DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 12(10), 1375-1393 (1986)

INSTRUMENTATION OF A VERTICAL HIGH SHEAR MIXER WITH A MOTOR SLIP MONITORING DEVICE

R. J. Timko*, J. L. Johnson†, G. W. Skinner,
S. T. Chen×, and H. A. Rosenberg

STUART PHARMACEUTICALS
Division of ICI Americas Inc.
Wilmington, Delaware 19897

ABSTRACT

The main impeller shaft of a vertical high shear mixer was instrumented with a device which measures motor slip and displays its output in percent horsepower. Response was proportional to mixer load. A warm-up period was required to minimize variability in output. High speed impeller operation showed more consistency in response than low speed impeller operation. During the

* Correspondence
† Present address is Hercules, Inc., Wilmington, Delaware
× Present address is CIBA Consumer Pharmaceuticals, Edison, New Jersey

 0363-9045/86/1210-1375$3.50/0

granulation process of the different test systems, a typical response profile showed a change in percent horsepower as the binder solution was added followed by a plateauing at about the proposed optimum mixing time. Additional studies to correlate this observation with granulation physical and compression characteristics are necessary.

INTRODUCTION

The purpose of a granulation procedure in the manufacturing process of a solid dosage form is to increase the uniformity of drug distribution, aid in improving material handling and flowability, and/or improve compression or bonding characteristics[1]. Monitoring of this step for reproducibility and optimization has generally been a subjective judgment. However, in the past two decades, there has been a growing desire for means which are capable of characterizing the granulation operation and detecting its endpoint.

A variety of instrumental techniques for this purpose have been put forth. Some monitor electronic and mechanical parameters of the granulating vessel[2-17]. Others attempt to quantify physical changes in the materials which occur during the massing process[18-22]. To date, none has been found universally acceptable for all granulations or all types of equipment.

This communication describes preliminary investigations on the use of motor slip measurements to monitor the granulation process in a vertical high shear mixer. Specifically, instrumentation of the unit along with the data on its reliability and reproducibility are presented.

EXPERIMENTAL

Instrumentation of the High Shear Mixer: A vertical high shear mixer[1] with a dual speed (875 rpm and 1750 rpm) alternating current motor was instrumented with a commercially available device[2] which is capable of detecting the slip characteristics of the motor.

1. Model MGT-70 Mixer/Granulator, Littleford Brothers, Inc., Florence, KY

2. Model 2340, Rexnord Instrument Products, Malvern, PA

This motor slip device, a motor load analyzer (MLA), as it is more traditionally referred to, consists of a magnetic sensor probe which is mounted on the shaft of the motor driving the impeller blade of the mixer, a junction box, and a signal analyzer. Signals from the sensor probe are translated into the electrical equivalent motor load and displayed as percent horsepower.

An MLA is designed to monitor motor load of a single speed alternating current induction motor. Because the high shear mixer used in this study has a dual speed motor, two MLA systems were required; one dedicated to low speed impeller operation, and one dedicated to high speed impeller operation. One sensor probe was installed with relay switches which activate the proper MLA unit depending upon the impeller speed.

Output from the MLAs was inputted to a strip chart recorder. Additionally, the MLAs were interfaced with a computer system containing software with a wide range of data analysis capabilities.

Test Systems: The response of the MLAs to load changes of materials of different bulk densities was examined using Microcrystalline Cellulose, NF[3], Lactose, NF[4], and Calcium Sulfate, NF[5]. Bulk density measurements[6] were made in triplicate. Various granulations were also used to evaluate the reliability and reproducibility of the instrumentation. It is not necessary to define the exact compositions of these granulations other than to indicate their general characteristics. There was a placebo system composed of Lactose, NF[7] and Microcrystalline Cellulose, NF granulated with either a 5% w/w aqueous povidone[8] solution or a 10% starch[9] paste dispersion. Also, there was an antihypertensive drug, microcrystalline cellulose, and povidone mixture

---

3. Avicel PH102, FMC Corporation, Newark, DE
4. Hydrous, Spray Dried Fast-Flo Grind, Foremost Whey Products, Barboo, WI
5. Anhydrous, U. S. Gypsum, Chicago, IL
6. Type TP-D Powder Characteristics Tester, Hoskawa Micromeritics Laboratory, Osaka, Japan
7. Hydrous, Regular Grind, Foremost Whey Products
8. USP, Plasdone K29-32, GAF Corporation, New York, NY
9. NF, Corn, A. E. Staley Manufacturing Company, Springfield, NJ.

granulated with Purified Water, USP. The antihypertensive compound had a low bulk density and was micronized.

RESULTS AND DISCUSSION

Motor slip is the difference between synchronous speed (no load) and operating speed (with load) of the rotating shaft. It increases with increasing motor load. During the granulation process, variations in motor load occur as the result of the changes in the physical characteristics of the materials. These variations are sensed by the probe mounted to the rotating motor shaft.

The prime advantage of an MLA over current measurement with an ammeter or power measurement with a wattmeter is its greater linearity of response over the range of motor loads. Current measurement is linear over a percent load range of about 70 to 110. At less than 70% load, the response is non-linear with only slight changes in the current reading. Thus, if the mixer is not fully loaded or if the granulation has an extremely low bulk density, there will not be much of

Table I.

No Load Baseline Trials

Average Percent Horsepower

	Low Speed							High Speed			
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 1	Day 2	Day 3	Day 4
TRIAL 1	9.9	24.9	17.9	12.8	13.9	10.6	13.9	10.8	10.4	13.4	13.3
2	12.5	23.3	--	13.8	--	12.3	13.5	9.8	9.6	12.5	12.8
3	14.1	23.0	--	15.3	--	13.6	20.9	--	9.5	12.2	12.5
4	--	--	--	21.6	--	12.9	19.5	--	12.6	13.8	13.7
5	--	--	--	20.7	--	--	18.9	--	12.1	12.5	12.8
6	--	--	--	27.2	--	--	--	--	11.9	12.2	12.0

	Low Speed	High Speed
OVERALL AVERAGE	16.8	12.0
STANDARD DEVIATION	4.93	1.32
RELATIVE STANDARD DEVIATION	29	11
99% CONFIDENCE INTERVAL	17.95 ± 10.72	12.0 ± 2.22

a change in current consumption. The MLA, on the other hand, has linearity in response over a range of 10 to 110% of motor loads[23].

In developing this system, it was necessary to determine the baseline load on the motor as sensed by the motor load analyzer. It was found that a 20 minute high speed warm-up was required to minimize baseline drift for both low and high speed impeller operation. During this warm-up period, the oil in the gearbox reaches operating temperature and any motor slip associated with a cold electric motor start-up is minimized.

Table I summarizes the results of the no-load trials. The individual reported values are an average value determined over a twenty (20) minute run time. Statistical analysis of these data have shown that the differences between the high and low baseline values were not significant. They were presumably induced by fluctuations within the MLA system; a high motor efficiency during high speed impeller operation is one likely source. Such variations cannot be eliminated and will always be present in this type of system.

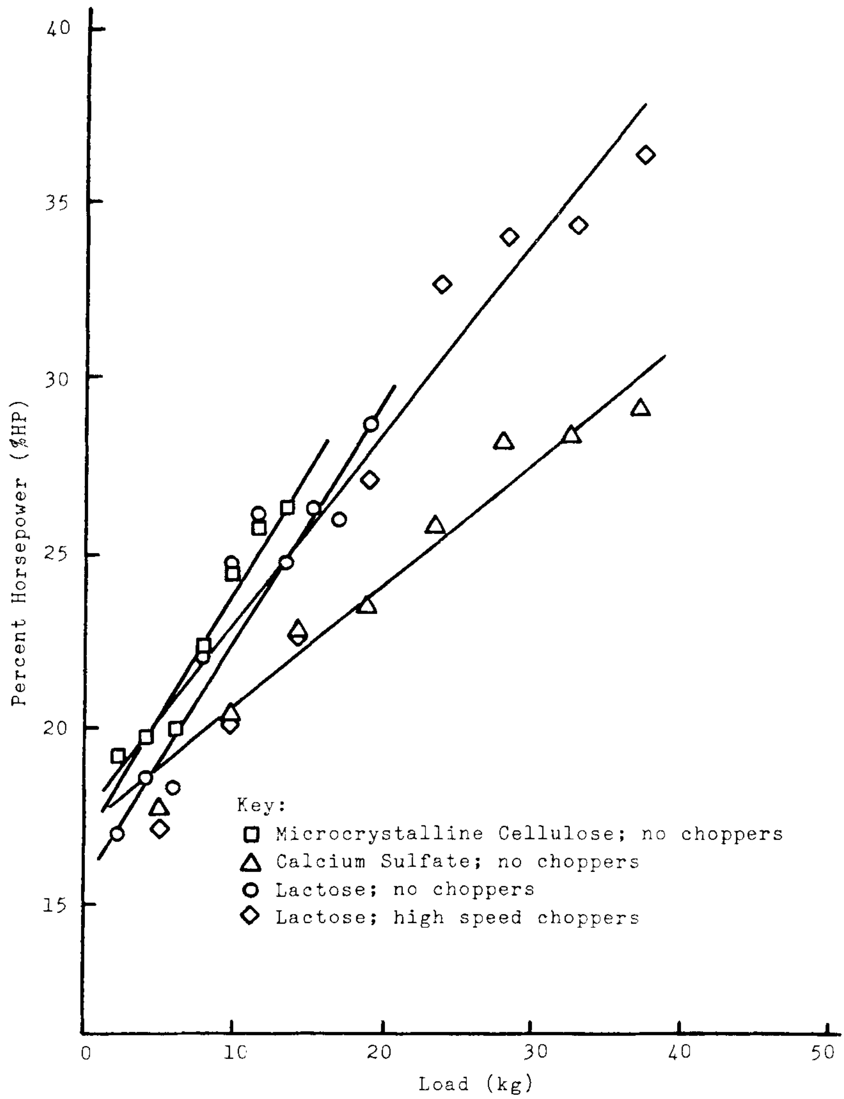

Figure 1

Motor Load Analyzer Output at Low Speed Impeller Operation versus Mixer Load for the Different Test Materials

They can be minimized by adjusting each run for the baseline value.

The response of the MLAs to load changes of materials of different bulk densities was examined using microcrystalline cellulose, lactose, and calcium sulfate. Bulk densities of these materials were determined to be about 0.31 g/cm^3, 0.65 g/cm^3, and 0.80 g/cm^3, respectively. For a given material, the percent horsepower output of the MLA was found proportional to the mixer load (Figures 1 and 2). The micromeritic properties of each material along with such phenomena as fluidization, generation of static charge, and the existence of active/passive mixing zones in the vessel may account for the differences in output between high and low impeller operation, and choppers on or off.

A typical MLA response profile for a 4:1 lactose/micro-crystalline cellulose mixture granulated with 2500 g of a 5% w/w aqueous povidone solution, and with high speed impeller and choppers, is presented in Figure 3. There was an increase in MLA output when the binder was added followed by a leveling off as the

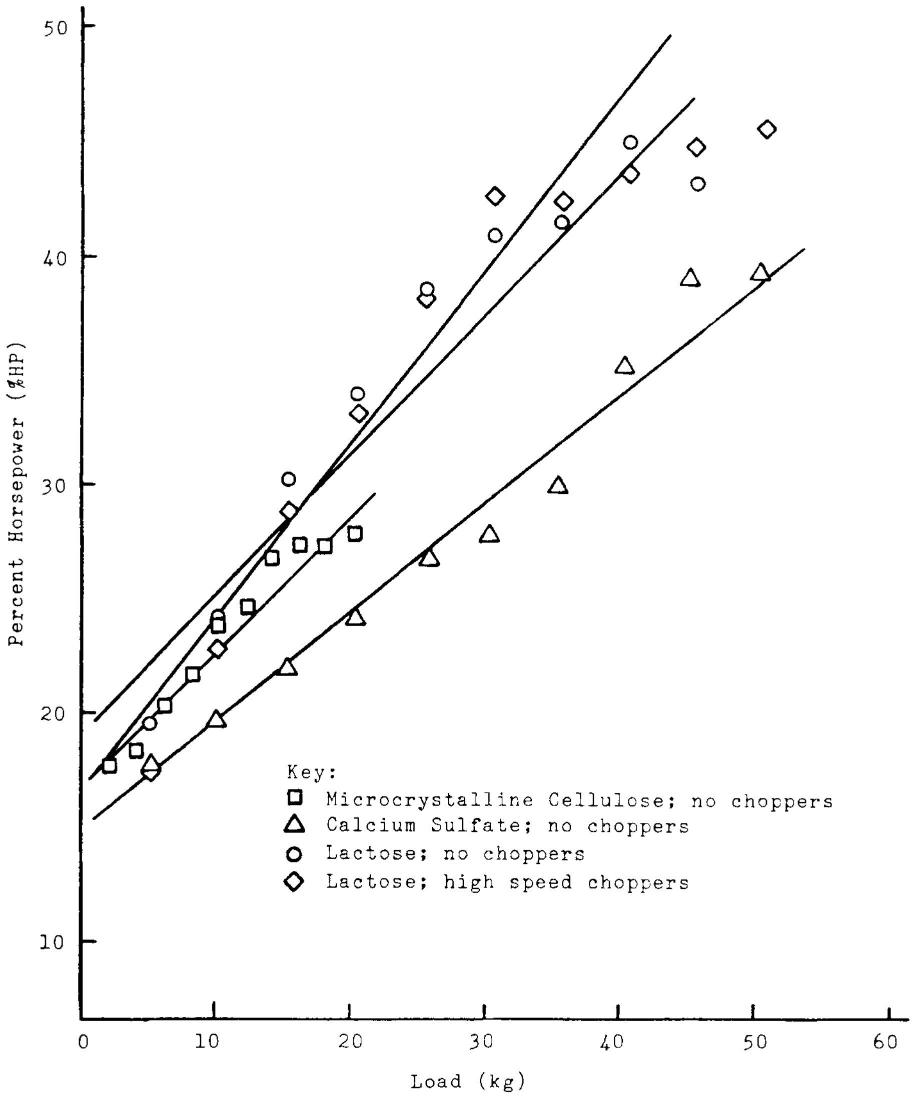

Figure 2

Motor Load Analyzer Output at High Speed Impeller Operation versus Mixer Load for the Different Test Materials

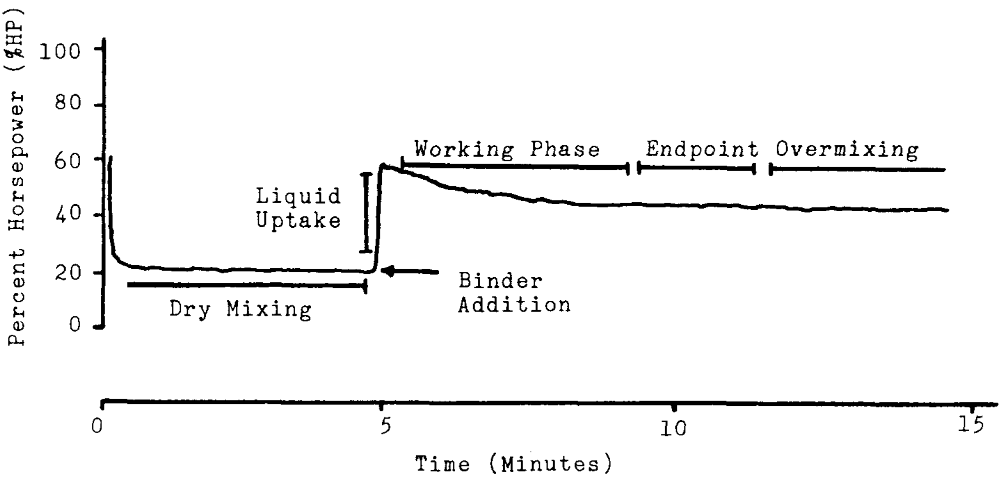

Figure 3

Motor Load Analyzer Output Profile of a 4:1 Lactose/ Microcrystalline Cellulose Mixture Granulated with 2500 g of a 5% Aqueous Povidone Solution and with High Speed Impeller and Choppers

povidone solution became distributed throughout the lactose/microcrystalline mixture.

The reproducibility of MLA response (Figure 4) is demonstrated with duplicate trials of this 4:1 lactose/microcrystalline cellulose system. The effect of high speed choppers operation on the MLA response profile is shown in Figure 5. When the choppers were on, MLA output was slightly lower than when they were off. This may be attributed to a change in the mixing

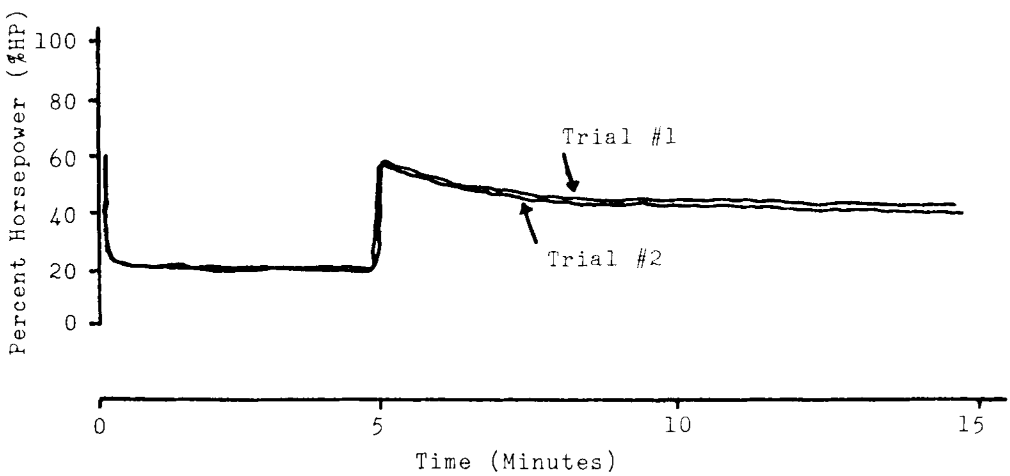

Figure 4

Reproducibility of Motor Load Analyzer Output for Duplicate Trials of a 4:1 Lactose/ Microcrystalline Cellulose Mixture Granulated with 2500 g of a 5% Aqueous Povidone Solution and with High Speed Impeller and Choppers

characteristics within the vessel resulting in less torque on the impeller.

Figure 6 shows a plot of MLA response at the completion of blending versus mixer load for a lactose based mixture granulated with 10% starch paste. The starch paste was added to the dry blended materials while mixing with high speed impeller and choppers. The wetted mass was then blended for an additional period of time. The motor load analyzer output profiles for this system were similar to that shown in

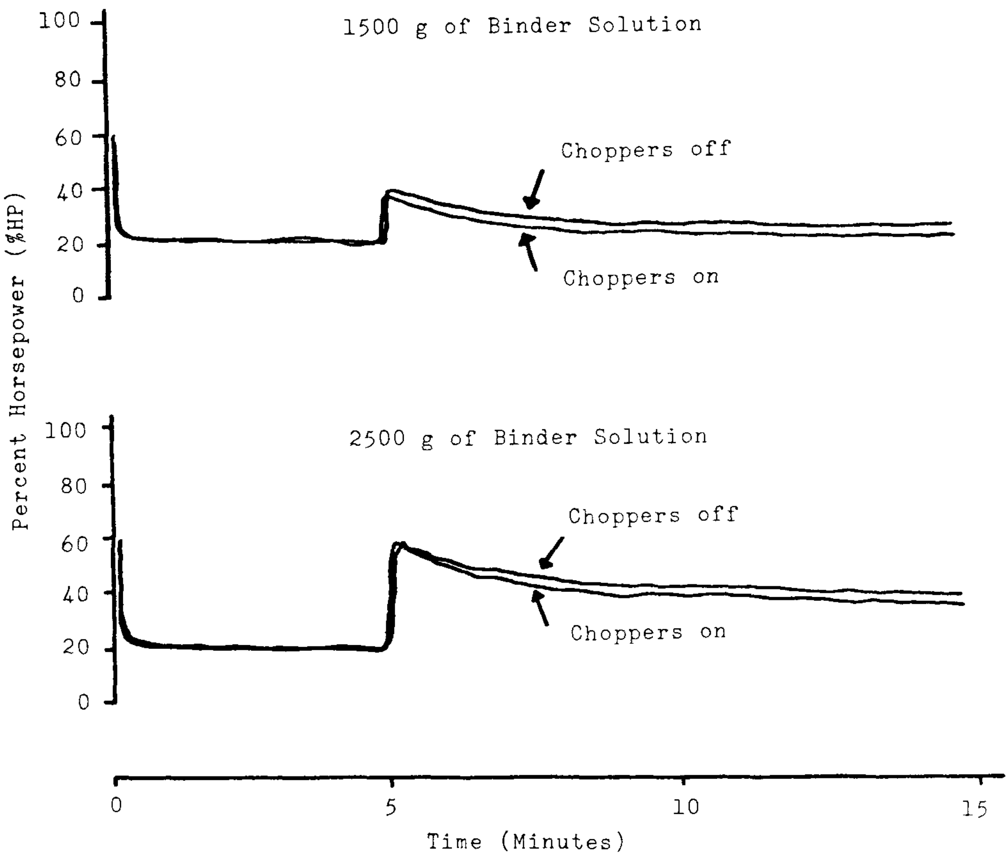

Figure 5

The Effect of High Speed Choppers Operation on the Motor Load Analyzer Output Profile of a 4:1 Lactose/Microcrystalline Cellulose Mixture Granulated with an Aqueous Povidone Solution

Figure 3 for the lactose/microcrystalline cellulose mixture granulated with aqueous povidone.

Figure 7 presents the MLA output profile for an antihypertensive drug mixture granulated with 3700 ml

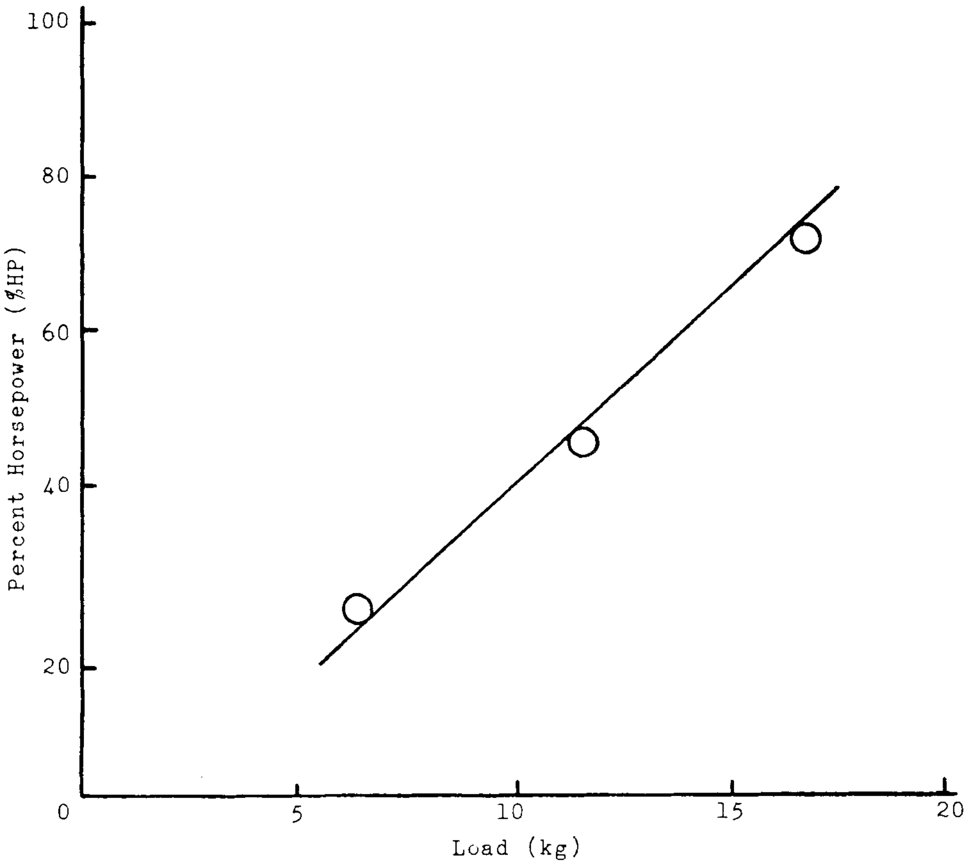

Figure 6

Motor Load Analyzer Output at the Completion of Mixing for a Lactose/Starch Paste Granulation

of Purified Water, USP. There was leveling of response at about the optimum mixing time for this granulation. Beyond this point, there was a gradual decrease in response with increased mixing time.

As demonstrated with Figures 3 and 7, several characteristic regions can be identified during the

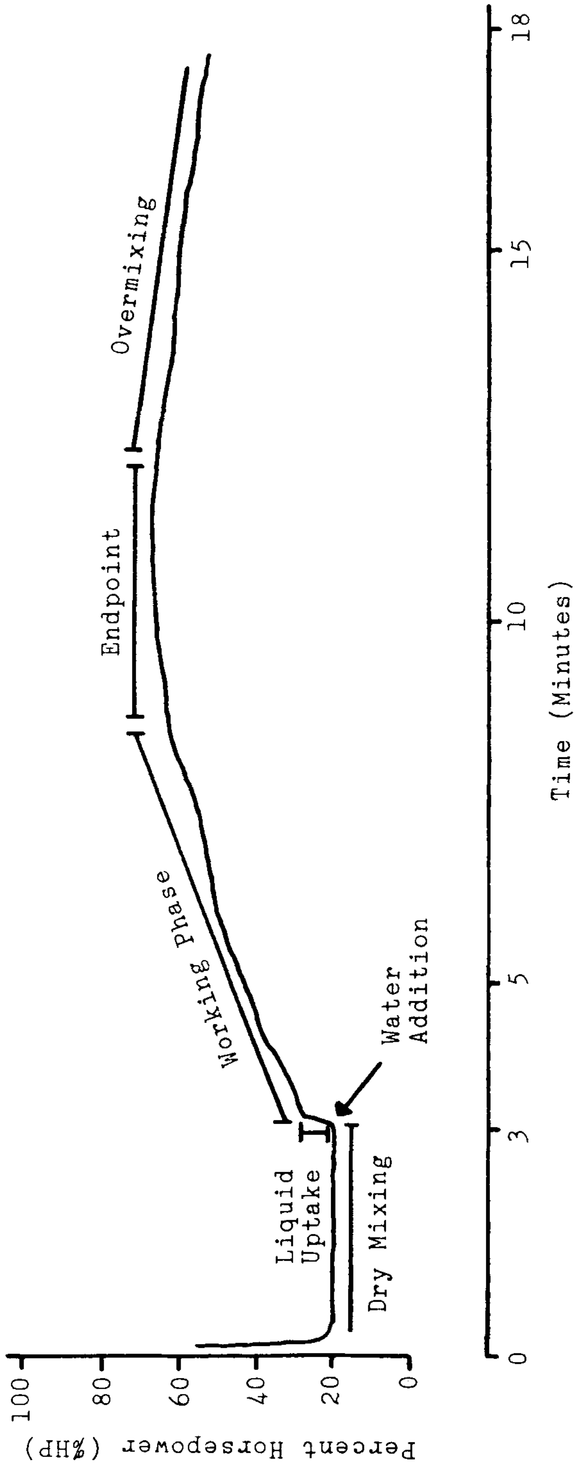

Figure 7

Motor Load Analyzer Output Profile for an Antihypertensive Drug Mixture Granulated with Purified Water, USP granulation process. They include the liquid uptake phase, the working phase, the optimum mixing range, and an over-agglomeration phase. The liquid uptake phase begins when the binder is added and lasts until it becomes distributed throughout the powder blend. During the working phase, agglomeration of the materials occurs; there is a constant change in granule size and composition. The optimum mixing range can be considered the granulation endpoint. It is probably an interval over which the agglomeration process is at some type of steady state. Granulation physical properties such as bulk density, particle size distribution, flowability, and compression characteristics are at their desired (optimum) levels. Past this endpoint region, the granulation becomes overworked. Its characteristics may become undesirable from processing and/or finished product viewpoints. Studies to confirm these observations are ongoing.

The data presented in this communication, although preliminary in nature, indicate that the described MLA system instrumented to a high shear mixer can reliably and with a good degree of reproducibility monitor the granulation process.

ACKNOWLEDGMENTS

A portion of this work was presented at the October 13, 1983 Eastern Regional Industrial Pharmaceutical Technology Meeting held in Morristown, New Jersey.

Appreciation is expressed to R. C. Gardner, J. S. Barrett, P. A. McHugh, W. E. Schoellkoph and Dr. B. Sachok for their technical expertise in aspects of this project.

REFERENCES

1. E. Shotton, J. A. Hersey, and P. E. Wray in "The Theory and Practice of Industrial Pharmacy," L. Lachman, H. A. Lieberman, and J. L. Kanig, Eds., Lea & Febiger, Philadelphia, PA., 1976, p 296

2. H. Leuenberger, Mfg. Chemist, May, 67 (1984)

3. Ibid., June, 53 (1984)

4. B. H. Hunter and D. Ganderton, J. Pharm. Pharmac., 25, Suppl., 71P (1973)

5. H.-P. Bier, H. Leuenberger, H. Sucker, Pharm. Ind., 41, 375 (1979)

6. H. Leuenberger, H.-P. Bier, and H. B. Sucker, Pharm. Tech., 4, 62 (1979)

7. N.-O. Lindberg, L. Leander, L. Wenngren, H. Helgesen, and B. Reenstierna, Acta Pharm. Suecica, 11, 603 (1974)

8. N.-O. Lindberg, L. Leander, P. G. Nilsson, and B. Reenstierna, ibid., 14, 191 (1977)

9. N.-O. Lindberg, *ibid.*, 14, 197 (1977)

10. N.-O. Lindberg, L. Leander, and B. Reenstierna, *Drug Dev. Ind. Pharm.*, 8, 775 (1982)

11. S. R. Ghanta, R. Srinivas, and C. T. Rhodes, *ibid.*, 10, 305 (1984)

12. N.-O. Lindberg, *ibid.*, 10, 45 (1984)

13. D. N. Travers, A. G. Rogerson and T. M. Jones, *J. Pharm. Pharmacol.*, 27, *Suppl.*, 3P (1975)

14. N.-O. Lindberg and C. Jönsson, *Drug Dev. Ind. Pharm.*, 9, 959 (1983)

15. J. Andersson and N.-O. Lindberg, *ibid.*, 9, 1495 (1983)

16. N.-O. Lindberg, C. Jönsson, and B. Holmquist, *ibid.*, 4, 917 (1985)

17. *Ibid.*, 11, 931 (1985)

18. D. Kay and P. C. Record, *Mfg. Chem. Aer. News*, 48, 45 (1978)

19. M. S. Spring, *Drug Dev. Ind. Pharm.*, 9, 1507 (1983)

20. W. C. Fry, W. C. Stagner, and K. C. Wichman, *J. Pharm. Sci.*, 73, 420 (1984)

21. W. C. Fry, W. C. Stagner, P. P. Wu, and K. C. Wichman, *Proceedings of the 4th International Symposium on Agglomeration*, Toronto, Ontario, Canada, June 2-5, 1985, p 497-501

22. W. C. Fry, P. P. Wu, K. C. Wichman, and W. C. Stagner, *Pharm. Tech. Conf. Proceed.*, Cherry Hill, New Jersey, September 10-12, 1985, p 358-367

23. Product Data Sheet, Series 2340 Motor Load Analyzer, Rexnord Instrument Products