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The Development of a Microwave Fluid-Bed Processor. I. Construction and Qualification of a Prototype Laboratory Unit

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The static bed- and planetary-type microwave dryers currently available to process pharmaceutical materials are not designed to use hot-air fluidization for the purpose of maximizing microwave energy inputs and particle drying. To take advantage of the benefits offered by fluidization, a 1-kg Uni-Gatt laboratory fluid bed processor was modified to support microwave-assisted fluid bed drying of several representative pharmaceutical granulations. The construction, design features, and validation of this new microwave fluid bed processor are presented.

KEY WORDS: microwave dryer; fluid-bed dryer; process equipment validation.

INTRODUCTION

Because of its efficiency and versatility with respect to particle agglomeration drying and coating capabilities, fluid-bed processing is commonly used in the pharmaceutical industry to manufacture solid dosage forms (1–7).

The use of microwave-assisted static bed and vacuum-type planetary mixer-dryers for pharmaceutical processing is a more recent development (8–11). Microwave-assisted vacuum dryers and processors have provided significant improvements in drying rates for aqueous-based granulations compared to conventional vacuum drying equipment (9,10).

Unassisted microwave heating (no vacuum or hot-air fluidization) through direct radiant energy coupling has poor evaporative drying qualities once moisture has been transferred by diffusion to the surface of solid particles (12–14). In contrast, fluid-bed drying possesses rapid evaporation rates for moisture but poor diffusional rates because of the poor thermal conductivity of most pharmaceutical solids. We therefore coupled microwave heating to fluid-bed drying to provide a more efficient transfer of energy to the granulating liquid. This process improves the rate of liquid migration to the particle surface and thereby rapidly removes the gas–liquid boundary film from such surfaces through flash evaporation in a moving bed and in the presence of a fluid stream of heated air.

Both Smith (15) and Rzepecak *et al.* (16) developed "microwave fluidized bed dryers." These earlier designs were either modified conveyor-type dryers for pasta manufacture or a modified conventional fluid-bed dryer where the drying cavity was configured to act as a waveguide. In this dryer, referred to as a "traveling wave applicator," microwaves propagate along the path of the traveling product and any remaining microwave energy not absorbed by the product is mechanically absorbed at the end of the microwave transmission path by a dummy load or load tubes. Traveling wave applicators are, therefore, intrinsically energy inefficient.

The purpose of the present work was to design and fabricate a laboratory size microwave fluid-bed processor (MFBP) in order to perform drying experiments with several representative pharmaceutical granulations. The design features of the new MFBP unit are discussed here.

EQUIPMENT DESIGN AND CONSTRUCTION

Fluid-Bed Dryer/Processor

All modifications described in Figs. 1 and 2 were performed on a basic laboratory size (approximately 1-kg) fluid-bed dryer/processor. The model chosen for study was a Uni-Glatt manufactured by Glatt GmbH, Binzen, Germany. The modifications to the dryer/processor are listed as follows.

Structural Modifications to Expansion Chamber

A circular hole was drilled into the left side of the expansion chamber and an appropriately sized No. 304 stainless-steel (SS) studded flange was welded to the outside wall (Fig. 2). All surfaces and joints were finely ground and polished to produce a sanitary and arc-free design. A circular pattern was chosen to give flexibility for 90° rotation of the waveguide. Although rotation of the waveguide was not extensively explored in Part II of this work (following paper), it was felt that the ability to attach a 90°-twist waveguide was an important design consideration in future studies.

The expansion chamber was chosen as the port of entry for the microwave source for several reasons. First, it is the largest product-containing cavity and allows the maximum number of energy modes within the dryer. Modes are created by randomly oriented reflected waves within an enclosed system. As the microwaves bounce back and forth, the amplitude of the electromagnetic (EM) wave can increase or decrease depending upon the phase of the reflected EM waves which interact. This situation is an example of what is termed a standing-wave phenomenon. Hence, the larger the cavity, the more opportunity for reflections.

Second, the only other convenient placement of the microwave entry port would be in the product bowl. Although this arrangement would permit more direct "contact" between the wet granulation and the incoming microwave energy, the reduction of energy modes due to the small volume and the high probability of producing near-field illumination with poorly fluidized material led to the design selection as depicted in Fig. 1. Near-field illumination describes the situation where there is a microwave-absorbing material, in this case wet granulation, located between the microwave entrance port and the rest of the drying cavity. Therefore,

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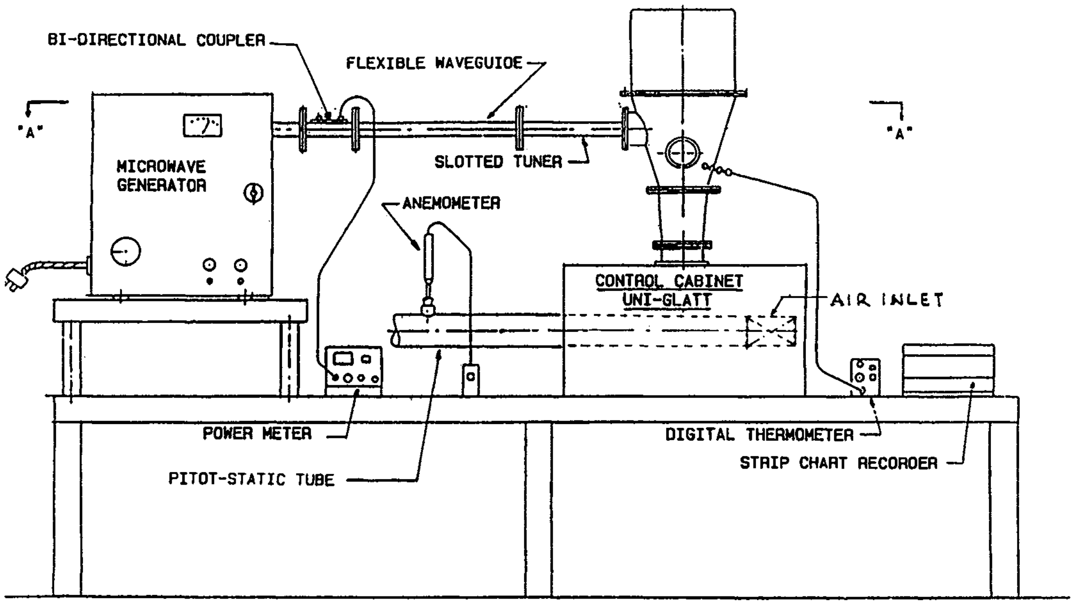

Fig. 1. Diagram of a laboratory-size microwave-assisted fluid-bed processor.

without granulation movement within the product bowl, the microwaves have no chance to enter and be reflected within the cavity and uniformly heat the granulation moisture. Third, if the microwave entrance was placed in the product bowl, the waveguide would have to be detached and reattached prior to each moisture determination and product changeover. This would make laboratory experimentation, equipment cleaning, and production-size drying difficult and time-consuming to perform.

Design of Microwave Entrance Plug

In order to allow the microwave energy to enter the expansion chamber while inhibiting fluidized particles from entering the microwave delivery system, a solid Teflon plug was placed at the microwave entrance of the expansion chamber. Teflon was chosen because of its inertness, machinability, and ability to permit radio frequencies (RF) to propagate with little distortion and energy loss. The plug was machined from a solid block of Teflon to close tolerances so as to provide a snug circular contoured face that conformed to the shape and curvature of the expansion chamber (Fig. 2).

Temperature Probe Guide and Stabilizer

A further modification was the attachment (welding) of a No. 304 SS fitting the lower right quadrant of the expansion

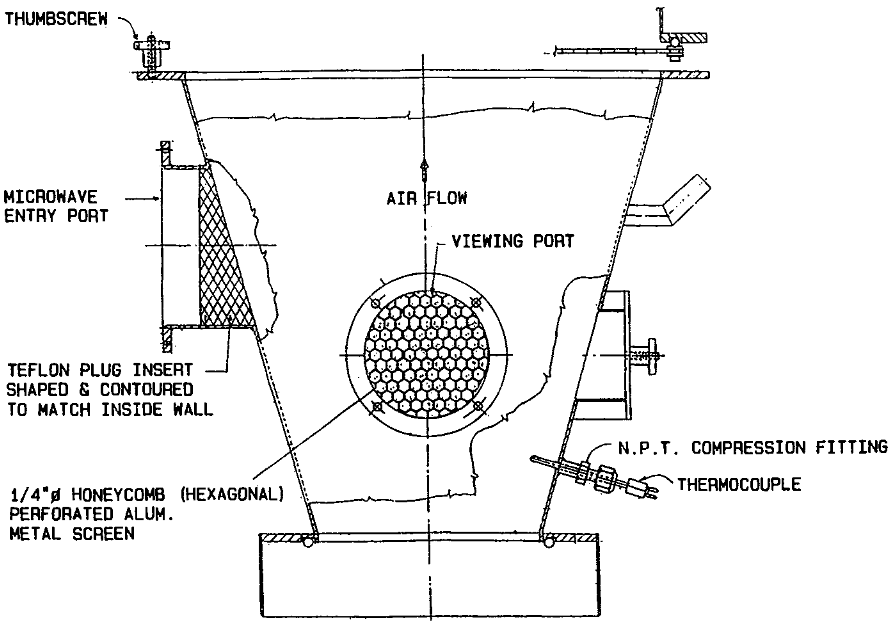

Fig. 2. Design of the expansion chamber for a microwave-assisted fluid-bed processor.

chamber. The 1/8-in. (3.2-mm) ID × 2-in. (50.8-mm)-long fitting was inserted to act as guide and holding device for a Type K thermocouple probe (Model N8439, Cole-Palmer Electronics, Chicago, IL). At the end of the tube, a National Pipe Thread (NPT) compression fitting was attached to provide a *secure* penetration depth of approximately 1/4 in. (6.4 mm) inside the expansion chamber (Fig. 2). The appropriate penetration depth of 1/4 in. was determined experimentally by employing a 1-liter load of water in the product bowl, and an input of 100 W of microwave power. The thermocouple was adjusted to varying depths until a nonfluctuating chamber temperature was obtained.

Installation of the Pilot-Static Tube

The final modification to the fluid-bed dryer was the attachment of an appropriately sized inlet straight duct (fabricated by Glatt Air Techniques, Inc., Ramsey, NJ) (Fig. 1). The purpose of the duct was to provide a means by which the volume of fluidizing air could be measured and monitored on a continuous basis. The cylindrical duct was constructed of galvanized steel, measuring 4 in. (101.6 mm) in diameter (ID) × 64 in. (1625.4 mm) in length, with a 90° bend and rectangular flange at the air inlet entrance of the dryer. The air inlet side of the duct to the point where laminar flow is assured was calculated to be 40 in. (1016 mm). At that length, two holes were drilled (one top, one bottom) and a small cylinder was welded to the top of the tube to allow the attachment of an electronic vane-wheel anemometer (Testovent 4000, TestoTerm Co., Mt. Freedom, NJ).

Microwave Source and Delivery System

The 2450-MHz Microwave Generator

The microwave generator (Model RES 131, Associated Sciences Research Foundation, Inc., Marlborough, NH) was designed to provide a variable output of 0 to approximately 1300 W. The frequency produced by the generator was a constant 2450 MHz (±15 MHz).

Microwave Monitoring System

A bidirectional coupler (Associated Sciences Research Foundation, Inc.) was chosen to permit easy and rapid monitoring of the forward and reverse microwave energy.

Forward Microwave Power Sensor. The forward coupler was equipped to provide -60 dB (or 10^{-6}) attenuation and the reverse coupler was to measure accurately the microwave power (watts) input into the fluid bed dryer. In addition, it was used to calibrate and qualify the microwave generator and permit easy routine checks during operation.

Reverse Microwave Power Sensor. The primary function of the reverse coupler was to measure the amount of reflected or unused microwave energy at any given point during the drying process.

Waveguide Assembly

A standard 18-in. (457-mm) WR340 flexible waveguide (Associated Sciences Research Foundation, Inc.) was installed between the bidirectional coupler and the slotted tuner.

Single-Slotted 2450-MHz Microwave Tuner

The final component of the delivery system was the slotted tuner (Associated Sciences Research Foundation, Inc.). The purpose of the tuner was to match the microwave power input with the load (granulation) present in the fluid bed dryer and thereby maximize the microwave energy efficiency. The slotted tuner was calibrated prior to each drying experiment (Part II; following paper).

Microwave Conductive Gaskets and Protective Screening

Design and Placement of Microwave Security Screens

The type of microwave security screen chosen was a nonwoven aluminum perforated plate obtained from McNichols Co., Carteret, NJ. The plate consisted of 1/4-in. (6.4-mm) hexagonal openings and a 79% open area. The slightly larger openings allowed adequate microwave protection but did not inhibit air flow between the expansion chamber and the filter housing. The screen for the viewing window was cut to fit the existing metal retaining ring, which held the viewing glass to the product bowl.

The security screen between the expansion chamber and the filter housing was designed so that the screen was welded between a perfectly matched pair of aluminum rings. These rings were of the exact dimensions (OD and ID) of the flange located atop the expansion chamber.

Microwave Conductive Gaskets and Sealants

In order to alleviate the possible problem of resistive heating, a commercially available metal-impregnated, compressible gasket was used (Chromerics, Woburn, MA). The main constituents are cross-linked silicone elastomer as the compressible polymer matrix and silver-plated aluminum as the conducting medium. In the gasket channel of the expansion chamber, cylindrical tubing, 5/16-in. (7.9-mm)-OD (Cho-Sil 5) was cut and bonded into the channel. The glue (Cho-Bond, a silicone-based adhesive which contains a high percentage of finely divided silver-plated copper particles that allow an uninterrupted metal-to-metal contact between the gasket and the adjacent metal ringed screen or flange. Between the screen and the filter housing, a flat, rectangular 1/2-in. (12.7-mm)-wide × 1/16-in. (1.58-mm)-thick metal impregnated gasket was used (Cho-Sil Model 1485). The gasket was cut to an appropriate size and bonded to the flange of the filter housing as described previously for the cylindrical (0 Type) gasket. The 0 profile-type gasket was again chosen to secure the product bowl to the expansion chamber. The gasket was cut and bonded to the gasket channel located on the bottom of the expansion chamber (Fig. 3).

Through preliminary trials it was determined that the product retaining screen, which is woven (100-mesh Dutch weave), did not cause resistive heating with microwave power inputs of up to 1000 W.

CALIBRATION AND QUALIFICATION

Calibration of the Bidirectional Coupler [Associated Sciences Research Foundation, Inc. (ASRF), Marlborough, NH] was performed by ASRF personnel using a Hewlett-Packard 8753 Network Analyzer. An HP4312 Power Meter

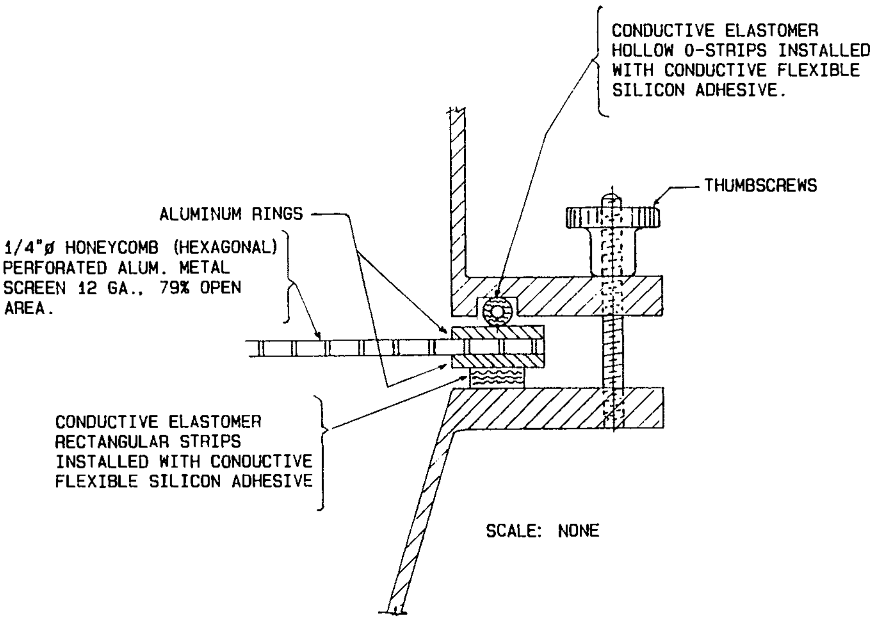

Fig. 3. Design of microwave security screening and conductive gasketing between the filter housing and the expansion chamber.

(Hewlett-Packard, Palo Alto, CA) and Temperature-Compensated Thermistor Mount (Model GIL-360-2, Struthers Electronics, Farmingdale, NY) were purchased from and calibrated by Electronics Research Labs (ERL), Camden, NJ, prior to their installation. Their function was to sense, transfer, and display the microwave power in either the forward or the reverse travel.

Using a freshly prepared starch granulation load (approximately 800 g or 90% of the product bowl capacity) microwave power was delivered into the fluid bed processor at 100-W increments as read on the power output meter located on the Generator. The actual forward power was then recorded from the previously calibrated HP 431C power meter. The range evaluated on the power output meter was 100–1100 W. The procedure was repeated 10 times, each with a new granulation load. The mean, standard deviation, and coefficient of variance were calculated for each 100-W power increment.

At the lower power inputs (100–400 W) there was a good agreement between anticipated power output and actual power outputs. At outputs of 500 W and greater, higher means were observed, although the coefficient of variance values remained consistent throughout the 100- to 1100-Watt range. The noted difference between the generator's power meter and the actual power output was due to the single-point calibration design of the power meter. A linear relationship was assumed when the power inputs of 250, 500, 750, and 1000 W were used during experimentation. The corrected settings were calculated using the following:

$$\frac{\text{output power setting}}{\text{actual power}} = \frac{\text{corrected output power setting}}{\text{desired power input}}$$

The corrected output power setting was then rounded to the nearest increment of 10 to be consistent with the precision of the generator's power meter. The corrected generator output settings which were used for all drying experiments were 250, 480, 700, and 940 for the reported outputs of 250, 500, 750, and 1000, respectively.

The Electronic Vane-Wheel Anemometer (Model Testovent 4000, distributed by TestoTerm, Mt. Freedom, NJ) was calibrated by the supplier. The anemometer was used to monitor accurately the fluidizing air velocity, and hence the air volume, during the drying process.

Product temperatures were monitored by an ⅛-in. (3.2-mm) OD × 12-in. (304.8-mm) L, cylindrical, Type K, bimetal probe (Model n8439). The temperature was read on a pre-calibrated Keithley 871, Type K, digital thermometer. Both units were purchased from Cole-Palmer Electronics, Chicago, IL.

Inlet air temperature and relative humidity were monitored using a Hygrotest 6100 (TestoTerm, Mt. Freedom, NJ). The unit was purchased with self-control and calibration set for the humidity sensors. The procedures as defined in the instruction manual were used to calibrate the instrument.

All microwave leak detection tests were performed via a calibrated Model HI 1501 survey meter to ensure that microwave leakage was below OSHA regulations of NMT 5 MW/cm^2 at 5 cm during processing. The calibration was performed by the manufacturer, Holaday, Eden Prairie, MN.

A Slotted Tuner (ASRF, Marlborough, NH) was used to "match" the microwave input with the load (granulation) present in the dryer. Proper tuning maximized the microwave absorbing efficiency by limiting the amount of reflected power back to the magnetron. The standard procedure used for calibration prior to each drying experiment for the different formulations reported in Part II is given as follows: Using a freshly granulated sample at 90–95% bowl capacity, approximately 100 W was inputted into the dryer. A brass screw was then positioned horizontally and vertically to a precise location where the lowest amount of reflected microwave power was measured. As each formulation presents a different load capacity, this procedure was repeated whenever a different formulation was dried.

DISCUSSION

Static-bed or planetary-type microwave dryers/processors currently available to process pharmaceutical materials cannot use warm-air fluidization for the purpose of maximizing microwave input energy during drying. To overcome this limitation, a vertical fluid bed processor with microwave assistance (MFBP) for batch operation was invented. A Uni-Glatt laboratory fluid-bed processor was modified to support the construction of the MFBP.

Design and Construction of the MFBP

The unit consisted of four major components, namely, the laboratory fluid-bed dryer/processor, the microwave source and delivery system, the auxiliary monitoring equipment for data retrieval and control of the drying process, and the microwave security screening and conductive gasketing. Reconstruction of the fluid-bed dryer/processor included modification of the expansion chamber (site for microwave power entry) and the addition of an inlet duct for air volume measurements. The expansion chamber was fitted with an appropriately sized 304 SS studded flange which provided microwave power entry into the drying cavity and the connection to the microwave delivery system. In order to inhibit fluidized particles from entering the microwave delivery system, Teflon, a microwave transparent material, was milled to the shape and curvature of the expansion chamber and placed at the microwave entry port. In addition, a temperature probe guide and stabilizer were attached to the lower right-hand quadrant of the expansion chamber.

The microwave source and delivery system consisted of a 2450-MHz microwave generator, a bidirectional coupler, a flexible waveguide, and a single-slotted tuner. The microwave generator provided a variable output of 0 to 1300 W at a frequency of 2450 MHz (±15 MHz). The bidirectional coupler allowed the sampling of forward and reverse microwave power through the waveguide. The forward coupler was used to calibrate and qualify the microwave generator and the reverse coupler was used on a continual basis to measure the reflected or unabsorbed microwave energy during the drying experiments in Part II of this report.

The addition of a single-slotted tuner to the microwave delivery system permitted an impedance match between the incoming microwave power and the wet granulation. This impedance "matching" was performed by adjusting the brass screw to an exact horizontal and vertical plane so as to reflect selectively the reverse flowing microwaves and reintroduce them to the drying chamber, thus minimizing microwave energy loss and maximizing drying efficiency.

The microwave security screening consisted of an aluminum perforated plate with 6.4-mm hexagonal openings and a 79% open area. The screening allowed adequate microwave protection at the viewing window and between the expansion chamber and the filter housing while permitting unimpeded air flow through the drying chamber. Rectangular and cylindrical microwave conductive gaskets were placed between the product loading bowl and the expansion chamber and between the expansion chamber and the filter housing in order to provide an electrical continuum within the drying chamber. The gaskets were commercially available and consisted of a cross-linked silicone elastomer for compressibility and silver-plated aluminum particles as a conducting medium.

The important features of the MFBP were (1) containment of the microwave energy within the drying chamber, (2) providing microwave leakage below OSHA regulations of 5 mW/cm^2 at 5 cm, and (3) promoting adequate reflection and dispersion of microwaves within the drying chamber. The above-mentioned features were possible due to proper selection and installation of microwave screening and conductive gaskets, the inclusion of a single-slotted tuner in the microwave delivery system, and matching microwave orientation (horizontal versus vertical) to the existing drying cavity design.

Design Modification

Other designs have been conceived and put into practice

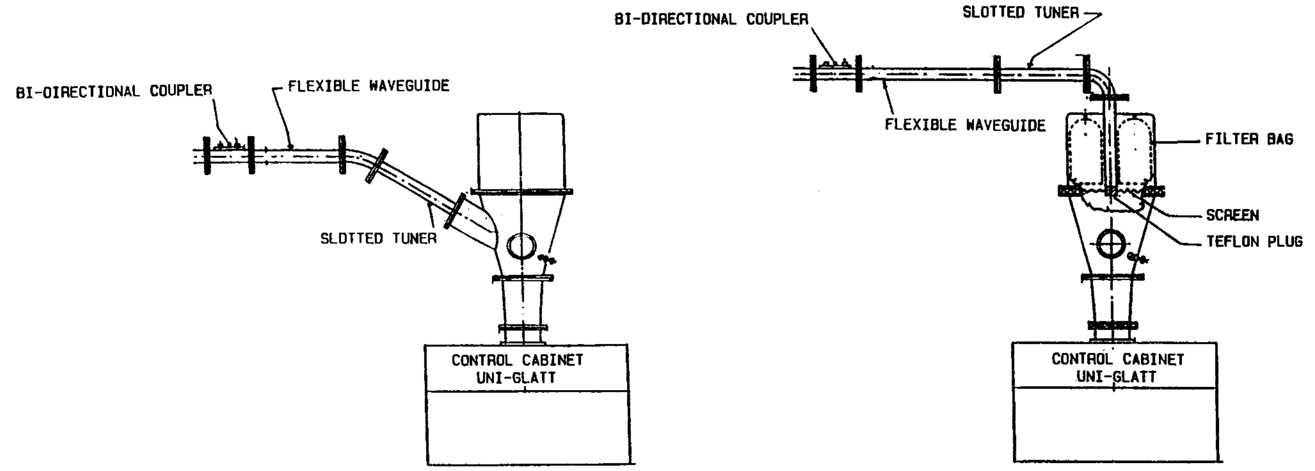

Fig. 4. (a) Diagram of a microwave-assisted fluid-bed processor with a microwave entry port at a 30° angle to the drying cavity. (b) Diagram of a microwave-assisted fluid-bed processor with a perpendicular placement of the microwave entry port to the drying cavity.

since the construction of the prototype MFBP. Figure 4a illustrates a MFBP with a microwave entrance 30° from horizontal. This design would "guide" the microwaves to a more dense region of fluidized material while utilizing the larger volume of the expansion chamber. A more radical design is shown in Fib. 4b. This concept takes advantage of a split-plenum design wherein the microwave entrance port would be incorporated into the steel septum between the two filter bags. This allows for the maximum exposure of microwaves to the fluidized material.

In addition, suggested improvements of ancillary equipment include a continuously variable tuner and the substitution of conductive gasketing with microwave chokes at critical component junctures.

CONCLUSION

The present 1-kg laboratory-size microwave-assisted fluid bed processor successfully combines the technologies of fluid-bed processing and microwave heating. The new equipment takes advantage of the fast evaporation rates, random particle travel, and multiprocessing capabilities of fluid bed drying. Moreover, the disadvantages of the slower initial drying rates and nonuniform moisture distributions that are normally associated with fluid-bed drying were eliminated through the introduction of microwave energy assistance. The MFBP also presents a safe and uncomplicated design for the introduction of microwaves to conventional fluid bed processors.

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