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USE OF MIXER-TORQUE MEASUREMENTS AS AN AID TO OPTIMIZING WET GRANULATION PROCESS

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ABSTRACT

Instrumentation designed for monitoring the wet granulation process is described. A Hobart mixer was instrumented with a slip ring torque sensor using a voltage of 5 volts D.C. to excite a strain gauge bridge. An amplifier was used to magnify the low signal levels produced by the strain gauge bridge and the gain was set at 179.6 so that 2 volts equals 200 inch ounce. The output was recorded using a Bascom-Turner recorder. The relative dynamic torque, was measured in millivolts as a function of granulating fluid added and time to optimize the granulation process using the planetary mixer. The instrumentation described in this paper has considerable potential for optimization and validation studies for wet granulation procedures.

INTRODUCTION

Wet granulation has been used pharmaceutically for many years and yet the detection of the desired granulation wet massing consistency ("end point") is still usually made by intuitive, subjective judgement. Progress in optimizing and validating wet granulation

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processes is seriously inhibited due to lack of an objective, quantifiable, reproducible measuring technique. Wet granulation is often used: (a) to improve flow, handling and resistance to segregation (1), (b) to improve bioavailability (2), (c) to improve homogeniety of low dose blends, (d) to overcome electrostatic properties of a powder blend (3), (e) to improve flow and compression characteristics of tablet matrices, or (f) to make in-situ complexes to stabilize the dosage forms. Wet granulation is often referred to as the most difficult unit operation to reproduce and scaleup because of the lack of a precise means to measure process variables and detect the end point.

Recognizing this problem, several researchers have attempted to quantifiably characterize the wet granulation process. Hunter and Ganderton described how measurement of power input to a commercial mixer can be monitored in an attempt to detect an "end point" of the wet massing process (4). The method is rather imprecise since the actual fraction of the energy supplied as useful work at mixer shaft is unknown. Lindberg and others (5) conducted preliminary experiments where they measured the bending moment, produced in the arm of an Artofex mixer, by means of strain gauges. Travers et al, (6) constructed a "torque arm" mixer of only about two kilograms capacity, where the mixer arm was driven by a motor mounted on a platform free to move in a horizontal plane on a ball-bearing race. A pin, fixed on the circumference of that platform, bears on the arm of a correx tension gauge and resists the torque developed as the mixer arm rotates in the mass. The angular displacement of the platform, which for small displacement is proportional to the developed torque, operates a displacement transducer.

In the present paper, we report a convenient method for instrumenting a Hobart mixer. Our preliminary data clearly demonstrates that the technique has considerable potential for wet granulation optimization and validation studies.

MATERIALS AND METHODS

A Model C-100 Hobart mixer[A], Model 1102-200 slip ring torque sensor[B], 1/4 HP explosion proof motor[C], strain gauge conditioner indicator[D], Model 4120 Bascom-Turner Recorder[E], two rubber block couplings[B], and two (0.375 x 22.0 x 6.5 in. and 0.375 x 28.75 x 15.0 x 6.5 in.) aluminum plates. Figure 1 shows the mode of instrumentation.

A Hobart mixer consists of (a) bowl support, bowl and lift-unit (#1), (b) base and pedestal unit (#2) and (c) transmission case unit as seen in Figure 1a. The back cover from base and pedestal unit was opened. The transmission unit (#3) was taken from the pedestal unit and its cover was removed and wiring disconnected. The motor was pulled from the transmission case unit and the windings removed from the shaft. An 0.375 x 22.0 x 6.5 in. aluminum support plate (#4) was installed on the pedestal unit. The transmission case unit cover was bored to make it possible to connect its driving shaft to the driving shaft of the slip ring transducer and the transmission case unit was then installed on top of the aluminum plate. The slip ring transducer was alligned accurately between the transmission unit and the 1/4 HP motor using aluminum support blocks. The driving shafts were connected with rubber block couplings, which could accomodate an angular misallignment of 1^{o}, parallel misallignment of 1/16 to 1/4 in. and axial play of 1/16 to 1/2 in. The entire unit

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[A]Hobart Manufacturing Co., Troy, Ohio

[B]Lebow Products, Eaton Corporation, Troy, Michigan 48099.

[C]General Electric, Fort Wayne, Indiana.

[D]Analog Devices, Norwood, MA 02062

[E]Bascom-Turner Instruments, Newton, MA 02158.

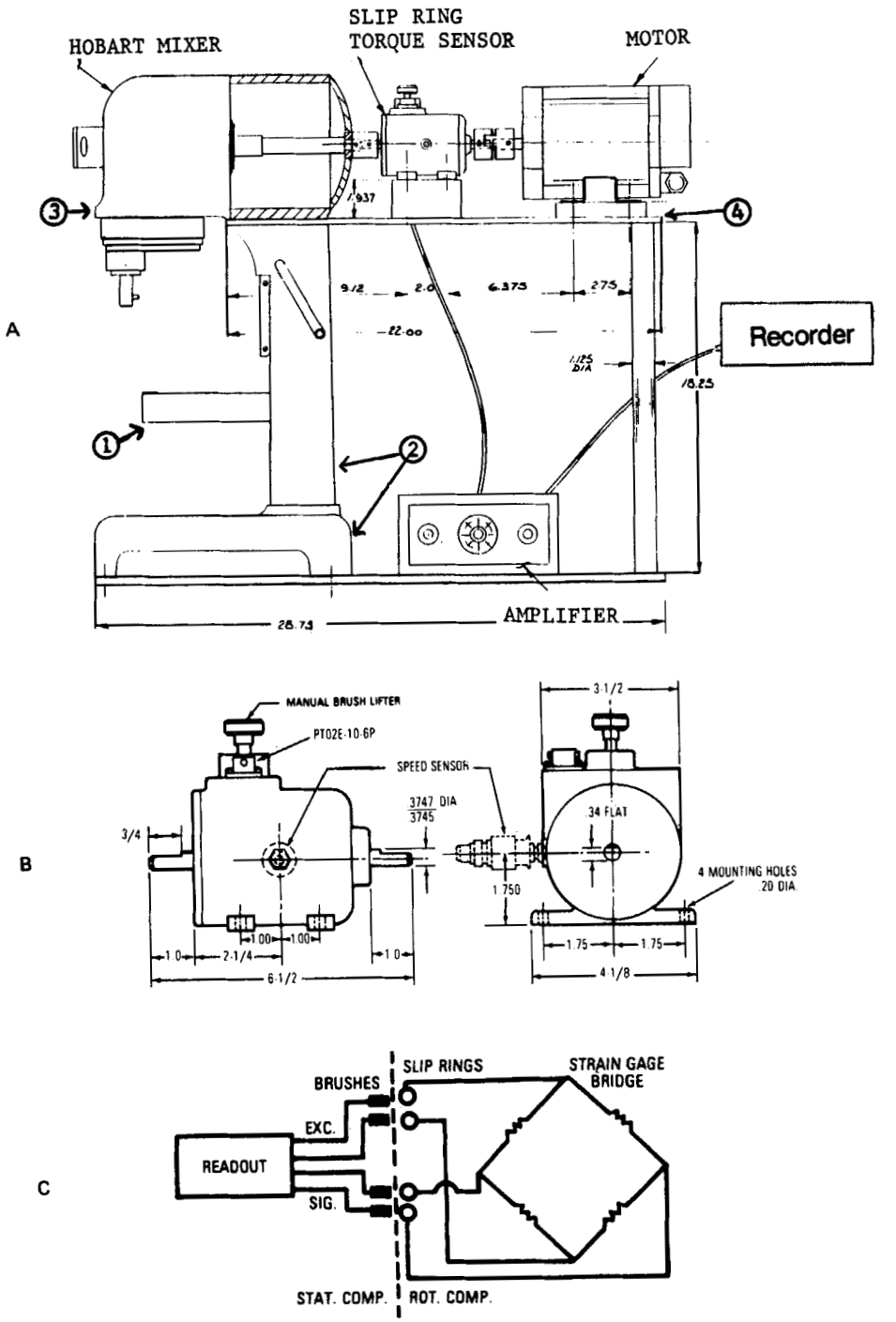

Figure 1a Side View of instrumented Hobart mixer.

Figure 1b Side view and Front view of slip ring torque sensor.

Figure 1c Schematic of slip ring rotating shaft torque measuring system.

was installed on second aluminum plate (0.375 x 28.75 x 15.0 x 6.5 in.) for stability. The back plate of the bowl support was shortened by about 0.375 in. to accommodate the aluminum plate which supports the slip ring unit and motor. The height of the bowl support was adjusted by turning the bowl lift stud. The transducer unit was connected to the amplifier, while the amplifier, in turn, was connected to the Bascom-Turner Model 4120 recorder. A voltage of 5V D.C. was used to excite the strain gauge bridge. The gain was set at 179.6 such that 2V output equalled 200 in. oz. (See Figure 1.)

For a preliminary wet granulation study to check out the instrumentation, powders of the following composition were used: 5100 g of lactose 80 mesh USP, 600 g of corn starch USP and 300 g of Povidone USP C-30. The materials were blended 30 minutes in a "V" shell blender and subdivided into six 1 kg lots. Six experiments were conducted under constant conditions to verify the reproducibility of the instrumentation. In each experiment, a 1 kg lot was placed in a 2.8 liter bowl (approximately 65% of bowl capacity) and was blended for five minutes at low speed in the instrumented Hobart mixer. Then, 200 ml of water was added at a constant rate (33.3 ml/minute) using a burette while mixing at low speed. Output in millivolts as a function of time was recorded using a Bascom-Turner recorder. Figure 2 shows results of three replicate experiments, where millivolts is plotted versus the percentage of granulating liquid added instead of time.

RESULTS AND DISCUSSION

The curve can be divided into five phases in relation to the amount of granulation liquid added. During the first phase, the powder blend is moistened without any increase in torque from the dry premix phase. There is no noticeable agglomeration of the particles in the first phase. In the second phase torque increases markedly as the solid particles begin to agglomerate. During the third phase, torque tends to decrease as proper granulation is achieved. Our intuition and experience indicate the

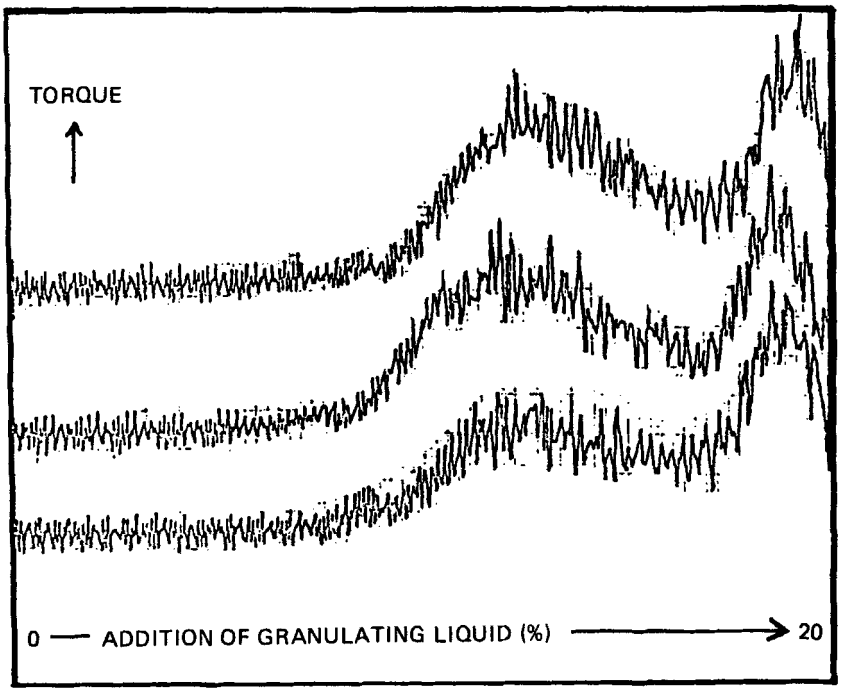

Figure 2 The three plots (Torque as a function of granulating liquid) placed one above the other to demonstrate the reproducibility of the replicate experiments.

end point of normal wet massing lies in phase 3 of the curve. Torque increases again during the fourth phase as the mass thickens. With further continuous addition of granulating liquid, the doughy mass which was pasty in the fourth phase, breaks down and slowly passes into a suspension with a marked decrease in torque (phase V). During wet granulation,torque varies as a result of a change in cohesive force and tensile strength of the agglomerates in the wet granulation bed. Therefore, interpretation of the torque curve may lend to better understanding and prediction of wet granulation parameters.

Depending on the purpose for which granulation is intended, the "end point" of the desired wet massing consistency may be optimally detected in different ways. In some cases, for example, dv/dt_{max} may be the best measure. In other systems the second

derivative may be more useful. Obviously, we require a greater quantity of data before any firm recommendations can be made.

Preliminary data suggest that an instrumented Hobart mixer can measure the relative torque as a function of time and should be useful to quantify the wet massing process and define the desired wet mass consistency end point. This in turn should help in the development of reproducible scaleup procedures where mass effect of material plays an important role. We have every reason to believe this instrumentation could be adapted to large scale equipment of similar type. It is also possible that an automated granulation process could be developed using this equipment with computer interface. Additional studies are in progress to further characterize the system and these results will appear in future reports.

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