most likely due to variations in flow rates. Pure powders flow in smooth regular patterns (Figure III) while the more complex a system becomes, the more likely variations are to occur in flow rates (Figure IV).

TABLE IV

RELATIONSHIP OF TABLET MEAN WEIGHT AND POWDER FLOW RATE

(A) Mg. Stearate (Percent)*	Flow Rate (Gm/Min.)	Mean Weight (Grams)	Coef. of Variation
1	323.3±17.6	714.7±5.2	0.73%
2	247.3± 7.2	714.3±4.1	0.58%
3	195.2± 6.7	704.8±3.5	0.50%
4	141.2±11.6	684.2±5.1	0.74%
5	117.1±19.8	658.4±6.8	1.04%

* QS w/ Emcompress (Edward Mendell Co. Inc.)

(B) Mixing Time (Minutes)**	Flow Rate (Gm/Min.)	Mean Weight (Grams)	Coef. of Variation
5	160.1± 5.3	698.5±3.3	0.47%
10	148.2±10.2	712.6±4.0	0.57%
15	132.4± 4.1	714.1±5.3	0.74%
30	118.5± 2.7	724.2±6.7	0.93%
45	112.9± 1.6	726.8±5.9	0.81%

**Emcompress + 2% Magnesium Stearate in Twin Shell w/ Impeller Bar

The greatest single value of an RPF is the fact that one may directly view a representation of actual mass flow. To see the variations and be able to scrutinize them or analyze them with appropriate statistics is obviously useful. These variations are the most likely key to defining product problems which develop due to flow. Figure V shows two flow graphs obtained when the present workers were investigating a formulation problem. This work was carried out on an RPF designed and made available by Dr. Garnet Peck at Purdue University. The tracings show two formulations which both flow reasonably. A hidden problem, hardly detectable with standard time orifice flow studies, was that another phenomena was occurring during the flow test. Tracing B shows a variable flow rate which developed as a trend. The concave tracing shows increasing mass flow rate over time. We conclude this was due to particulate separation occuring in the hopper due to the large particle

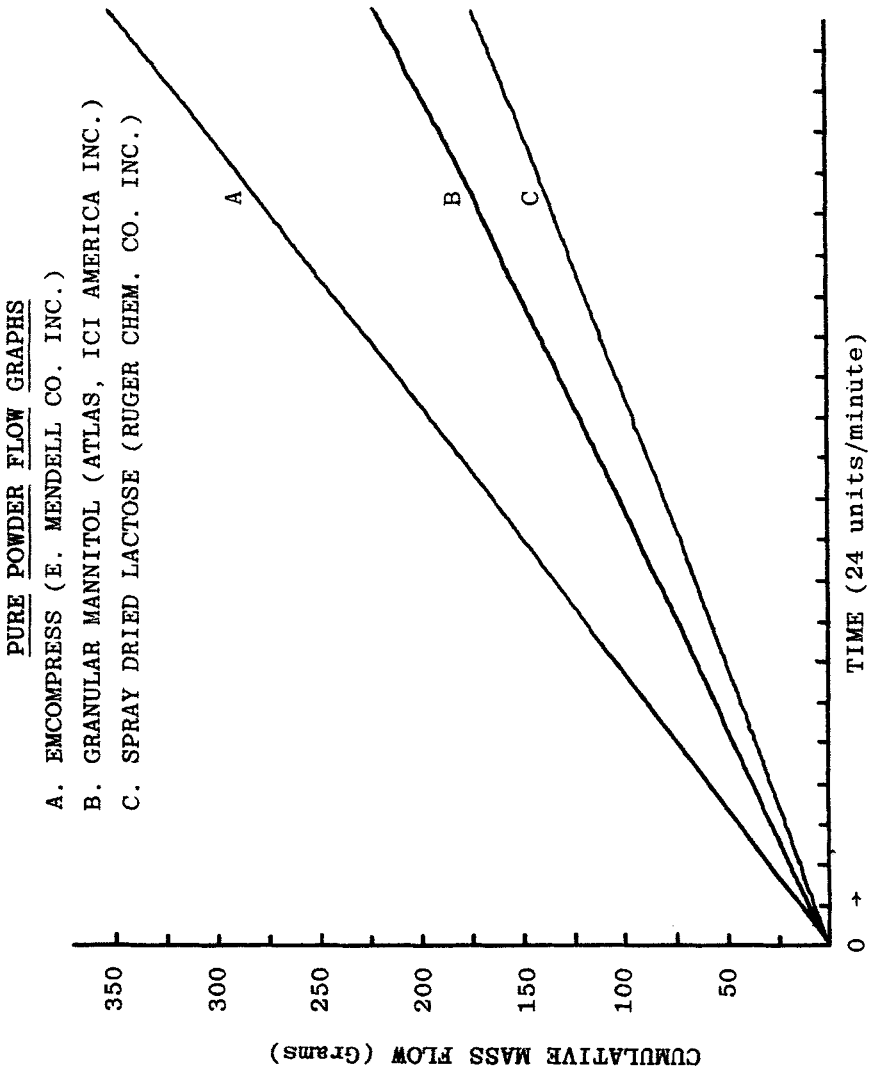

PURE POWDER FLOW GRAPHS
A. EMCOMPRESS (E. MENDELL CO. INC.)
B. GRANULAR MANNITOL (ATLAS, ICI AMERICA INC.)
C. SPRAY DRIED LACTOSE (RUGER CHEM. CO. INC.)
A
B
C
CUMULATIVE MASS FLOW (Grams)
350
300
250
200
150
100
50
0
TIME (24 units/minute)

FIGURE III

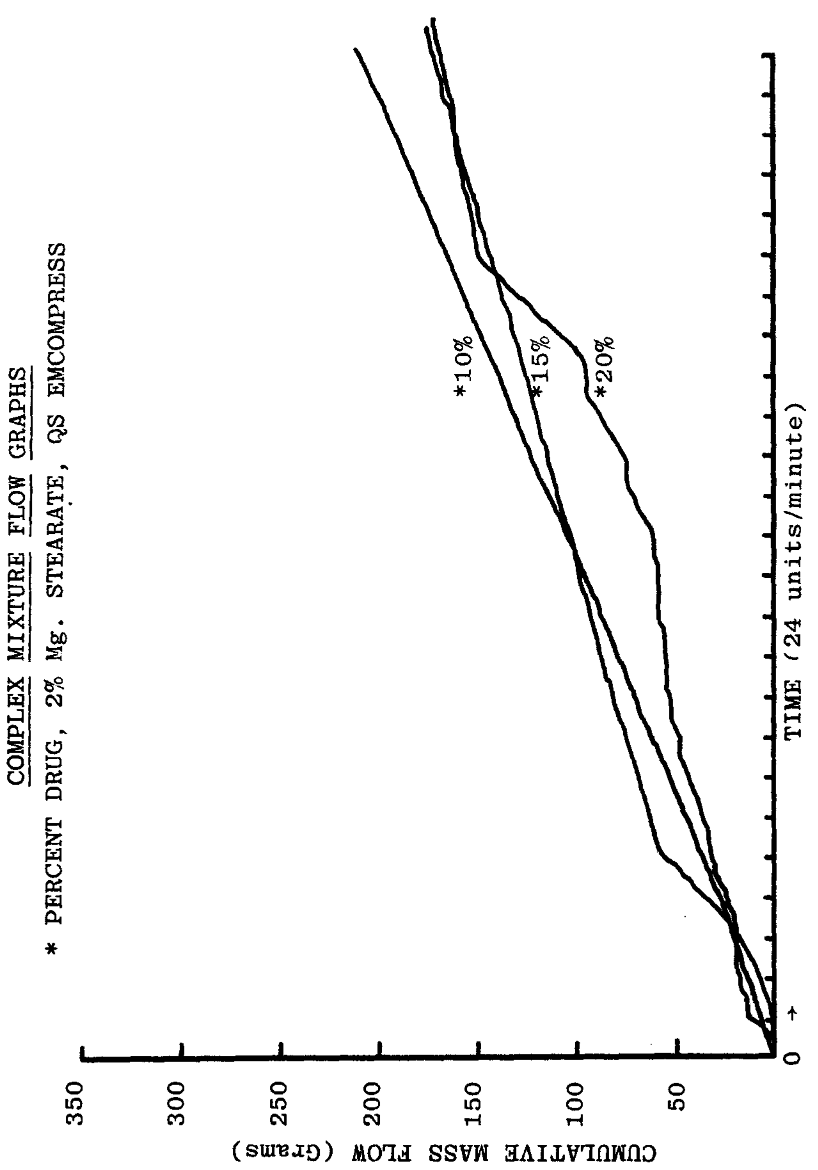
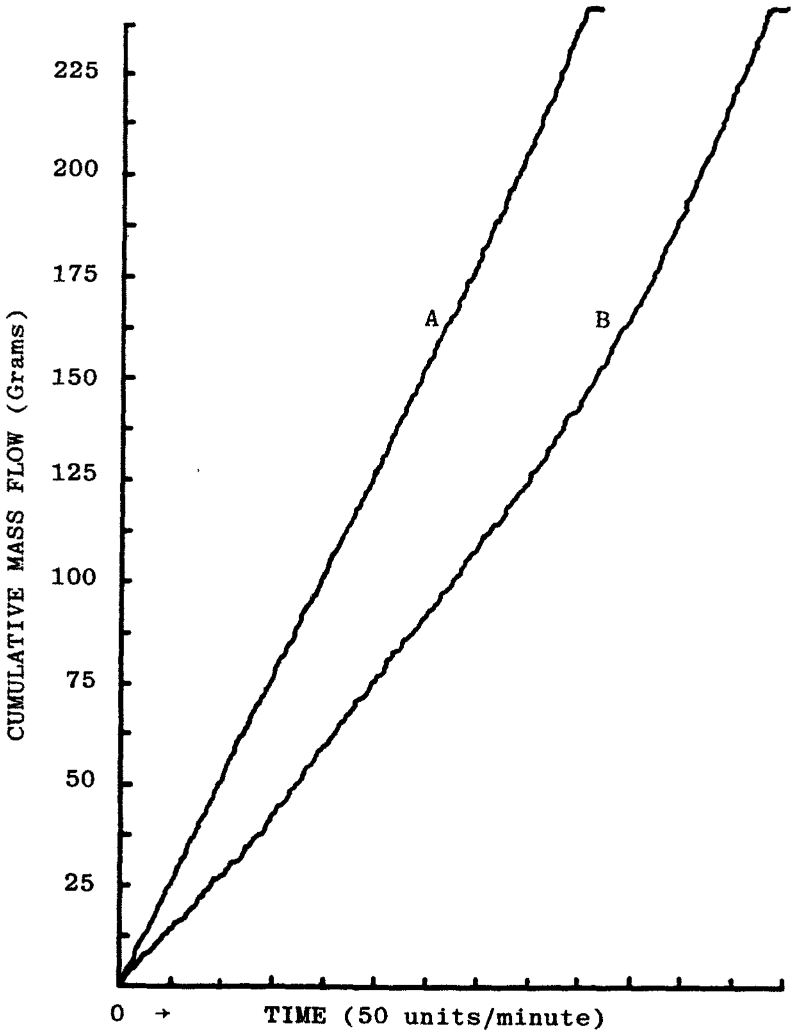

COMPLEX MIXTURE FLOW GRAPHS
* PERCENT DRUG, 2% Mg. STEARATE, QS EMCOMPRESS
*10%
*15%
*20%
350
300
250
200
150
100
50
0
CUMULATIVE MASS FLOW (Grams)
TIME (24 units/minute)

FIGURE IV

COMPLEX MIXTURE FLOW GRAPHS

A. 10% Drug, 2% Cabosil, 2% Mg. Stearate, QS Lactose SD

B. 10% Drug, 2% Cabosil, 2% Mg. Stearate, QS Gran. Manni



Data from Peck Flowmeter, Purdue University, School of Pharmacy and Pharmacal Sciences

FIGURE V

size of the mannitol. This type of variation trend was also detectable in other tracings showing convex and combination variation trends. These trends may have led to content uniformity problems in the finished product if not detected in the flow studies.

Some investigators have stated that orifice low techniques are not useful for powders with particles less than 100 microns. (13) These workers have implied that only shear cell tests can provide useful information regarding flow characteristics of cohesive powders. It is true that shear cell determinations can provide a wealth of information related to powder handling characteristics, but the complexity of the equipment required to carry out shear studies, and the crucial accuracy involved in the set up and experimentation make the simple RPF a viable apparatus for even these studies. It is not necessary to carry out numerous trials to determine the proper consolidating conditions needed for proper shear results, nor are the multiple runs needed to establish a valuable yield loci necessary when running flow studies. The complex mathematics involved in calculating useful shear cell parameters also makes it less likely that this type of equipment will be routinely used in preformulation, quality control, and in-process testing as we are proposing the RPF can.

Further it is quite possible that with further work RPF's will be used to measure even the cohesive powders in pure form. Because it is possible for these powders to flow in production situations, by use of actual production conditions in RPF studies success is likely. Since it is possible to use actual hoppers and also make the addition of suitable vibrations encountered by powders during normal production, RPF data will probably in the future yield useful data on cohesive powders as well as solve related problems in formulations such as particulate segregation in hoppers due to vibration.

CONCLUSIONS

The examples reported in this paper show that R.P.F.'s have considerable potential in the following areas:

(a) basic preformulation studies, including selection of raw materials,

(b) optimization and validation studies of formulations,

(c) in process quality controls during manufacturing,

and (d) evaluation of the design of equipment, such as mixers or hoppers.

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