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# (54) USE OF A LAYER OF SOLID FUEL, METHOD FOR PRODUCING SUCH A LAYER AND ASSOCIATED HEATING UNIT

VERWENDUNG EINER SCHICHT AUS FESTEM BRENNSTOFF, VERFAHREN ZUM ERSTELLEN EINER SOLCHEN SCHICHT UND ZUGEHÖRIGE HEIZVORRICHTUNG

UTILISATION D’UNE COUCHE DE COMBUSTIBLE SOLIDE, PROCÉDÉ POUR FABRIQUER UNE TELLE COUCHE ET UNITÉ DE CHAUFFAGE CORRESPONDANTE

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**(Cont. next page)**

- **PATENT ABSTRACTS OF JAPAN vol. 006, no. 158 (C-120), 19 August 1982 (1982-08-19) -& JP 57 078968 A (DAINIPPON PRINTING CO LTD), 17 May 1982 (1982-05-17)**

## Description

### Field

**[0001]** This disclosure relates to heating units capable of rapidly heating the substrate to essentially uniform temperature across the surface and to articles and methods employing such heating units.

### Introduction

**[0002]** Self-contained heat sources are employed in a wide-range of industries, from food industries for heating food and drink to outdoor recreation industries for providing hand and foot warmers to medical applications for inhalation devices. Many self-contained heating sources are based on either an exothermic chemical reaction or on ohmic heating. For example, self-heating units that produce heat by an exothermic chemical reaction often have at least two compartments, one for holding a heat producing composition and one for holding an activating solution. The two compartments are separated by a frangible seal that when broken allows mixing of the components to initiate an exothermic reaction to generate heat (see for example U.S. Patent Nos. 5,628,304; 4,773,389; 6,289,889). This type of non-combustible, self-heating unit is suitable for heating food, drink, or cold toes and fingers, since the heat production is relatively mild. Another common source for self-contained heat is ohmic heating. In ohmic heating a current is passed through an electrically resistive material to generate heat that is transmitted to an adjacent article. This mode of heat production has been employed to vaporize or heat a volatile substance, for example tobacco, for inhalation by a user. Cigarette holders and pipe bowls having an electrical resistance coil to generate heat in order to volatilize tobacco flavors have been described (U.S. Patent Nos. 2,104,266; 4,922,901; 6,095,143). Heating of drugs other than tobacco by ohmic heating have also been described. For example, WO 94/09842 to Rosen describes applying a drug to an electrically resistive surface and heating the surface to vaporize the drug for inhalation. Ohmic heating has the advantage of facilitating precise control of the energy applied to determine the heat generated. However, in many ohmic heating systems, and in particular for small systems where limited energy is available, such as, for example, when using batteries, there can be a substantial delay on the order of seconds or minutes between the time heating is initiated and maximum temperature is achieved. Moreover, for small devices, such as for example, portable medical devices, where the power source comprises a battery, ohmic heating can be expensive and bulky.

**[0003]** Another approach for providing a controlled amount of heat is using electrochemical interactions. Here, components that interact electrochemically after initiation in an exothermic reaction are used to generate heat. Exothermic electrochemical reactions include reactions of a metallic agent and an electrolyte, such as a mixture of magnesium granules and iron particles as the metallic agent, and granular potassium chloride crystals as the electrolyte. In the presence of water, heat is generated by the exothermic hydroxylation of magnesium, where the rate of hydroxylation is accelerated in a controlled manner by the electrochemical interaction between magnesium and iron, which is initiated when the potassium chloride electrolyte dissociates upon contact with the liquid water. Electrochemical interactions have been used in the smoking industry to volatilize tobacco for inhalation (U.S. Patent Nos. 5,285,798; 4,941,483; 5,593,792).

**[0004]** The aforementioned self-heating methods are capable of generating heat sufficient to heat an adjacent article to several hundred degrees Celsius in a period of several minutes. There remains a need in the art for a device capable of rapid heat production, *i.e.*, on the order of seconds and fractions of seconds, capable of heating with essential uniformity an article to within a defined temperature range, and which is suitable for use in articles to be used by people.

**[0005]** US 5,322,018 relates to an igniter that is said to provide rapid longitudinal and radial propagation of the ignition reaction.

**[0006]** US 4,193,388 relates to a container which, it is said, can be designed to heat its outer surface as to sterilize it, or to heat its inner surface and any contents therewithin.

### Summary

**[0007]** This disclosure relates to the use of a layer of an essentially homogenous slurry of a selected mass of a solid fuel according to claim 1.

**[0008]** This disclosure relates also to a method for providing an essentially homogenous and uniform coating of dry solid fuel, according to claim 15, and to a heating unit according to the claim 28.

**[0009]** It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of certain embodiments, as claimed.

### Description of the Drawings

**[0010]**

Fig. 1A is a cross-sectional illustration of a heating unit according to certain embodiments.

Fig. 1B is a perspective illustration of a heating unit as disclosed herein, but not an embodiment of the claimed invention.

Fig. 2A is a cross-sectional illustration of a heating unit having a cylindrical geometry as disclosed herein, but not an embodiment of the claimed invention.

Fig. 2B is a perspective illustration of a heating unit having a cylindrical geometry as disclosed herein, but not an embodiment of the claimed invention.

Fig. 2C is a cross-sectional illustration of a cylindrical heating unit similar to the heating unit of Figs. 2A-2B but having a modified igniter design as disclosed herein, but not an embodimenet of the claimed invention.

Fig. 2D is a cross-sectional illustration of a cylindrically-shaped heating unit that includes a thermal shunt as disclosed herein but not an embodiment of the claimed invention.

Fig. 3 is a schematic cross-sectional illustration of a chemical heating unit having two pressure transducers for measuring the internal pressure during and after ignition of the solid fuel.

Figs. 4A-4F are thermal images of a cylindrically-shaped heating unit measured using an infrared thermal imaging camera at post-ignition times of 100 milliseconds (Fig. 4A), 200 milliseconds (Fig. 4B), 300 milliseconds (Fig. 4C), 400 milliseconds (Fig. 4D), 500 milliseconds (Fig. 4E), and 600 milliseconds (Fig. 4F).

Figs. 5A-5B are thermal images showing the temperature uniformity of the exterior substrate surface expanse 400 milliseconds after ignition of two cylindrically-shaped heating units.

Figs. 6A-6C show schematic illustrations of the generation of drug vapor from a drug supply unit carrying a film of drug on the exterior substrate surface (Fig. 6A); ignition of the heating unit (Fig. 6B); and generation of a wave of heat effective to vaporize the drug film (Fig. 6C).

Figs. 7A-7E are high speed photographs showing the generation of thermal vapor from a drug supply unit as a function of time following ignition of the solid fuel.

Fig. 8 shows a drug delivery device containing a heating unit as part of an inhalation drug delivery device for delivery of an aerosol comprising a drug.

Figs. 9A-9C show drug supply units for use in drug delivery devices designed for delivering multiple drug doses.

Figs 10A-10B show illustrations of a perspective view (Fig. 10A) and an assembly view (Fig. 10B) of a thin film drug supply unit.

Figs. 11A-11B show cross-sectional illustrations of thin film drug supply units comprising multiple doses.

Fig. 12 shows a relationship between the mass of a solid fuel coating and the peak temperature of the exterior surface of a substrate according to certain embodiments.

Fig. 13A is an illustration of a cross-sectional view of a heating unit having an impulse absorbing material disposed within the unit.

Fig.13B is an illustration of a cross-sectional view of a cylindrical heating unit having an impulse absorbing material disposed within the unit.

Fig. 13C is an illustration of a cross-sectional view of a heating unit having an impulse absorbing material and an additional pressure reducing element disposed with the enclosure.

Fig. 14 shows the measured pressure within heating units comprising glass fiber mats following ignition of the solid fuel.

Fig. 15 shows the temperature at various positions within a heating unit following ignition of the solid fuel.

Fig. 16 is a schematic illustration of an igniter comprising an initiator composition disposed on an electrically resistive heating element.

Fig.17 shows peak internal pressure within sealed heating units following ignition of a thin film layer of solid fuel comprising a metal reducing agent and a metal-containing oxidizer.

Fig. 18 shows the relationship of the yield and purity of an aerosol comprising a specific pharmaceutical compound using different substrate temperatures obtained from different masses of solid fuel.

Fig. 19 shows a temperature profile of a heating unit substrate following ignition of the solid fuel.

## Description of Various Embodiments

**[0011]** Unless otherwise indicated, all numbers expressing quantities of ingredients, reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about."

**[0012]** In this application, the use of the singular includes the plural unless specifically stated otherwise. In this application, the use of "or" means "and/or" unless stated otherwise. Also, terms such as "element" or "component" encompass both elements and components comprising one unit and elements and components that comprise more than one subunit unless specifically stated otherwise.

*COATED SUBSTRATES AND TEMPERATURE CONTROL*

**[0013]** **Fig. 1A** shows an example of a substrate **12,** such as those used in this invention. The substrate can be formed from a thermally-conductive material. Thermally-conductive materials are well known, and typically include, but are not limited to, metals, such as aluminum, iron, copper, stainless steel, and the like, alloys, ceramics, and filled polymers. The substrate can be formed from one or more such materials and in certain embodiments, can have a multilayer structure. For example, the substrate can comprise one or more films and/or coatings and/or multiple sheets or layers of materials. In certain embodiments, portions of the substrate can be formed from multiple sections. In certain embodiments, the multiple sections forming the substrate of the heating unit can have different thermal properties. A substrate can be of any appropriate geometry, the rectangular configuration shown in **Fig. 1A** is merely exemplary. A substrate can also have any appropriate thickness and the thickness of the substrate can be different in certain regions. Substrate **12,** as shown in **Fig. 1A,** has an interior surface **14** and an exterior surface **16.** Heat can be conducted from interior surface **14** to exterior surface **16.** An article or object placed adjacent or in contact with exterior surface **16** can receive the conducted heat to achieve a desired action, such as warming or heating a solid or fluid object, effecting a further reaction, or causing a phase change. In certain embodiments, the conducted heat can effect a phase transition in a compound in contact, directly or indirectly, with exterior surface **16.**

**[0014]** Solid fuels can be used to heat the substrates rapidly. The energy released during an exothermic reaction using solid fuels can be used to provide the temperature rise required to heat directly or indirectly a material adjacent to the exterior surface. In certain embodiments, the substrate **12** has an expanse of a solid fuel **20**, in direct contact with or adjoining interior surface **14.**

**[0015]** The solid fuel can be any appropriate shape and have any appropriate dimensions. For example, as shown in **Fig. 1A,** solid fuel **20** can comprise a surface expanse **26** and side expanses **28, 30.** As shown in **Fig. 1B,** heating unit **40** comprises a substrate **42** having an exterior surface **44** and an interior surface **46.** Solid fuel **48,** is in the shape of a hollow rod extending the length of substrate **42** and exhibiting a diameter less than that of interior surface **46.** It can be appreciated that a finned or ribbed exterior surface can provide a high surface area that can be useful to facilitate heat transfer from the solid fuel to an article or composition in contact with the surface.

**[0016]** The components of the solid fuel can react in an exothermic reaction to produce heat. For example, the solid fuel can react in an exothermic oxidation-reduction reaction or an intermetallic alloying reaction. An oxidation-reduction reaction refers to a chemical reaction in which one compound gains electrons and another compound loses electrons. The compound that gains electrons is referred to as an oxidizing agent, and the compound that loses electrons is referred to as a reducing agent. An example of an oxidation-reduction reaction is a chemical reaction of a compound with molecular oxygen ($O_2$) or an oxygen-containing compound that adds one or more oxygen atoms to the compound being oxidized. During the oxidation-reduction reaction, the molecular oxygen or the oxygen-containing compound is reduced by the compound being oxidized. The compound providing oxygen acts as the oxidizer or oxidizing agent. The compound being oxidized acts as the reducing agent. Oxidation-reduction reactions can be exothermic, meaning that the reactions generate heat. An example of an exothermic oxidation-reduction reaction is the thermite reaction of a metal with a metal oxidizing agent. According to the invention, a solid fuel comprises a metal reducing agent and a metal-containing oxidizing agent.

**[0017]** The metal reducing agent and the oxidizing agent can be in the form of a powder. The term "powder" refers to powders, particles, prills, flakes, and any other particulate that exhibits an appropriate size and/or surface area to sustain self-propagating ignition. For example, the powder can comprise particles exhibiting an average diameter ranging from 0.1 $\mu$m to 200 $\mu$m.

**[0018]** A metal reducing agent can include, but is not limited to molybdenum, magnesium, calcium, strontium, barium, boron, titanium, zirconium, vanadium, niobium, tantalum, chromium, tungsten, manganese, iron, cobalt, nickel, copper, zinc, cadmium, tin, antimony, bismuth, aluminum, and silicon. In certain embodiments, a metal reducing agent can include aluminum, zirconium, and titanium. A metal reducing agent can comprise more than one metal reducing agent.

**[0019]** An oxidizing agent can comprise oxygen, an oxygen based gas, and/or a solid oxidizing agent. In this disclosure, an oxidizing agent comprises a metal-containing oxidizing agent. A metal-containing oxidizing agent includes, but is not limited to, perchlorates and transition metal oxides. Perchlorates can include perchlorates of alkali metals or alkaline earth metals, such as, but not limited to, potassium perchlorate ($KClO_4$), potassium chlorate ($KClO_3$), lithium perchlorate ($LiClO_4$), sodium perchlorate ($NaClO_4$), and magnesium perchlorate [$Mg(ClO_4)_2$]. Transition metal oxides that function as oxidizing agents include, but are not limited to, oxides of molybdenum, such as $MoO_3$, iron, such as $Fe_2O_3$, vanadium ($V_2O_5$), chromium ($CrO_3$, $Cr_2O_3$), manganese ($MnO_2$), cobalt ($Co_3O_4$), silver ($Ag_2O$), copper ($CuO$), tungsten ($WO_3$), magnesium ($MgO$), and niobium ($Nb_2O_5$). The metal-containing oxidizing agent can include more than one metal-containing oxidizing agent.

**[0020]** In certain embodiments, the metal reducing agent forming the solid fuel can be selected from zirconium and aluminum, and the metal-containing oxidizing agent can be selected from $MoO_3$ and $Fe_2O_3$.

**[0021]** The ratio of metal reducing agent to metal-containing oxidizing agent can be selected to determine the ignition temperature and the burn characteristics of the solid fuel. An exemplary chemical fuel can comprise 75% zirconium and 25% $MoO_3$, percentage based on weight. In certain embodiments, the amount of metal with is a reducing agent can range from 60% by weight to 90% by weight of the total dry weight of the solid fuel. In certain embodiments, the amount of metal-containing oxidizing agent can range from 10% by weight to 40% by weight of the total dry weight of the solid fuel. The amount of oxidizing agent in the solid fuel can be related to the molar amount of the oxidizers at or near the eutectic point for the fuel composition. The oxidizing agent can be the major component and in others the metal reducing agent can be the major component. Those of skill in the art are able to determine the appropriate amount of each component based on the stoichiometry of the chemical reaction and/or by routine experimentation. Also as known in the art, the particle size of the metal and the metal-containing oxidizer can be varied to determine the burn rate, with smaller particle sizes selected for a faster burn (see, for example, U.S. Patent No. 5,603,350).

**[0022]** In certain embodiments, a solid fuel can comprise additive materials to facilitate, for example, processing and/or to determine the thermal and temporal characteristics of a heating unit during and following ignition of the solid fuel. An additive material can be reactive or inert. An inert additive material will not react or will react to a minimal extent during ignition and burning of the solid fuel. The additive can comprise inorganic or organic materials.

**[0023]** In certain applications, particularly, where it is desirous to produce a minimal amount of gas, such as for example, in a sealed heating unit, the additive material can be inorganic materials. These inorganic materials can function as binders, adhesives, gelling agents, thixotropic agents, and/or surfactants. Examples of gelling agents include, but are not limited to, clays such as Laponite®, Montmorillonite, Cloisite®, metal alkoxides, such as those represented by the formula $R\text{-}Si(OR)_n$ and $M(OR)_n$ where n can be 3 or 4, and M can be Ti, Zr, Al, B or other metals, and collidal particles based on transition metal hydroxides or oxides. Examples of binding agents include, but are not limited to, soluble silicates such as Na- or K-silicates, aluminum silicates, metal alkoxides, inorganic polyanions, inorganic polycations, and inorganic sol-gel materials, such as alumina or silica-based sols.

**[0024]** The solid fuel adheres to the surface of the substrate and the constituents of the solid fuel adhere to each other, and maintain physical integrity. It can be useful that the solid fuel remain adhered to the substrate surface and maintain physical integrity during processing, storage, and use during which time the solid fuel coating can be exposed to a variety of mechanical and environmental conditions. As discussed above, several additives, such as those disclosed herein, can be incorporated into the solid fuel to impart adhesion and physical robustness to the solid fuel coating.

**[0025]** The solid fuel can comprise Laponite®, and in particular Laponite® RDS, as an inert additive material. Laponite® is a synthetic layered silicate, and in particular a magnesium phyllosilicate, with a structure resembling that of the natural clay mineral hectorite ($Na_{0.4}Mg_{2.7}Li_{0.3}Si_4O_{10}(OH)_2$). Laponite® RD is a commercial grade material which, when added to water, rapidly disperses to form a gel when hydrated (Southern Clay Products, Gonzales, TX). Laponite® RD has the following chemical analysis in weight percent: 59.5% $SiO_2$ : 27.5% MgO: 0.8% $Li_2O$ : 2.8% $Na_2O$. Laponite® RDS (Southern Clay Products, Gonzales, TX) is a commercially available sol-forming grade of Laponite® modified with a polyphosphate dispersing agent, or peptizer, to delay rheological activity until the Laponite® RDS is added as a dispersion into a formulation. A sol refers to a colloid having a continuous liquid phase in which solid is suspended in a liquid. Laponite® RDS has the following chemical analysis in weight percent: 54.5% $SiO_2$ : 26% MgO : 0.8% $Li_2O$ : 5.6% $Na_2O$ : 4.1% $P_2O_5$. In the presence of electrolytes, Laponites® can act as gelling and thixotropic agents. Thixotropy refers to the property of a material to exhibit decreased viscosity under shear.

**[0026]** When incorporated into a solid fuel composition comprising a metal which is a reducing agent and a metal-containing oxidizing agent, such as any of those disclosed herein, in addition to imparting gelling and thixotropic properties, Laponite® RDS can also act as binder.

**[0027]** An example of the preparation of a solid fuel comprising Laponite® RDS and the application of the solid fuel to a metal foil substrate are described in Example 1.

**[0028]** Other useful additive materials include glass beads, diatomaceous earth, nitrocellulose, polyvinylalcohol, and other polymers that may function as binders. The solid fuel can comprise more than one additive material. The components of the solid fuel comprising the metal, oxidizing agent and/or additive material and/or any appropriate aqueous- or organic-soluble binder, can be mixed by any appropriate physical or mechanical method to achieve a useful level of dispersion and/or homogeneity. The solid fuel can be degassed.

**[0029]** In addition, to the enhanced binding properties of the solid fuels with additive, other advantages of using inorganic additives include stability of the additive up to very high temperatures and lack of, or minimal release of, any toxic gases by the additive. In an enclosed system, this lack of additional gas production from the inorganic additive also reduces or minimizes the possibility of rupture of the enclosed heating unit.

**[0030]** Tables 1A-1E summarize solid fuel compositions including the additives used. The weight ratio of the components comprising certain solid fuel compositions are provided.

**Table 1A: Examples of Solid Fuel Compositions (wt%)**

| Component | Fuel #1 | Fuel #2 | Fuel #3 | Fuel #4 | Fuel #5 | Fuel #6 | Fuel #7 | Fuel #8 |
|---|---|---|---|---|---|---|---|---|
| Zirconium (Zr) | 70-90 | | | | | 20-40 | 20-30 | |
| Titanium (Ti) | | 70-92 | | | | | | 60-80 |
| Iron (Fe) | | | 70-90 | | | | | |
| Magnesium (Mg) | | | | 20-40 | 40-60 | | | |
| Boron (B) | | | | | | | | 20-40 |
| Potassium perchlorate ($KClO_4$) | 10-30 | 8-30 | 10-30 | | | | | |
| Lead Oxide (PbO) | | | | | 40-60 | | | |
| Tungsten Oxide ($WO_3$) | | | | | | 60-80 | | |
| Barium Chromate ($BaCrO_4$) | | | | | | | 70-80 | |
| Teflon | | | | 60-80 | | | | |

**Table 1B: Examples of Solid Fuel Compositions (wt%)**

| Component | Fuel #9 | Fuel #10 | Fuel #11 | Fuel #12 | Fuel #13 | Fuel #14 | Fuel #15 | Fuel #16 |
|---|---|---|---|---|---|---|---|---|
| Zirconium (Zr) | | | | 21 | | | 10-50 | |
| Titanium (Ti) | 60-80 | | 70-92 | | 82 | 55 | 33-81 | |
| Iron (Fe) | | | 0-84 | | | | | |
| Aluminum (Al) | | 20-40 | | | | 20 | | |
| Nickel (Ni) | | 60-80 | | | | | | |
| Boron (B) | | | | | | 25 | | |
| Potassium perchlorate ($KClO_4$) | | | 8-30 | | | | 9-17 | 50 |
| Potassium chlorate ($KClO_3$) | | | | | 18 | | | |
| Tungsten Oxide ($WO_3$) | 20-40 | | | | | | | |
| Barium Chromate ($BaCrO_4$) | | | | 64 | | | | |
| Zirconium Carbide (ZrC) | | | | | | | | 50 |
| Diatomaceous Earth | | | | 15 | | | | |

**Table 1C: Examples of Solid Fuel Compositions (wt%)**

| Component | Fuel #17 | Fuel #18 | Fuel #19 | Fuel #20 | Fuel #21 | Fuel #22 | Fuel #23 | Fuel #24 |
|---|---|---|---|---|---|---|---|---|
| Zirconium (Zr) | | 50-65 | | | 50-72 | 30-80 | 65 | 55-70 |
| Titanium (Ti) | | | 20-70 | | | | | |
| Boron (B) | | | | 15 | | | | |
| Potassium Perchlorate ($KClO_4$) | 52.5 | | | | | | | |
| Molybdenum Oxide ($MoO_3$) | | 0-50 | 30-80 | | | 20-70 | | 25-33 |
| Iron Oxide ($Fe_2O_3$) | | 0-50 | | 85 | 28-50 | | 25 | |
| Zirconium Hydride ($ZrH_2$) | 47.5 | | | | | | | |
| Diatomaceous Earth | | balance | | | | | 10 | 5-12 |

**Table 1D: Examples of Solid Fuel Compositions (wt%)**

| Component | Fuel #25 | Fuel #26 | Fuel #27 | Fuel #28 | Fuel #29 | Fuel #30 | Fuel #31 | Fuel #32 | Fuel #33 |
|---|---|---|---|---|---|---|---|---|---|
| Zirconium (Zr) | 35-50 | 63-69 | 70 | 34 | 66.5-69 | 66.5-74.6 | 54-66.5 | 69 | 69 |
| Titanium (Ti) | 20-35 | | | | | | | | |
| Molybdenum Oxide $MoO_3$ | 30 | 27-29.5 | 30 | 54 | 28.5-29 | 24.87-29 | 28.5-34 | 29.85 | 29.85 |
| Nitrocellulose | | | excess | | | 0.53-4.5 | | 0.5 | 0.5 |
| Cab-O-Sil | | 4-7.5 | | | | | | | |
| Glass Fiber | | | | 12 | | | | | 0.65 |
| Glass Microsphere | | | | | | | | 0.65 | |
| Polyvinyl Alcohol | | | | | 2.5-4.5 | | | | |
| High Vacuum Grease | | | | | | | 5-12 | | |

**Table 1E: Examples of Solid Fuel Compositions (wt%)**

| Component | Fuel #34 | Fuel #35 | Fuel #36 | Fuel #37 | Fuel #38 | Fuel #39 | Fuel #40 | Fuel #41 | Fuel #42 | Fuel #43 |
|---|---|---|---|---|---|---|---|---|---|---|
| Zirconium (Zr) | 66.5-69 | 69.65 | 69.7-74.6 | 49-59.5 | | | 47-70 | | 40 | 20 |
| Magnesium (Mg) | | | | | | 40 | | | | |
| Aluminum (Al) | | | | | 36-70 | | | 50-55 | 30 | |
| Silicon (Si) | | | | | | | | | | 30 |
| Potassium chlorate ($KClO_3$) | | | | | | | 0-3 | | | |
| Bismuth Oxide ($Bi_2O_3$) | | | | | | | | | | 50 |
| Molybdenum Oxide ($MoO_3$) | 28.5-29 | 29.85 | 24.9-29.8 | 21-25.5 | 30-64 | 40 | 23.1-38 | 45-50 | 30 | |
| Diatomaceous Earth | | | | 19-25 | | | balance or excess | | | |
| Nitrocellulose | | | | 0.5 | | | 0.4-2 | 1 | | |
| Glass Beads | | | | | | 20 | | | | |
| Carboxymethyl cellulose | | | | | | | | | | excess |
| Polyvinyl alcohol | | | 0.5 | | | | | | | |
| 40% Aqueous $SiO_2$ | 2-5 | | | | | | | | | |
| Viton-A | | 0.5 | | | | | | | | |

**[0031]** While the use of additives in the solid fuel can improve the binding properties of the solid fuel, it also can improve the ease of use and manufacturability of substrates coated with such fuel. In particular, use of additives can make it possible to use wet-coating techniques, such as, for example, but not limitation, dip coating, spray coating, roller coating, gravure coating, reverse roll coating, gap coating e.g. with a wire wound coating rod e.g. in a bar coater, metering rod coating, slot die coating, curtain coating, and air knife coating, as means for deposition of a fuel powder on a substrate surface, such as, for example, either inside, or on, a cylindrical type surface such as the internal surface of the substrate in **Fig. 1B**, or on a flat surface such as a foil as is shown in **Fig 10A**.

**[0032]** The use of solid fuel slurries with additives for coating a substrate can provide for better mixing of the materials, enhanced adherence properties, and more control over the even disbursement of the solid fuel on a surface. While preparing a physical mixture of solid fuel powders as an essentially homogeneous layer around the walls of a cylindrical device can be done, it is problematic, especially if the materials used have differences in densities, particle sizes, shapes, surface volume ratios; and lack chemically attractive surface-surface interactions. (Essentially homogeneous is defined, for purposes herein, as essentially uniform; and when applied to a mixture of two or more components, it refers to a basically uniform distribution of the various different particles throughout the mixture. This is in contrast to a heterogeneous mixture of components where various components tend to aggregate and there is settling out of the higher density particles.) Use of a core for dispersing mixtures of fuel powders to an interior surface of a substrate, allows one to control the gap or layer thickness of the solid fuel layer, however, it does not prevent other problems such as segregation of the particles in the mixture. Inadequate homogeneity as to the fuel mixture itself, due to ineffective mixing can result in inconsistent heating of the exterior surface of the substrate. Mixing can be facilitated and even automated when done as a slurry as opposed to a dry powder.

**[0033]** Additionnally, lack of homogeneity as to the fuel thickness on, or in, contact with an interior surface of a substrate can also result in inconsistent heating of the exterior surface of a substrate. Coating adherence and ease of application can be enhanced by the use of slurries with additives.

**[0034]** The solid fuel is disposed on a substrate as a coating or thin layer, wherein the thickness of the thin layer of solid fuel ranges from 0.00254 cm (0.001 inches) to 0.0762 cm (0.030 inches) by use of wet coating.

**[0035]** Substrates such as, for example, substrates **510** shown in **Fig. 10A**, can be coated to a nearly homogeneous thickness to form a thin coating or a thin layer of solid fuel **512** on the interior region of the substrate corresponding to the exterior surface on which the drug **514** is disposed. The thickness of the substrate, its thermal conductivity, its heat capacity, the thickness of the thin layer of solid fuel **512**, and the composition of solid fuel **512** can determine the maximum temperature (peak temperature) as well as the temporal and spatial dynamics of the temperature profile produced by the burning of the solid fuel.

**[0036]** Studies using thin solid fuel layers having a thickness ranging from 0.00254 cm (0.001 inches) to 0.0227 cm (0.005 inches) demonstrate that the maximum temperature reached by a thin film substrate on which the solid fuel is disposed can be linear with the mass of solid fuel applied. For example, as shown in **Fig. 12** for several different solid fuel compositions, for a 0.00254 cm (0.001 inch) to 0.00762 cm (0.0003 inch) thick layer of $Zr/MoO_3$ solid fuel having a mass ranging from 0.13 g to 0.25 g, the maximum temperature reached by the substrate during burn is linear. Other studies with solid fuel layers having a mass ranging from 0.12 g to 0.24 g demonstrate linearity over a temperature ranging from 375 °C to 625 °C. It will be appreciated that one skilled in the art can establish similar relationships for other solid fuel compositions and configurations. Such studies demonstrate that the temperature reached by the substrate when the solid fuel is burned can be established by controlling the amount of solid fuel applied to the substrate.

**[0037]** Measurements of the substrate surface temperature after firing demonstrate that thin coatings or layers of a solid fuel comprising a metal reducing agent and a metal-containing oxidizing agent can produce uniformity of temperature on the exterior surface of the substrate. Uniformity of temperature is defined herein to exist when the temperature in degrees Celsius of the exterior surface of the substrate, corresponding to the fuel coated area of the interior surface of the substrate, is within a standard deviation of 50° C from the average surface temperature obtained, as measured within 100 milliseconds after completion of propagation of the ignited fuel flame front. A temperature profile of a substrate forming a heating unit substantially as shown in **Figs. 10A** and **10B** and described in Example 9 following ignition of the solid fuel is shown in **Fig. 19**. **Fig. 19** shows the average surface temperature at various positions across two dimensions of a 3.302 cm x 3.302 cm (1.3 inch x 1.3 inch) substrate 0.25 seconds following ignition of a 0.0041 cm (0.00163 inch) thick coating of solid fuel. The average surface temperature of the effective heated area was about 400°C.

**[0038]** In certain applications, such as for example, vaporization of a drug off the substrate of a heating unit, uniformity of heating of the substrate is critical as it facilitates the production of an aerosol comprising a high purity drug or pharmaceutical composition and maximizes the yield of drug initially deposited on the substrate forming an aerosol.

## *HEATING UNITS*

**[0039]** An embodiment of a heating unit is shown in **Fig. 1A**. Heating unit **10** comprises a substrate **12** with a thin layer or coating of solid fuel **20** in contact with the interior surface **14** of substrate **12**. Solid fuel is ignited to generate a self-sustaining oxidation-reduction reaction. Once a portion of the solid fuel is ignited, the heat generated by the oxidation-reduction reaction can ignite adjacent unburned fuel until all of the fuel is consumed in the process of the chemical reaction. The exothermic oxidation-reduction reaction can be initiated by the application of energy to at least a portion of the solid fuel. Energy absorbed by the solid fuel or by an element in contact with the solid fuel can be converted to heat. When the solid fuel becomes heated to a temperature above the auto-ignition temperature of the reactants, e.g. the minimum temperature required to initiate or cause self-sustaining combustion in the absence of a combustion source or flame, the oxidation-reduction reaction will initiate, igniting the solid fuel in a self-sustaining reaction until the fuel is consumed.

**[0040]** Energy can be applied to ignite the solid fuel using a number of methods. For example, a resistive heating element can be positioned in thermal contact with the solid fuel, which when a current is applied, can heat the solid fuel to the auto-ignition temperature. An electromagnetic radiation source can be directed at the solid fuel, which when absorbed, can heat the solid fuel to its auto-ignition temperature. An electromagnetic source can include lasers, diodes, flashlamps and microwave sources. RF or induction heating can heat the solid fuel source by applying an alternating RF field that can be absorbed by materials having high magnetic permeability, either within the solid fuel, or in thermal contact with the solid fuel. The source of energy can be focused onto the absorbing material to increase the energy density to produce a higher local temperature and thereby facilitate ignition. In certain embodiments, the solid fuel can be ignited by percussive forces.

**[0041]** The auto-ignition temperature of a solid fuel comprising a metal which is a reducing agent and a metal-containing oxidizing agent as disclosed herein can range of 400 °C to 500 °C. While such high auto-ignition temperatures facilitate safe processing and safe use of the solid fuel under many use conditions, for example, as a portable medical device, for the same reasons, to achieve such high temperatures, a large amount of energy must be applied to the solid fuel to initiate the self-sustaining reaction. Furthermore, the thermal mass represented by the solid fuel can require that an impractically high temperature be applied to raise the temperature of the solid fuel above the auto-ignition temperature. As heat is being applied to the solid fuel and/or a support on which the solid fuel is disposed, heat is also being conducted away. Directly heating a solid fuel can require a substantial amount of power due to the thermal mass of the solid fuel and support.

**[0042]** As is well known in the art, for example, in the pyrotechnic industry, sparks can be used to safely and efficiently ignite fuel compositions. Sparks refer to an electrical breakdown of a dielectric medium or the ejection of burning particles. In the first sense, an electrical breakdown can be produced, for example, between separated electrodes to which a voltage is applied. Sparks can also be produced by ionizing compounds in an intense laser radiation field. Examples of burning particles include those produced by friction and break sparks produced by intermittent electrical current. Sparks of sufficient energy incident on a solid fuel can initiate the self-sustaining oxidation-reduction reaction.

**[0043]** When sufficiently heated, the exothermic oxidation-reduction reaction of the solid fuel can produce sparks, as well as radiation energy. Thus, reliable, reproducible and controlled ignition of the solid fuel can be facilitated by the use of an initiator composition capable of reacting in an exothermic oxidation-reduction reaction. The initiator composition can comprise the same or similar reactants as those comprising the solid fuel. The initiator composition can be formulated to maximize the production of sparks having sufficient energy to ignite a solid fuel. Sparks ejected from an initiator composition can impinge upon the surface of the solid fuel, causing the solid fuel to ignite in a self-sustaining exothermic oxidation-reduction reaction. The igniter can comprise a physically small, thermally isolated heating element on which is applied a small amount of an initiator composition capable of producing sparks or the initiator composition can be placed directly on the fuel itself and ignited by a variety of means, including, for example, optical or percussive.

**[0044]** As shown in **Fig. 1A**, heating unit **10** can include an initiator composition **50** which can ignite a portion of solid fuel **20**. As shown in **Fig. 1A**, initiator composition **50** can be positioned proximate to the center region **54** of solid fuel **20**. Initiator composition **50** can be positioned at other regions of solid fuel **20**, such as toward the edges. A heating unit can comprise more than one initiator composition where the more than one initiator composition **50** can be positioned on the same or different side of solid fuel **20**. Initiator composition **50** can be mounted in a retaining member **56** that is integrally formed with substrate **12** and/or secured within a suitably sized opening in substrate **12**. Retaining member **56** and substrate **12** can be sealed to prevent release outside heating unit **10** of reactants and reaction products produced during ignition and burning of solid fuel **20**. Electrical leads **58a**, **58b** in electrical contact with initiator composition **50** can extend from retaining member **56** for electrical connection to a mechanism configured to activate (not shown) initiator composition **50**.

**[0045]** Initiator compositions capable of producing sparks upon exposure to heat, force, or a spark are known, for example, in the pyrotechnic field and the photoflash industry. An initiator composition can comprise at least one metal, such as those described herein, and at least one oxidizing agent, such as, for example, a chlorate or perchlorate of an alkali metal or an alkaline earth metal or metal oxide and others disclosed herein. An initiator composition can include at least one binder and/or additive material such as a gelling agent and/or binder. Examples of additive materials including gelling agents and/or binders are disclosed herein. Additive materials can be useful in determining certain processing, ignition, and/or burn characteristics of the initiator composition.

**[0046]** Fig. **2A** shows a longitudinal cross-sectional illustration of a heating unit. **Fig. 2B** shows a corresponding perspective illustration illustrating the unassembled individual components shown in **Fig. 2A**. As shown in **Fig. 2A**, heating unit **60** can include a substrate **62** that is generally cylindrical in shape and terminates at one end in a tapered nose portion **64** and at the other end in an open receptacle **66**. Substrate **62** has interior and exterior surfaces **68**, **70**, respectively, which define an inner region **72**. An inner backing member **74** can be cylindrical in shape and can be located within inner region **72**. The opposing ends **76**, **78** of backing member **74** can be open. Backing member **74** can comprise a heat-conducting or heat-absorbing material, depending on the desired thermal and temporal dynamics of the heating unit. When constructed of a heat-absorbing material, backing member **74** can reduce the maximum temperature reached by substrate **62** after ignition of the solid fuel **80**.

**[0047]** Solid fuel **80** comprising, for example, any of the solid fuels described herein, can be confined between substrate **62** and backing member **74** or can fill inner region **72**. Solid fuel 80 can adjoin interior surface **68** of substrate **62**.

**[0048]** Initiator composition **82** can be positioned in open receptacle **66** of substrate **62**, and can be configured to ignite solid fuel **80**. A retaining member **84** can be located in open receptacle **66** and can be secured in place using any suitable mechanism, such as for example, bonding or welding. Retaining member **84** and substrate **62** can be sealed to prevent release of the reactants or reaction products produced during ignition and burn of initiator composition **82** and solid fuel **80**. Retaining member **84** can include a recess **86** in the surface facing inner region **72**. Recess **86** can retain initiator composition **82**. In certain embodiments, an electrical stimulus can be applied directly to initiator composition **82** via leads **88**, **90** connected to the positive and negative termini of a power source, such as a battery (not shown). Leads **88**, **90** can be connected to an electrically resistive heating element placed in physical contact with the initiator composition **82** (not shown). In certain embodiments, leads **88**, **90** can be coated with the initiator composition **82**.

**[0049]** Referring to **Fig. 2A**, application of a stimulus to initiator composition **82** can result in the generation of sparks that can be directed from open end **78** of backing member **74** toward end **76**. Sparks directed toward end **76** can contact solid fuel **80**, causing solid fuel **80** to ignite. Ignition of solid fuel **80** can produce a self propagating wave of ignited solid fuel **80**, the wave traveling from open end **78** toward nose portion **64** and back toward retaining member **84** held within receptacle end **66** of substrate **62**. The self-propagating wave of ignited solid fuel **80** can generate heat that can be conducted from interior surface **68** to exterior surface **70** of substrate **62**.

**[0050]** A heating unit is illustrated in **Fig. 2C**. As shown in **Fig. 2C**, heating unit **60** can comprise a first initiator composition **82** disposed in recess **86** in retaining member **84** and a second initiator composition **94** disposed in open end **76** of backing member **74**. Backing member **74**, located within inner region **72**, defines an open region **96**. Solid fuel **80** is disposed within the inner region between substrate **62** and backing member **74**. Sparks generated upon application of an electrical stimulus to first initiator composition **82**, through leads **88**, **90**, can be directed through open region **96** toward second initiator composition **94**, causing second initiator composition **94** to ignite and generate sparks. Sparks generated by second initiator composition **94** can then ignite solid fuel **80**, with ignition initially occurring toward the nose portion of substrate **62** and traveling in a self propagating wave of ignition to the opposing end.

**[0051]** The igniter can comprise a support and an initiator composition disposed on the support. The support can be thermally isolated to minimize the potential for heat loss. In this way, dissipation of energy applied to the combination of assembly and support can be minimized, thereby reducing the power requirements of the energy source, and facilitating the use of physically smaller and less expensive heat sources. In certain applications, for example, with battery powered portable medical devices, such considerations can be particularly useful. It can be useful that the energy source be a small low cost battery, such as a 1.5 V alkaline battery. The initiator composition can comprise a metal reducing agent and metal-containing oxidizing agent.

**[0052]** A metal reducing agent can include, but is not limited to molybdenum, magnesium, calcium, strontium, barium, boron, titanium, zirconium, vanadium, niobium, tantalum, chromium, tungsten, manganese, iron, cobalt, nickel, copper, zinc, cadmium, tin, antimony, bismuth, aluminum, and silicon. A metal reducing agent can include aluminum, zirconium, and titanium. A metal reducing agent can comprise more than one metal reducing agent. An oxidizing agent can comprise oxygen, an oxygen based gas, and/or a solid oxidizing agent. An oxidizing agent can comprise a metal-containing oxidizing agent. A metal-containing oxidizing agent includes, but is not limited to, perchlorates and transition metal oxides. Perchlorates can include perchlorates of alkali metals or alkaline earth metals, such as but not limited to, potassium perchlorate ($KClO_4$), potassium chlorate ($KClO_3$), lithium perchlorate ($LiClO_4$), sodium perchlorate ($NaClO_4$), and magnesium perchlorate [$Mg(ClO_4)_2$]. Transition metal oxides that function as oxidizing agents include, but are not limited to, oxides of molybdenum, such as $MoO_3$, iron, such as $Fe_2O_3$, vanadium ($V_2O_5$), chromium ($CrO_3$, $Cr_2O_3$), manganese ($MnO_2$), cobalt ($Co_3O_4$), silver ($Ag_2O$), copper ($CuO$), tungsten ($WO_3$), magnesium ($MgO$), and niobium ($Nb_2O_5$). The metal-containing oxidizing agent can include more than one metal-containing oxidizing agent.

**[0053]** The ratio of metal reducing agent to metal-containing oxidizing agent can be selected to determine the appropriate burn and spark generating characteristics. The amount of oxidizing agent in the initiator composition can be related to the molar amount of the oxidizers at or near the eutectic point for the fuel composition. The oxidizing agent can be the major component and in others the metal reducing agent can be the major component. Those of skill in the art are able to determine the appropriate amount of each component based on the stoichiometry of the chemical reaction and/or by routine experimentation. Also as known in the art, the particle size of the metal and the metal-containing oxidizer can be varied to determine the burn rate, with smaller particle sizes selected for a faster burn (see, for example, WO 2004/011396).

**[0054]** An initiator composition can comprise additive materials to facilitate, for example, processing, enhance the mechanical integrity and/or determine the burn and spark generating characteristics. The additive materials can be inorganic materials and can function as binders, adhesives, gelling agents, thixotropic, and/or surfactants. Examples of gelling agents include, but are not limited to, clays such as Laponite®, Montmorillonite, Cloisite®, metal alkoxides such as those represented by the formula $R\text{-}Si(OR)_n$ and $M(OR)_n$ where n can be 3 or 4, and M can be Ti, Zr, Al, B or other metals, and colloidal particles based on transition metal hydroxides or oxides. Examples of binding agents include, but are not limited to, soluble silicates such as Na- or K-silicates, aluminum silicates, metal alkoxides, inorganic polyanions, inorganic polycations, inorganic sol-gel materials such as alumina or silica-based sols. Other useful additive materials include glass beads, diatomaceous earth, nitrocellulose, polyvinylalcohol, guor gum, ethyl cellulose, cellulose acetate, polyvinylpyrrolidone, fluorocarbon rubber (Viton) and other polymers that can function as a binder. The initiator composition can comprise more than one additive material. The components of the initiator composition comprising the metal, metal-containing oxidizing agent and/or additive material and/or any appropriate aqueous- or organic-soluble binder, can be mixed by any appropriate physical or mechanical method to achieve a useful level of dispersion and/or homogeneity. Additive materials can be useful in determining certain processing, ignition, and/or burn characteristics of the initiator composition. The particle size of the components of the initiator can be selected to tailor the ignition and burn rate characteristics as is known in the art (see for example U.S. Patent No. 5,739,460).

**[0055]** An initiator composition can comprise at least one metal, such as those described herein, and at least one oxidizing agent, such as, for example, a chlorate or perchlorate of an alkali metal or an alkaline earth metal or metal oxide and others disclosed herein.

**[0056]** Examples of initiator compositions include compositions comprising 10% Zr : 22.5% B : 67.5% $KClO_{3.}$; 49.0% Zr : 49.0 % $MoO_3$ and 2.0% nitrocellulose, and 33.9% Al : 55.4% $MoO_3$ : 8.9% B : 1.8 nitrocellulose; 26.5% Al : 51.5% $MoO_3$ : 7.8%B : 14.2% Viton, in weight percent.

**[0057]** Other initiator compositions can be used. For example, an initiator composition that can ignite upon application of a percussive force comprises a mixture of sodium chlorate ($NaClO_3$), phosphorous (P), and magnesium oxide (MgO).

**[0058]** Energy sufficient to heat the initiator composition to the auto-ignition temperature can be applied to the initiator composition and/or the support on which the initiator composition is disposed. The energy source can be any of those disclosed herein, such as resistive heating, radiation heating, inductive heating, optical heating, and percussive heating. In applications wherein the initiator composition is capable of absorbing the incident energy, the support can comprise a thermally insulating material. The incident energy can be applied to a thermally conductive support that can heat the initiator composition above the auto-ignition temperature by thermal conduction.

**[0059]** The energy source can be an electrically resistive heating element. The electrically resistive heating element can comprise any material that can maintain integrity at the auto-ignition temperature of the initiator composition. The heating element can comprise an elemental metal such as tungsten, an alloy such as Nichrome, or other material such as carbon. Materials suitable for resistive heating elements are known in the art. The resistive heating element can have any appropriate form. For example, the resistive heating element can be in the form of a wire, filament, ribbon or foil. The electrical resistance of the heating unit can range from 2 Ω to 4 Ω. The appropriate resistivity of the heating element can at least in part be determined by the current of the power source, the desired auto ignition temperature, or the desired ignition time. The auto-ignition temperature of the initiator composition can range from 200 °C to 500 °C. The resistive heating element can be electrically connected, and suspended between two electrodes electrically connected to a power source.

**[0060]** The support can comprise one or more heating units.

**[0061]** An igniter comprising a resistive heating element is illustrated in **Fig. 16**. As shown in **Fig. 16**, resistive heating element **716** is electrically connected to electrodes **714**. Electrodes **714** can be electrically connected to an external power source such as a battery (not shown). As shown in **Fig. 16**, electrodes **714** are disposed on a laminate material **712** such as a printed circuit material. Such materials and methods of fabricating such flexible or rigid laminated circuits are well known in the art. Laminate material **712** can comprise a material that will not degrade at the temperatures reached by resistive heating element **716**, by the exothermic reaction including sparks generated by initiator composition **718**, and at the temperature reached during burning of the solid fuel. For example, laminate **712** can comprise Kapton®, a fluorocarbon laminate material or FR4 epoxy/fiberglass printed circuit board. Resistive heating element **716** is positioned in an opening **713** in laminate **712**. Opening **713** thermally isolates resistive heating element **716** to minimize thermal dissipation and facilitate transfer of the heat generated by the resistive heating element to the initiator composition, and can provide a path for sparks ejected from initiator composition **718** to impinge upon a solid fuel (not shown).

**[0062]** As shown in **Fig. 16**, initiator composition **718** is disposed on resistive heating element **716**.

**[0063]** The following procedure was used to apply the initiator composition to resistive heating elements.

**[0064]** A 0.002 cm (0.0008 inch) diameter Nichrome wire was soldered to Cu conductors disposed on a 0.005 inch thick FR4 epoxy/fiberglass printed circuit board (Onanon). The dimensions of the igniter printed circuit board were 4.62 x 0.64 cm (1.82 inches by 0.25 inches). Conductor leads can extend from the printed circuit board for connection to a power source. In certain embodiments, the electrical leads can be connected to an electrical connector.

**[0065]** The igniter printed circuit board was cleaned by sonicating (Branson 8510R-MT) in DI water for 10 minutes, dried, sprayed with acetone and air dried.

**[0066]** The initiator composition comprised 0.68 grams nano-aluminum (40-70 nm diameter, Argonide Nanomaterial Technologies, Sanford, FL), 1.23 grams of nano-$MoO_3$ (EM-NTO-U2; Climax Molybdenum, Henderson, CO), and 0.2 grams of nano-boron (33,2445-25G; Aldrich). A slurry comprising the initiator composition was prepared by adding 8.6 mL of 4.25% Viton/A500 (4.25 grams Viton in 100 mL amyl acetate (Mallinckrodt)) solution.

**[0067]** A 1.1 uL drop of slurry was deposited on the heating element, dried for 20 minutes, and another 0.8 uL drop of slurry comprising the initiator composition was , deposited on the opposite side of the heating element.

**[0068]** Application of 3.0 V through a 1,000$\mu$F capacitor from two A76 alkaline batteries to the Nichrome heating element ignited the Al : $MoO_3$ : B initiator composition within 1 to 50 msec, typically within 1 to 6 msec. When positioned within 0.12" inches of the surface of a solid fuel comprising a metal reducing agent and a metal-containing oxidizing agent such as, for example, a fuel comprising 76.16% Zr: 19.04% $MoO_3$ : 4.8% Laponite® RDS, the sparks produced by the initiator composition ignited the solid fuel to produce a self-sustaining exothermic reaction. A 1 $\mu$L drop of the slurry comprising the initiator composition can be deposited onto the surface of the solid fuel adjacent the initiator composition disposed on the resistive heating element to facilitate ignition of the solid fuel.

**[0069]** The initiator composition comprising Al : $MoO_3$ : B adhered to the Nichrome wire and maintained physical integrity following mechanical and environmental testing including temperature cycling (-25 °C ↔ 40 °C), drop testing, and impact testing.

**[0070]** As shown in **Fig. 2D** heating units can include a thermal shunt **98**, shown in **Fig. 2D** as a cylindrical rod disposed within the heating unit. The thermal shunt can be incorporated into the solid fuel expanse as a particulate, the thermal shunt can comprise the backing member and/or the thermal shunt can be a separate element as shown. The thermal shunt can be in direct contact with the solid fuel and/or can indirectly contact the solid fuel. A thermal shunt can be capable of absorbing heat such that incorporation of a thermal shunt in a heating unit can control or reduce the maximum temperature reached by the exterior surface of the substrate forming the heating unit. For example, the thermal shunt can comprise a material capable of undergoing a phase change at or above the ignition temperature of the solid fuel. Examples of phase change materials include low melting point metals such as tin, low melting point alloys such as Wood's metal and leadtin alloys, inorganic salts, and mixtures thereof. The thermal shunt can comprise a material that can release absorbed heat to prolong the heating time of the heating unit. A thermal shunt can comprise at least one material exhibiting a high heat capacity, such as, for example, copper, aluminum, stainless steel and glass. Examples of materials that can release absorbed heat include sugars, waxes, metal salts and other materials capable of melting during burning of the solid fuel and then undergoing crystallization as the heating unit cools, thus generating exothermic heat of crystallization, and mixtures thereof. Other materials capable of functioning as thermal shunts include porous and fibrous materials such as porous ceramic membranes and/or fiber mats, and the like. Such materials can exhibit a high surface area that can facilitate heat transfer from the reactants and reaction products to the material matrix. In certain applications, the porous and/or fibrous materials do not react with the reactants or reaction products produced during ignition and burn, and do not degrade and/or produce gaseous products at the temperatures achieved by the heating unit. The thermal shunt material can comprise fibers including, but not limited to, metal fibers, silica fibers, glass fibers, graphite fibers, and/or polymer fibers.

**[0071]** In certain embodiments, the heating unit described and illustrated in **Fig. 1A** can be used in applications wherein rapid heating is useful. In certain embodiments, a portion of the substrate can reach a maximum (peak) temperature in less than three seconds (3 sec), in certain embodiments less than 1 second (1 sec), in certain embodiments less than 500 milliseconds, and in certain embodiments less than 250 milliseconds.

**[0072]** A heating unit substantially as illustrated in **Fig. 2B** was fabricated to measure the temperature of the exterior surface of the substrate following ignition of a solid fuel. Referring to **Fig. 2B**, cylindrical substrate **62** was approximate 3.81 cm (1.5 inches) in length and the diameter of open receptacle 66 was 1.524 cm (0.6 inches). Solid fuel **80** comprising 75% Zr : 25% $MoO_3$ in weight percent was placed in the inner region in the space between the backing member **74** and the interior surface of substrate **62**. A first initiator composition **82** comprising 5 mg of 10% Zr : 22.5% B : 67.5% $KClO_3$ in weight percent was placed in the depression of the retaining member and 10 mg of a second initiator composition **94** of 10% Zr : 22.5% B : 67.5% $KClO_3$ in weight percent was placed in the open end **76** of backing member **74** near the tapered portion of heating unit **60**. Electrical leads **88**, **90** from two 1.5 V batteries provided a current of 0.3 Amps to ignite first initiator composition **82**, thus producing sparks to ignite second initiator composition **94**. Both initiators were ignited within 1 to 20 milliseconds following application of the electrical current. Sparks produced by second initiator composition **94** ignited solid fuel **80** in the tapered nose region **64** of the cylinder. Thermocouples placed on the exterior surface of substrate **62** were used to monitor the substrate surface temperature as a function of time. The exterior substrate surface reached a maximum temperature of 400 °C in less than 100 milliseconds.

**[0073]** Upon ignition of the solid fuel, an exothermic oxidation-reduction reaction produces a considerable amount of energy in a short time, such as for example, in certain embodiments less than 1 second, in certain embodiments less than 500 milliseconds, and in certain embodiments less than 250 milliseconds. Examples of exothermic reactions include electrochemical reactions and metal oxidation-reduction reactions. When used in enclosed heating units, by minimizing the quantity of reactants and the reaction conditions the reaction can be controlled but can result in a slow release of heat and/or a modest temperature rise. However, in certain applications, it can be useful to rapidly heat a substrate to temperatures in excess of 200 °C within 1 second or less. Such rapid intense thermal pulses can be useful for vaporizing pharmaceutical compositions to produce aerosols. A rapid intense thermal pulse can be produced using an exothermic oxidation-reduction reaction and in particular a thermite reaction involving a metal and a metal-containing oxidizing agent. Concomitant with the rapid generation of heat, there can be a rapid generation of gaseous products and unreacted reactants with high translational energies. When sealed within an enclosure, the exothermic oxidation-reduction reaction can generate a significant increase in pressure.

**[0074]** Energy produced by the exothermic reaction, whether thermal, optical, mechanical, e.g. particle ejection, or chemical can generate a significant pressure when contained with a sealed enclosure. In certain embodiments, a solid fuel capable of reacting in an exothermic oxidation-reduction reaction can be used to form a heating unit. For example, solid fuel as disclosed herein can be used to thermally vaporize a drug coating to produce an aerosol of a drug for medical applications. In certain applications, such as in portable medical devices, it can be useful to contain the pyrothermic materials and products of the exothermic reaction and other chemical reactions resulting from the high temperatures within the enclosure. While containing the exothermic reaction can be accomplished by adequately sealing the enclosure to withstand the internal pressures resulting from the burning of the solid fuel as well as an initiator composition if present, it can be useful to minimize the internal pressure to ensure the safety of the heating device and facilitate device fabrication.

**[0075]** The pressure within the substrate can increase during and after ignition and burning of the initiator composition and the solid fuel. The increase in pressure can depend, at least in part, on the amount and composition of the solid fuel, the relative amounts of the fuel components, the density and/or degree of compaction of the solid fuel, the particle size of the fuel components, the configuration of the substrate, the amount of initiator, and/or the composition of the initiator. A solid fuel, an initiator composition, and a substrate configuration can be selected to control the pressure increase and maintain the maximum pressure within a useful operating range. The initiator composition and solid fuel can produce gas phase reaction products during ignition and burn. Thus, the pressure within the substrate can be managed by minimizing the amount of initiator composition and solid fuel disposed within the heating unit. One of skill can experimentally determine the minimum amount of initiator composition needed to reliably ignite the solid fuel. One of skill can also determine the properties, configuration, and placement of the solid fuel within a heating unit to achieve a useful substrate temperature.

**[0076]** The internal pressure of a heating unit can be managed or reduced by constructing the substrate, backing, and any other internal components from materials that produce minimal gas products at elevated temperatures. Pressure can be managed or reduced by providing an interior volume wherein gas can be collected and/or vented when the initiator and solid fuel are burned. The interior volume can include a porous or fibrous material having a high surface area and a large interstitial volume. The interstitial volume can contain a gas generated as a result of the initiator and solid fuel reactions and can thereby reduce the pressure within the enclosure and collisions of the reactants and reaction products with the matrix of the porous or fibrous material can efficiently transfer the internal and translational energy.

**[0077]** The internal pressure of a heating unit during and after burning of an initiator composition and a solid fuel can vary depending on the parameters discussed above. The internal pressure of heating units was measured using the fixture illustrated in **Fig. 3**. As shown in **Fig. 3**, heating unit **300** comprises a substantially-cylindrically shaped substrate **302** having a closed nose portion **304** and an open receiving end **306**. A backing member **308** is disposed within the interior region of substrate **302**. Backing member **308** is cylindrical in shape but of overall smaller dimensions than that of substrate **302**. Tapered nose portion **310** defines an opening **312** in backing member **308**. Opposing end **314** from tapered nose portion **310** of backing member **308** is open. The interior surface of substrate **302** and the exterior surface of backing member **308** define an annular shell or a gap into which a solid fuel **316** can be disposed. A plug **320** is sized for insertion into open receiving end **306** of substrate **302** and is securely sealed by an O-ring **322**. Electrodes **324** in contact with an initiator composition (not shown) disposed within heating unit **300** extend through plug **320** for electrical connection to a power source (not shown) external to heating unit **300**. Pressure transducer **326** for measuring the steady state pressure via line **328** within heating unit **300** can be mounted on plug **320**. A dynamic pressure transducer **330** can be provided for monitoring the pressure within heating unit **300** via line **332**.

**[0078]** A heating unit equipped with two pressure transducers, as illustrated in **Fig. 3**, was used to simultaneously measure the dynamic pressure and steady state pressure within a heating unit of a type as shown in **Fig. 2**. For dynamic pressure measurement, a high frequency shock wave/blast ICP pressure sensor (PCB, model 113A24, maximum pressure = $7.0\text{x}10^6$ Pa (1,000 psig)) combined with a line powered ICP signal conditioner (PCB, model 484B06) was used. For steady state pressure measurement, a subminiature millivolt output type pressure transducer (Omega Engineering, model PX600-500GV, maximum pressure = $3.5\times10^6$Pa (500 psig)) and a high performance strain gauge indicator with analog output (PCB, DP41-S-A) were used. Signals generated by the pressure transducers were recorded and stored using two oscilloscopes. To minimize the influence of pressure measurement on the performance of the heating unit, the volume of lines **328** and **332** were designed so as not to exceed 2% of the total unfilled internal volume of the heating unit. The measured internal pressure ranged from $7.9\times10^5$Pa to $2.3\times10^6$Pa (100 psig to 300 psig), and depended primarily on the compositions of the solid fuel. The contribution of the initiator composition to the internal pressure was a maximum $7.9\times10^5$Pa (100 psig).

**[0079]** Measurments of the peak internal pressure within sealed heating units, of a type as shown in **Fig. 10**, following ignition of a thin film layer of solid fuel comprising a metal reducing agent and a metal-containing oxidizer are shown in **Fig. 17.** The experimental arrangement used to generate the results shown in **Fig.17** is described in Example 2. **Fig. 17** shows that the peak pressure within a heating unit can range from $1.7\times10^5$Pa to $3.8\times10^5$Pa (10 psig to 40 psig) and correlates with the peak temperature of the exterior surface of the substrate. Also, as shown in **Fig. 17,** the peak pressure within the heating unit, as well as the peak temperature of the substrate surface can for the particular heating units measure, depend on the composition of the solid fuel, and the thickness of the foil substrate.

**[0080]** The internal pressure within a heating unit can also be managed or reduced by incorporating materials capable of absorbing, adsorbing or reacting with gas phase reaction products. The surface of the material may intrinsically be capable of absorbing. adsorbing or reacting with the gaseous products, or can be coated or decorated with, for example, elements, compounds and/or compositions. The immediate burst of pressure resulting from the solid fuel burn can be reduced by locating an impulse absorbing material and/or coating within the heating unit. A heating unit comprising an impulse absorbing material is schematically illustrated in **Fig. 13.**

**[0081]** **Figs. 13A-C** show a thermally conductive substrate **210,** such as metal foil on which is disposed a coating of a solid fuel **212.** Solid fuel **212** comprises a metal which is a reducing agent and a metal-containing oxidizing agent capable of forming an oxidation-reduction reaction. In **Figs. 13A-C** thermally conductive substrate **210** is sealed using a sealant **220** to an enclosure **218** to form the heating unit. Sealant **220** can be an adhesive or any other methods for forming a seal, such as for example, welding, soldering, fastening or crimping. An impulse absorbing material **214** is disposed between the interior surface of enclosure **218** and the interior surfaces of substrate **210** and the solid fuel **212.** As shown in **Figs. 13A-C,** impulse absorbing material fills the interior volume defined by the interior surfaces of the heating unit. The impulse absorbing material can fill a portion of the interior volume defined by the interior surfaces of the heating unit (not shown). The thickness of the impulse absorbing material, e.g. the dimension between the interior surface of solid fuel **212** and the interior surface of enclosure **218** can be any appropriate thickness to reduce the initial pressure impulse resulting from the burning of solid fuel **212** to an appropriate level. The appropriate thickness can vary at least in part on the amount of solid fuel, the solid fuel composition, and/or the physical characteristics of the impulse absorbing material such as porosity, density, and composition and the maximum acceptable pressure within the enclosure. It will be appreciated that above a certain thickness, additional impulse absorbing material can have limited effect on reducing the peak pressure within the heating unit. The impulse absorbing material can comprise one or more materials and one or more layers of impulse absorbing material. In certain applications wherein multiple layers of impulse absorbing materials are used, each layer can comprise the same or different material. In **Fig 13C,** an element **216** overlays impulse absorbing material **214.** Element **216** can be the same or a different impulse absorbing material, and can include a getter. **Fig 13B** illustrates a cross-sectional view of a cylindrical heating unit comprising a substrate **210,** a layer of solid fuel **212,** and a central region filled with an impulse absorbing material **214.**

**[0082]** The impulse absorbing material can comprise a material which can absorb the thermal and translational energy of the reactants and reaction products produced during burning of the solid fuel, and if present, an initiator composition. An initiator composition comprising, for example, any of the initiator compositions disclosed herein, can be incorporated into the sealed heating unit to initiate the self-sustaining exothermic reaction of the solid fuel. An impulse absorbing material can present a high surface area to absorb the pressure impulse of thermally and translationally hot molecules and which does not react at the temperatures reached within the heating unit during and following the burn of the solid fuel. Examples of such materials include porous materials such as ceramic membranes, and fibrous materials such as fiber mats. Hot molecules physically and/or thermally ejected from the burning solid fuel can pass through the interstitial spaces defined by porous or fibrous matrix to access a large surface area, which upon collision, can facilitate transfer of thermal and translational energy to the matrix of the impulse absorbing material, thereby reducing the peak pressure within the heating unit.

**[0083]** Examples of porous membranes include, but are not limited to ceramic membranes, fluorocarbon membranes, alumina membranes, polymer membrane and membranes formed from sintered metal powders. Examples of fibrous materials include, but are not limited to, glass, silica, carbon, graphite, metals, and high temperature resistant polymers. Sponge materials can also be used. The porosity and density of the impulse absorbing material can be selected to reduce the peak pressure by an appropriate amount. For a given amount of solid fuel, composition of solid fuel, and heating unit dimensions, the appropriate porosity and density of the impulse absorbing material can be determined empirically. It can be useful to have the pores sufficiently large to facilitate entry of the thermally and translationally hot molecules to the interior of an impulse absorbing material, or to one or more additional layers of impulse absorbing materials with different porosity and/or composition to facilitate transfer of energy from the hot molecules to the impulse absorbing material.

**[0084]** The effect of incorporating glass fiber mats on the internal pressure of a heating unit is shown in **Fig. 14.** Glass fiber mats were placed over a coating of solid fuel comprising an average mass of 177 mg of 80% Zr: 20% $MoO_3$ disposed on a 0.01 cm (0.004 inch) thick stainless steel foil, and the pressure within the enclosure measured following ignition of the solid fuel. Each glass fiber mat was 0.1 cm (0.040 inches) thick. As shown in **Fig. 14,** glass fiber mats significantly reduced the peak internal pressure of the heating unit. When a single mat was used, the maximum pressure within the sealed enclosure was $2.5 \times 10^5$Pa (22 psig) when two mats were used the maximum pressure was $1.9 \times 10^5$Pa (13 psig), and when 5 mats were used, the peak pressure was $1.6 \times 10^5$Pa (9 psig).

**[0085]** The ability of glass fiber mats to reduce the temperature within a heating unit is shown in **Fig. 15.** The same experimental arrangement as described for **Fig. 14** was used. The peak temperature measured between the solid fuel and the first mat was about 515 °C and 325 °C, between the first and second mats was about 200°C and 180 °C, and between the second and third mats was less than 100 °C, thus demonstrating that the internal and translational energy of the reactants and reaction products is transferred to the impulse absorbing materials.

**[0086]** As demonstrated by the results shown in **Fig. 14,** the residual pressure, e.g. the pressure 10 seconds or more after solid fuel ignition, in the heating unit was insensitive to the presence of an impulse absorbing material. Without being limited by theory, the residual pressure can be the result of gases evolved and/or produced during the burning of the solid fuel. Possible gas sources include hydrogen bonded to the metal reducing agent, and unreacted oxygen produced during the oxidation reaction and unreacted gaseous intermediates. For example, oxygen generated by the metal-containing oxidizing agent may not immediately react with the metal reducing agent, but rather can proceed through several gaseous reaction intermediates.

**[0087]** The residual pressure within a heating unit can be reduced by including materials capable of gettering the residual gaseous reaction products. Such materials can be included with the impulse absorbing material, intrinsic to the impulse absorbing material, and/or applied to the impulse absorbing material as a coating, deposit, layer, and the like. The getter can be coated or deposited onto a support disposed within a heating unit and/or on one or more interior surfaces of the heating unit.

**[0088]** Getters are materials capable of absorbing, adsorbing and/or reacting with gases and can be used to improve and/or maintain a vacuum, and/or to purify gases. Absorption refers to the process by which one material is retained by another, such as the attachment of molecules of a gas or vapor to a solid surface by physical forces. Adsorption refers to the increase in the concentration of a dissolved substance at the interface of a condensed and a gaseous or liquid phase. Getters are used for example in the semiconductor industry to reduce residual gases in high vacuum systems. In certain embodiments, getters capable of removing hydrogen gas, $H_2$, and molecular oxygen, $O_2$, can include, but are not limited to, compositions including metals and nonmetals, such as Ta, Zr, Tb, Ti, Al, Mg, Ba, Fe, and P. Examples of getters useful for removing $H_2$ gas include, but are not limited to, sintered Zr/graphite powders, Zr/ Al compositions, Zr/V/Fe, polymer-bound getters such as PdO/zeolite dispersed in a polymer matrix, and polydiene hydrogenation catalyst compositions. Iron-based and polymeric getters have been developed to absorb $O_2$. Carbon and/or graphite based materials can be used to adsorb and/or absorb $H_2$ and $O_2$. A getter can also adsorb, absorb and/or react with volatile intermediate products or the unreacted reactants of the exothermic oxidation-reduction reaction such as, for example, $MoO_x$, CO, $CO_2$, and $N_2$.

**[0089]** A getter can be applied to a substrate by any appropriate method. It can be useful to provide a large surface area of getter to rapidly and efficiently reduce the residual gas pressure. This can be accomplished, for example, by providing a getter formed from a porous material, such as a sintered powder, or a fibrous material. The getter can be applied to the surface of a porous or fibrous material.

**[0090]** Certain applications of heating units were used to examine the burn propagation speed of the solid fuel following ignition. The burn propagation speed refers to the speed of the burn front, which separates unburned and burned solid fuel regions. The burn propagation speed can be determined at least in part by the solid fuel composition, the particle size of the components of the solid fuel, the density or level of compaction of the solid fuel, the shape and dimensions of the solid fuel, the material forming the heating unit, and/or any internal components such as a backing member. The temporal and spatial characteristics of the burn propagation speed for cylindrically-shaped heating units were evaluated by monitoring the surface temperature of heating units using an infrared thermal imaging camera (FLIR Systems, Thermacam SC3000).

**[0091]** Thermal images of a cylindrically-shaped heating unit measured by infrared thermal imaging as a function of time, in milliseconds, are shown in **Figs. 4A-4F.** The construction of the heating unit used to produce the thermal images is provided in Example 3. The substrate was 1.5 cm in diameter and 4.5 cm in length In **Figs. 4A-4F,** two images are shown in each panel. In both images, white areas in color correspond to a surface temperature of 500 °C and black areas correspond to a surface temperature of 25 °C. The top image corresponds to a front view of the heating unit and the lower image corresponds to a rear view of the heating unit, which was obtained from a reflection in a mirror mounted behind the unit. **Fig. 4A** shows the extent of the self-propagating wave of ignited solid fuel 100 milliseconds after ignition. **Figs. 4B-4E,** taken at 200, 300, 400, and 500 milliseconds after ignition, respectively, show that the wave of ignited fuel continued to propagate along the axial direction of the heating unit. The image shown in **Fig. 4F** was taken at 600 milliseconds after ignition, at which time the entire surface of the substrate was heated, indicating that the solid fuel was consumed. The data gathered from this and other studies using various solid fuel compositions and heating unit configurations demonstrated that the burn propagation speed can range from 1.5 cm/sec to 50 cm/sec. Thus, the speed at which heat is transferred to a substrate forming the heating unit can be tailored as useful for certain applications.

**[0092]** In other studies, heating units as described in Examples 4A and 4B were fabricated and the surface temperature uniformity was evaluated by infrared thermal imaging. Heating units prepared for these studies differed from those used in the investigation of burn propagation speed only in the mass ratio of metal and oxidizing agent used to form the solid fuel. Thermal images taken 400 milliseconds after igniting the solid fuel are shown in **Figs. 5A-5B.** The image shown in **Fig. 5A** corresponds to a heating unit comprising the solid fuel composition described in Example 4A and the image in **Fig. 5B** to a heating unit comprising the solid fuel composition described in Example 4B. The dimensions of the heated area were 1.5 cm by 4.5 cm. The exterior substrate surface of the heating unit used to produce the image shown in **Fig. 5B** is more uniform than that of the heating unit shown in **Fig. 5A**. The substrate surface temperature can be more uniform in heating units designed for axial flame propagation. In certain applications, the substrate surface temperature is considered uniformly heated if no more than 10% of the exterior surface exhibits a temperature 50 °C to 100 °C less than the average temperature of the remaining 90% of the exterior surface.

**[0093]** In certain embodiments, it can be useful that at least a portion of the exterior surface of the substrate be heated to a uniform temperatures, and that the heated portion be heated at a similar rate. Uniform heating of at least a portion of the substrate can be facilitated by reducing the thermal mass of the substrate in the region to be heated and/or by controlling the amount of solid fuel generating heat. Uniform heating of the exterior surface of the substrate can be useful for vaporizing a compound disposed on the exterior substrate surface in a short period of time to form an aerosol comprising the vaporized compound having high yield and purity. As an example, uniform heating of a 3.3cm by 3.3cm (1.3 inch by 1.3 inch) substrate area can be achieved by applying a 0.0041 ± 0.00093cm (0.00163± 0.000368 inch) thick layer of solid fuel onto a 0.01cm (0.004 inch) thick foil. Upon ignition, the surface of the foil opposing the surface on which 0.18 g of the solid fuel is applied can reach a maximum temperature of 440 °C over the 3.3cm by 3.3cm (1.3 inch by 1.3 inch) area at 250 msec after ignition. As will be appreciated by one of skill in the art, the fuel thickness selected will depend on the fuel composition, the foil thickness, and the desired temperature.

**[0094]** Examples 5-7 provide heating units prepared and evaluated for pressure during burn, burn propagation speed, and substrate temperature uniformity. The heating unit described in Example 5 was comprised of a solid fuel composition of Zr, $MoO_3$, $KClO_3$, nitrocellulose, and diatomaceous earth. After remote ignition of the solid fuel from the tip of the heating unit (opening **312** in **Fig. 3**), the internal pressure increased to 150 psig during the burn period of 0.3 seconds. One minute after burn, the residual pressure was under $5.2x10^5$Pa (60 psig). The burn propagation speed was measured by infrared thermal imaging to be 13 cm/sec. With respect to surface temperature uniformity, no obvious cold spots were observed. (A cold spot, for purposes of Examples 5-7 herein, is defined as a portion of the surface exhibiting a temperature which is 50 °C to 100 °C less than the average temperature of the remaining 90% of the exterior surface.)

**[0095]** The heating unit prepared as described in Example 6 contained a solid fuel composition comprised of Zr, $MoO_3$, and nitrocellulose. The gap or annular shell between the substrate and backing member was 0.05cm (0.020 inches). The external surface of the backing member was coated with initiator composition to increase the burn propagation speed. The solid fuel was remotely ignited from the tip of the heating unit (opening **312** in **Fig. 3**). The internal pressure increased to $1.45x10^6$Pa (200 psig) during the reaction period of 0.25 seconds, and the residual pressure was under $5.2x10^5$Pa (60 psig). The burn propagation speed was 15 cm/sec. With respect to surface temperature uniformity, no obvious cold spots were observed.

**[0096]** The heating unit prepared as described in Example 7 contained a solid fuel composition of Al, $MoO_3$, and nitrocellulose. The solid fuel was placed in a 0.05 cm (0.020-inch) annular shell gap between the substrate and the backing member. The solid fuel was directly ignited near the plug. The internal pressure increased to $2.17x10^6$Pa (300 psig) during the reaction period of less than 5 milliseconds. The residual pressure was under $5.2x10^5$Pa (60 psig). The exterior surface of the substrate was uniformly heated, with between 5 percent to 10 percent of the exterior surface exhibiting a temperature 50 °C to 100 °C less than that of the remaining exterior surface.

## *DRUG SUPPLY UNIT*

**[0097]** Certain arrangements include a drug supply unit comprising, a heating unit as described herein. A drug supply unit can be used in a drug delivery device where a drug is to be thermally vaporized and then condensed for administration to a user. The drug condensate can be administered by inhalation, nasal ingestion, or topically. Drug refers to any compound for therapeutic use or non-therapeutic use, including therapeutic agents and substances, Therapeutic agent refers to any compound for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and any compound used in the mitigation or treatment of symptoms of disease. Whereas, substances refer to compounds used for a non-therapeuttc use, typically for a recreational or experimental purpose.

**[0098]** **Figs. 6A-6C** schematically illustrate cross-sectional views of a drug supply unit **100** comprising a heating unit similar to that described in **Fig. 2B.** More specifically, **Figs. 6A-6C** illustrate a drug supply unit **100** having a film of drug disposed on the exterior substrate surface **(Fig. 6A);** ignition of the heating unit **(Fig. 6B);** and generation of a wave of heat effective to vaporize the drug film **(Fig. 6C).** With initial reference to **Fig. 6A,** drug supply unit **100** comprises a heating unit **102**, similar to that described in **Fig. 2B.** In **Figs. 6A-B,** a substantially cyllindrically-shaped, heat-conductive substrate **104** has an exterior surface **106** and an interior surface **108,** which define an inner region **112.** A film **110** of drug can be disposed on all or a portion of exterior surface **106.**

**[0099]** Film**110** can be applied to exterior substrate surface **106** by any appropriate method and can depend at least in part on the physical properties of the drug and the final thickness of the film. Methods of applying a drug to the exterior substrate surface include, but are not limited to, brushing dip coating, spray coating, screen printing, roller coating, inkjet printing, vapor-phase deposition, spin coating, and the like. The drug can be prepared as a solution comprising at least one solvent and applied to the exterior surface. A solvent can comprise a volatile solvent such as, for example, but not limitation, acetone or isopropanol. The drug can be applied to the exterior surface of the substrate as a melt. The drug can be applied to a support having a release coating and transferred to a substrate from the support. For drugs that are liquid at room temperature, thickening agents can be admixed with the drug to produce a viscous composition comprising the drug that can be applied to the exterior substrate surface by any appropriate method, including those described herein. A film of compound can be formed during a single application or can be formed during repeated applications to increase the final thickness of the film. The final thickness of a film of drug disposed on the exterior substrate surface can be less than 50 $\mu$m, less than 20 $\mu$m and less than 10 $\mu$m, the film thickness can range from 0.02 $\mu$m to 20 $\mu$m, and can range from 0.1 $\mu$m to 10 $\mu$m.

**[0100]** The film can comprise a therapeutically effective amount of at least one drug. Therapeutically effective amount refers to an amount sufficient to affect treatment when administered to a patient or user in need of treatment. Treating or treatment of any disease, condition, or disorder refers to arresting or ameliorating a disease, condition or disorder, reducing the risk of acquiring a disease, condition or disorder, reducing the development of a disease, condition or disorder or at least one of the clinical symptoms of the disease, condition or disorder, or reducing the risk of developing a disease, condition or disorder or at least one of the clinical symptoms of a disease or disorder. Treating or treatment also refers to inhibiting the disease, condition or disorder, either physically, e.g. stabilization of a discernible symptom, physiologically, e.g., stabilization of a physical parameter, or both, and inhibiting at least one physical parameter that may not be discernible to the patient. Further, treating or treatment refers to delaying the onset of the disease, condition or disorder or at least symptoms thereof in a patient which may be exposed to or predisposed to a disease, condition or disorder even though that patient does not yet experience or display symptoms of the disease, condition or disorder. In certain embodiments, the drug film can comprise one or more pharmaceutically acceptable carriers, adjuvants, and/or excipients. Pharmaceutically acceptable refers to approved or approvable by a regulatory agency of the Federal or a state government or listed in the U.S Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly in humans.

**[0101]** As shown in **FIGS. 6A-6C**, substrate **104** of drug supply unit **100** can define an inner region **112** in which a solid fuel **114** can be disposed. As shown, solid fuel **114** can be disposed as an annular shell defined by interior substrate surface **108** and an inner, cylindrical backing member **118**. A first initiator composition **120** can be located at one end of cylindrical backing member **118** and a second initiator composition **122** can be located at the opposing end of cylindrical backing member **118**. First initiator composition **120** can be in physical contact with an electrically resistive heating element via electrical leads **124**, **126** to a power source (not shown).

**[0102]** As shown in **Figs. 6B**, application of an electrical current provided by a power source (not shown) to leads **124**, **126** can cause initiator composition **120** to produce sparks, such as sparks **128**, **130** that can be directed toward second initiator composition **122**. Ignition of second initiator composition **122** can ignite solid fuel **114** in the region indicated by arrows **132**, **134**. Igniting solid fuel **114** in the region indicated by arrows **132**, **134** effectuates a self-propagating wave of burning solid fuel, as schematically illustrated in **Fig. 6C**. In **Fig. 6C**, the self-propagating burn is indicated by arrows **136**, **138**, **140**,**142** with the solid fuel burn propagating from the point of ignition through the solid fuel. As the solid fuel burns, heat can be produced that can be conducted through substrate **104** causing vaporization of drug film **110** disposed on external substrate surface **106**. In **Fig. 6C**, thermally vaporized drug is illustrated as the "cloud" of drug **144**. As illustrated in **Fig. 6C**, vaporization of the drug occurs in the direction of arrows **136**, **138**, **140**, **142**, where the film nearest the ignition point of the solid fuel is vaporized first, followed by vaporization in regions along the length of drug supply unit **100**. As shown in **Fig. 6C**, thermally vaporized drug **144** is illustrated at the tapered region of drug supply unit **100**, and drug film not yet vaporized from the exterior surface **106** is illustrated at point **110**.

**[0103]** **Figs. 7A-7E** represent high-speed photographs showing the thermal generation of a vapor from a drug supply unit similar to that described in **Figs. 6A-6C**. **Fig. 7A** shows a heat-conductive substrate 4 cm in length coated with a 3 $\mu$m to 5 $\mu$m thick film of the therapeutic agent alprazolam. The drug-coated substrate was placed in a chamber through which a stream of air was flowing in an upstream-to-downstream direction, indicated by the arrow in **Fig. 7A**, at a rate of 15 L/min. Solid fuel contained in the heating unit was ignited to heat the substrate. The progression of drug vaporization from the exterior surface of the drug supply unit was monitored using real-time photography. **Figs. 7B-7E** show the sequence of thermal vaporization at time intervals of 150 msec, 250 msec, 500 msec, and 1,000 msec, following ignition of an initiator composition, respectively. The cloud of thermal vapor formed from the drug film is visible in the photographs. Complete vaporization of the drug film was achieved in less than 1,000 msec.

**[0104]** The drug supply unit is configured such that the solid fuel heats a portion of the exterior surface of the substrate to a temperature sufficient to thermally vaporize the drug within at least 3 seconds following ignition of the solid fuel, within 1 second following ignition of the solid fuel, within 800 milliseconds following ignition of the solid fuel, within 500 milliseconds following ignition of the solid fuel, or within 250 milliseconds following ignition of the solid fuel.

**[0105]** A drug supply unit can generate an aerosol comprising a drug that can be inhaled directly by a user and/or can be mixed with a delivery vehicle, such as a gas, to produce a stream for delivery, e.g., via a spray nozzle, to a topical site for a variety of treatment regimens, including acute or chronic treatment of a skin condition, administration of a drug to an incision site during surgery, or to an open wound.

**[0106]** Rapid vaporization of a drug film can occur with minimal thermal decomposition of the drug. For example less than 10% of the drug is decomposed during thermal vaporization, or less than 5% of the drug is decomposed during thermal vaporization. A drug can undergo a phase transition to a liquid state and then to a gaseous state, or can sublime, i.e., pass directly from a solid state to a gaseous state. A drug can include a pharmaceutical compound. The drug can comprise a therapeutic compound or a non-therapeutic compound. A non-therapeutic compound refers to a compound that can be used for recreational, experimental, or pre-clinical purposes. Classes of drugs that can be used include, but are not limited to, anesthetics, anticonvulsants, antidepressants, antidiabetic agents, antidotes, antiemetics, antihistamines, anti-infective agents, antineoplastics, antiparkisonian drugs, antirheumatic agents, antipsychotics, anxiolytics, appetite stimulants and suppressants, blood modifiers, cardiovascular agents, central nervous system stimulants, drugs for Alzheimer's disease management, drugs for cystic fibrosis management, diagnostics, dietary supplements, drugs for erectile dysfunction, gastrointestinal agents, hormones, drugs for the treatment of alcoholism, drugs for the treatment of addiction, immunosuppressives, mast cell stabilizers, migraine preparations, motion sickness products, drugs for multiple sclerosis management, muscle relaxants, nonsteroidal anti-inflammatories, opioids, other analgesics and stimulants, opthalmic preparations, osteoporosis preparations, prostaglandins, respiratory agents, sedatives and hypnotics, skin and mucous membrane agents, smoking cessation aids, Tourette's syndrome agents, urinary tract agents, and vertigo agents.

**[0107]** Examples of anesthetic include ketamine and lidocaine.

**[0108]** Examples of anticonvulsants include compounds from one of the following classes: GABA analogs, tiagabine, vigabatrin; barbiturates such as pentobarbital; benzodiazepines such as clonazepam; hydantoins such as phenytoin; phenyltriazines such as lamotrigine; miscellaneous anticonvulsants such as carbamazepine, topiramate, valproic acid, and zonisamide.

**[0109]** Examples of antidepressants include amitriptyline, amoxapine, benmoxine, butriptyline, clomipramine, desipramine, dosulepin, doxepin, imipramine, kitanserin, lofepramine, medifoxamine, mianserin, maprotoline, mirtazapine, nortriptyline, protriptyline, trimipramine, venlafaxine, viloxazine, citalopram, cotinine, duloxetine, fluoxetine, fluvoxamine, milnacipran, nisoxetine, paroxetine, reboxetine, sertraline, tianeptine, acetaphenazine, binedaline, brofaromine, cericlamine, clovoxamine, iproniazid, isocarboxazid, moclobemide, phenyhydrazine, phenelzine, selegiline, sibutramine, tranylcypromine, ademetionine, adrafinil, amesergide, amisulpride, amperozide, benactyzine, bupropion, caroxazone, gepirone, idazoxan, metralindole, milnacipran, minaprine, nefazodone, nomifensine, ritanserin, roxindole, S-adenosylmethionine, escitalopram, tofenacin, trazodone, tryptophan, and zalospirone.

**[0110]** Examples of antidiabetic agents include pioglitazone, rosiglitazone, and troglitazone.

**[0111]** Examples of antidotes include edrophonium chloride, flumazenil, deferoxamine, nalmefene, naloxone, and naltrexone.

**[0112]** Examples of antiemetics include alizapride, azasetron, benzquinamide, bromopride, buclizine, chlorpromazine, cinnarizine, clebopride, cyclizine, diphenhydramine, diphenidol, dolasetron, droperidol, granisetron, hyoscine, lorazepam, dronabinol, metoclopramide, metopimazine, ondansetron, perphenazine, promethazine, prochlorperazine, scopolamine, triethylperazine, trifluoperazine, triflupromazine, trimethobenzamide, tropisetron, domperidone, and palonosetron.

**[0113]** Examples of antihistamines include astemizole, azatadine, brompheniramine, carbinoxamine, cetrizine, chlorpheniramine, cinnarizine, clemastine, cyproheptadine, dexmedetomidine, diphenhydramine, doxylamine, fexofenadine, hydroxyzine, loratidine, promethazine, pyrilamine and terfenidine.

**[0114]** Examples of anti-infective agent include compounds selected from one of the following classes: antivirals such as efavirenz; AIDS adjunct agents such as dapsone; aminoglycosides such as tobramycin; antifungals such as fluconazole; antimalarial agents such as quinine; antituberculosis agents such as ethambutol; β-lactams such as cefmetazole, cefazolin, cephalexin, cefoperazone, cefoxitin, cephacetrile, cephaloglycin, cephaloridine; cephalosporins, such as cephalosporin C, cephalothin; cephamycins such as cephamycin A, cephamycin B, and cephamycin C, cephapirin, cephradine; leprostatics such as clofazimine; penicillins such as ampicillin, amoxicillin, hetacillin, carfecillin, carindacillin, carbenicillin, amylpenicillin, azidocillin, benzylpenicillin, clometocillin, cloxacillin, cyclacillin, methicillin, nafcillin, 2-pentenylpenicillin, penicillin N, penicillin O, penicillin S, penicillin V, dicloxacillin; diphenicillin; heptylpenicillin; and metampicillin; quinolones such as ciprofloxacin, clinafloxacin, difloxacin, grepafloxacin, norfloxacin, ofloxacine, temafloxacin; tetracyclines such as doxycycline and oxytetracycline; miscellaneous anti-infectives such as linezolide, trimethoprim and sulfamethoxazole.

**[0115]** Examples of anti-neoplastic agents include droloxifene, tamoxifen, and toremifene.

**[0116]** Examples of antiparkisonian drugs include amantadine, baclofen, biperiden, benztropine, orphenadrine, procyclidine, trihexyphenidyl, levodopa, carbidopa, andropinirole, apomorphine, benserazide, bromocriptine, budipine, cabergoline, eliprodil, eptastigmine, ergoline, galanthamine, lazabemide, lisuride, mazindol, memantine, mofegiline, pergolide, piribedil, pramipexole, propentofylline, rasagiline, remacemide, ropinerole, selegiline, spheramine, terguride, entacapone, and tolcapone.

**[0117]** Examples of antirheumatic agents include diclofenac, hydroxychloroquine and methotrexate.

**[0118]** Examples of antipsychotics include acetophenazine, alizapride, amisulpride, amoxapine, amperozide, aripiprazole, benperidol, benzquinamide, bromperidol, buramate, butaclamol, butaperazine, carphenazine, carpipramine, chlorpromazine, chlorprothixene, clocapramine, clomacran, clopenthixol, clospirazine, clothiapine, clozapine, cyamemazine, droperidol, flupenthixol, fluphenazine, fluspirilene, haloperidol, loxapine, melperone, mesoridazine, metofenazate, molindrone, olanzapine, penfluridol, pericyazine, perphenazine, pimozide, pipamerone, piperacetazine, pipotiazine, prochlorperazine, promazine, quetiapine, remoxipride, risperidone, sertindole, spiperone, sulpiride, thioridazine, thiothixene, trifluperidol, triflupromazine, trifluoperazine, ziprasidone, zotepine, and zuclopenthixol.

**[0119]** Examples of anxiolytics include alprazolam, bromazepam, oxazepam, buspirone, hydroxyzine, mecloqualone, medetomidine, metomidate, adinazolam, chlordiazepoxide, clobenzepam, flurazepam, lorazepam, loprazolam, midazolam, alpidem, alseroxlon, amphenidone, azacyclonol, bromisovalum, captodiamine, capuride, carbcloral, carbromal, chloral betaine, enciprazine, flesinoxan, ipsapiraone, lesopitron, loxapine, methaqualone, methprylon, propanolol, tandospirone, trazadone, zopiclone, and zolpidem.

**[0120]** An example of an appetite stimulant is dronabinol.

**[0121]** Examples of appetite suppressants include fenfluramine, phentermine and sibutramine.

**[0122]** Examples of blood modifiers include cilostazol and dipyridamol.

**[0123]** Examples of cardiovascular agents include benazepril, captopril, enalapril, quinapril, ramipril, doxazosin, prazosin, clonidine, labetolol, candesartan, irbesartan, losartan, telmisartan, valsartan, disopyramide, flecanide, mexiletine, procainamide, propafenone, quinidine, tocainide, amiodarone, dofetilide, ibutilide, adenosine, gemfibrozil, lovastatin, acebutalol, atenolol, bisoprolol, esmolol, metoprolol, nadolol, pindolol, propranolol, sotalol, diltiazem, nifedipine, verapamil, spironolactone, bumetanide, ethacrynic acid, furosemide, torsemide, amiloride, triamterene, and metolazone.

**[0124]** Examples of central nervous system stimulants include amphetamine, brucine, caffeine, dexfenfluramine, dextroamphetamine, ephedrine, fenfluramine, mazindol, methyphenidate, pemoline, phentermine, sibutramine, and modafinil.

**[0125]** Examples of drugs for Alzheimer's disease management include donepezil, galanthamine and tacrin.

**[0126]** Examples of drugs for cystic fibrosis management include CPX, IBMX, XAC and analogues; 4-phenylbutyric acid; genistein and analogous isoflavones; and milrinone.

**[0127]** Examples of diagnostic agents include adenosine and aminohippuric acid.

**[0128]** Examples of dietary supplements include melatonin and vitamin-E.

**[0129]** Examples of drugs for erectile dysfunction include tadalafil, sildenafil, vardenafil, apomorphine, apomorphine diacetate, phentolamine, and yohimbine.

**[0130]** Examples of gastrointestinal agents include loperamide, atropine, hyoscyamine, famotidine, lansoprazole, omeprazole, and rebeprazole.

**[0131]** Examples of hormones include: testosterone, estradiol, and cortisone.

**[0132]** Examples of drugs for the treatment of alcoholism include naloxone, naltrexone, and disulfiram.

**[0133]** Examples of drugs for the treatment of addiction it is buprenorphine.

**[0134]** Examples of immunosupressives includemycophenolic acid, cyclosporin, azathioprine, tacrolimus, and rapamycin.

**[0135]** Examples of mast cell stabilizers include cromolyn, pemirolast, and nedocromil.

**[0136]** Examples of drugs for migraine headache include almotriptan, alperopride, codeine, dihydroergotamine, ergotamine, eletriptan, frovatriptan, isometheptene, lidocaine, lisuride, metoclopramide, naratriptan, oxycodone, propoxyphene, rizatriptan, sumatriptan, tolfenamic acid, zolmitriptan, amitriptyline, atenolol, clonidine, cyproheptadine, diltiazem, doxepin, fluoxetine, lisinopril, methysergide, metoprolol, nadolol, nortriptyline, paroxetine, pizotifen, pizotyline, propanolol, protriptyline, sertraline, timolol, and verapamil.

**[0137]** Examples of motion sickness products include diphenhydramine, promethazine, and scopolamine.

**[0138]** Examples of drugs for multiple sclerosis management include bencyclane, methylprednisolone, mitoxantrone, and prednisolone.

**[0139]** Examples of muscle relaxants include baclofen, chlorzoxazone, cyclobenzaprine, methocarbamol, orphenadrine, quinine, and tizanidine.

**[0140]** Examples of nonsteroidal anti-inflammatory drugs include aceclofenac, acetaminophen, alminoprofen, amfenac, aminopropylon, amixetrine, aspirin, benoxaprofen, bromfenac, bufexamac, carprofen, celecoxib, choline, salicylate, cinchophen, cinmetacin, clopriac, clometacin, diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, indoprofen, ketoprofen, ketorolac, mazipredone, meclofenamate, nabumetone, naproxen, parecoxib, piroxicam, pirprofen, rofecoxib, sulindac, tolfenamate, tolmetin, and valdecoxib.

**[0141]** Examples of opioid drugs include alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, carbiphene, cipramadol, clonitazene, codeine, dextromoramide, dextropropoxyphene, diamorphine, dihydrocodeine, diphenoxylate, dipipanone, fentanyl, hydromorphone, L-alpha acetyl methadol, lofentanil, levorphanol, meperidine, methadone, meptazinol, metopon, morphine, nalbuphine, nalorphine, oxycodone, papaveretum, pethidine, pentazocine, phenazocine, remifentanil, sufentanil, and tramadol.

**[0142]** Examples of other analgesic drugs include apazone, benzpiperylon, benzydramine, caffeine, clonixin, ethoheptazine, flupirtine, nefopam, orphenadrine, propacetamol, and propoxyphene.

**[0143]** Examples of opthalmic preparation drugs include ketotifen and betaxolol.

**[0144]** Examples of osteoporosis preparation drugs alendronate, estradiol, estropitate, risedronate and raloxifene.

**[0145]** Examples of prostaglandin drugs include epoprostanol, dinoprostone, misoprostol, and alprostadil.

**[0146]** Examples of respiratory agents include albuterol, ephedrine, epinephrine, fomoterol, metaproterenol, terbutaline, budesonide, ciclesonide, dexamethasone, flunisolide, fluticasone propionate, triamcinolone acetonide, ipratropium bromide, pseudoephedrine, theophylline, montelukast, zafirlukast, ambrisentan, bosentan, enrasentan, sitaxsentan, tezosentan, iloprost, treprostinil, and pirfenidone

**[0147]** Examples of sedative and hypnotic drugs include butalbital, chlordiazepoxide, diazepam, estazolam, flunitrazepam, flurazepam, lorazepam, midazolam, temazepam, triazolam, zaleplon, zolpidem, and zopiclone.

**[0148]** Examples of skin and mucous membrane agents include isotretinoin, bergapten and methoxsalen.

**[0149]** Examples of smoking cessation aids include nicotine and varenicline.

**[0150]** An example of a Tourette's syndrome agent includes pimozide.

**[0151]** Examples of urinary tract agents include tolteridine, darifenicin, propantheline bromide, and oxybutynin.

**[0152]** Examples of vertigo agents include betahistine and meclizine.

**[0153]** A drug can further comprise substances to enhance, modulate and/or control release, aerosol formation, intrapulmonary delivery, therapeutic efficacy, therapeutic potency, stability, and the like. For example, to enhance therapeutic efficacy a drug can be co-administered with one or more active agents to increase the absorption or diffusion of the first drug through the pulmonary alveoli, or to inhibit degradation of the drug in the systemic circulation. A drug can be co-administered with active agents having pharmacological effects that enhance the therapeutic efficacy of the drug. A drug can comprise compounds that can be used in the treatment of one or more diseases, conditions, or disorders. A drug can comprise more than one compound for treating one disease, condition, or disorder, or for treating more than one disease, condition, or disorder.

## THIN FILM DRUG SUPPLY UNIT

**[0154]** A thin film drug supply unit is illustrated in **Figs. 10A-10B**. **Fig. 10A** illustrates a perspective view, and **Fig. 10B** an assembly view of a thin film drug supply unit **500**. Thin film drug supply unit **500** comprises, as shown in **Fig. 10B**, a thin film heating unit **530** on which is disposed a drug **514** to be thermally vaporized. As shown in **Fig.10A**, thin film heating unit **530** comprises a first and a second substrate **510**, and a spacer **518**.

**[0155]** As shown, first and second substrates **510** include an area comprising solid fuel **512** disposed on the interior surface, and an area comprising a drug **514** to be vaporized disposed on the exterior surface. First and second substrates **510** can comprise a thermally conductive material such as those described herein, including, for example, metals, ceramics, and thermally conductive polymers. Substrates **510** can comprise a metal, such as, but not limited to, stainless steel, copper, aluminum, and nickel or an alloy thereof. Substrates can have one or more layers, and the multiple layers can comprise different materials. For example, a substrate can comprise multiple layers of laminated metal foils, and/or can comprise thin films of one or more materials deposited on the surface. The multiple layers can be used for example to determine the thermal properties of the substrate and/or can be used to determine the reactivity of the surface with respect to a compound disposed on the exterior surface. A multilayer substrate can have regions comprising different materials. The thickness of substrates **510** can be thin to facilitate heat transfer from the interior to the exterior surface and/or to minimize the thermal mass of the device. In certain embodiments, a thin substrate can facilitate rapid and homogeneous heating of the exterior surface with a lesser amount of solid fuel compared to a thicker substrate. Substate **510** can also provide structural support for solid fuel **512** and drug film **514**. In certain embodiments, substrates **510** can comprise a metal foil. The thickness of substrates **510** can range from 0.00254 cm to 0.05 cm (0.001 inches to 0.020 inches), in certain embodiments from 0.00254 cm to 0.0254 cm (0.001 inches to 0.010 inches) from 0.005 cm to 0.015 cm (0.002 inches to 0.006 inches), and from 0.005 cm to 0.0127 cm (0.002 inches to 0.005 inches). The use of lesser amounts of solid fuel can facilitate control of the heating process as well as facilitate miniaturization of a drug supply unit.

**[0156]** The thickness of substrates **510** can vary across the surface. For example, a variable thickness can be useful for controlling the temporal and spatial characteristics of heat transfer and/or to facilitate sealing of the edges of substrates **510**, for example, to spacer **518**, opposing substrate **510**, or to another support (not shown). In certain embodiments, substrates **510** can exhibit a homogeneous or nearly homogeneous thickness in the region of the substrate on which solid fuel **512** and drug **514** are disposed to facilitate achieving a homogeneous temperature across that region of the substrate on which the solid fuel is disposed. Homogeneous heating of the substrate can facilitate the production of an aerosol comprising a high purity of a drug or pharmaceutical composition and maximize the yield of drug initially deposited on the substrate forming an aeresol.

**[0157]** Substrates **510** can comprise an area of solid fuel **512** disposed on the interior surface, e.g. the surface facing opposing substrate **510**. An appropriate amount of solid fuel **512** can in part be determined by the thermal vaporization or sublimation temperature of the drug, the amount of drug to be vaporized, the thickness and thermal conductivity of the substrate, the composition of the solid fuel, and the temporal characteristics of the intended thermal vaporization process. Solid fuel **512** can be applied to substrate **510** using any appropriate method. For example, solid fuel **512** can be applied to substrate **510** by brushing, dip coating, screen printing, roller coating, spray coating, inkjet printing, stamping, spin coating, and the like. To facilitate processing, solid fuel **510** can comprise at least one additive material, and/or a solvent, as disclosed herein. In certain embodiments, solid fuel **512** can be formed as a preformed sheet that can be cut to a specific dimension and subsequently applied to substrate **510**. The solid fuel can be applied to a support, and transferred to a substrate as a preformed section. In this disclosure solid fuel **512** is applied to a portion of substrates **510** as a thin film or layer.

**[0158]** Solid fuel **512** can comprise a mixture of $Zr/MoO_3$, $Zr/Fe_2O_3$, $Al/MoO_3$, or $Al/Fe_2O_3$. In certain embodiments, the amount of metal which is a reducing agent can range from 60 wt% to 90 wt%, and the amount of metal-containing oxidizing agent can range from 40 wt% to 10 wt%. Higher ratios of metal reducing agent can cause the solid fuel to burn slower and at a lower temperature, whereas lower ratios of metal reducing agent can cause the solid fuel to burn faster and reach a higher maximum temperature. Regardless of the weight percent ratios of the metal reducing agent and metal-containing oxidizing agent, a solid fuel can comprise a stoichiometric amount of metal which is a reducing agent and metal-containing oxidizing agent. For example, the balanced $Zr : Fe_2O_3$ metal oxidation-reduction reaction can be written as:

$$3\,Zr + 2\,Fe_2O_3 \rightarrow 3\,ZrO_2 + 4\,Fe$$

A stoichiometric amount of $Zr : Fe_2O_3$ for this reaction is 1 : 1.67 by weight.

**[0159]** Drug **514** can be disposed on the exterior surface of substrates **510**. The amount of drug **514** disposed on the exterior surface of substrate **510** can be any appropriate amount. For example, the amount of drug **514** can be a therapeutically effective amount. A therapeutically effective amount can be determined by the potency of the drug, the clinical indications, and the mode of administration. Thin film drug supply unit can be configured to thermally vaporize more than 95% of the drug, and in certain applications, greater than 98% of the drug, with minimal degradation of the drug. The aerosol formed using a drug supply unit can comprise greater than 90% of a drug applied to a substrate, and in certain applications greater than 95% of a drug applied to a substrate. The yield and purity of the aerosol can be controlled by and selected based on the temporal characteristics and magnitude of the thermal impulse transferred to the compound.

**[0160]** The relationship of the yield and purity of an aerosol comprising a pharmaceutical compound on the substrate temperature and mass of solid fuel for certain embodiments is shown in **Fig. 18**. Thin film drug supply units substantially as shown in **Figs. 10A** and **10B**, and described in Example 9 were used to produce the measurements shown in **Fig. 18**. The experimental arrangement used to analyze the percent yield and percent purity of the aerosol comprising a vaporized drug is described in Example 10. As shown in **Fig. 18**, at substrate temperatures ranging from about 355° C to about 425° C, the percent yield of drug forming the aerosol was greater than about 85% and the percent purity was greater than about 90%. The percent yield refers to the ratio of the total solid weight of the aerosol to the weight of the drug initially deposed on the substrate times 100. Factors that can reduce the percent yield include incomplete vaporization of the drug and redeposition of the drug on the substrate.

**[0161]** The percent purity, with respect to the aerosol purity, refers to the fraction of drug composition in the aerosol/ the fraction of drug composition in the aerosol plus drug degradation products times 100. Thus purity is relative with regard to the purity of the starting material. For example, when the starting drug or drug composition used for substrate coating contained detectable impurities, the reported purity of the aerosol does not include those impurities present in the starting material that were also found in the aerosol, e.g., in certain cases if the starting material contained a 1%

impurity and the aerosol was found to contain the identical 1% impurity, the aerosol purity may nevertheless be reported as >99 % pure, reflecting the fact that the detectable 1% purity was not produced during the vaporization-condensation aerosol generation process.

**[0162]** Factors that can reduce the percent purity of the aerosol include degradation of the drug during thermal vaporization. Depending at least in part on the composition and thermal properties of a particular drug or pharmaceutical composition, the appropriate thermal vaporization temperature to produce an aerosol comprising the particular drug or pharmaceutical composition having high yield and purity can be determined as set forth in U.S. application Serial No. 10/718,982, filed November 20, 2003.

**[0163]** Drug **514** can be applied to substrate **510** using any appropriate method, such as for example, brushing, dip coating, screen printing, roller coating, spray coating, inkjet printing, stamping, vapor deposition, and the like. Drug **514** can also be applied to a support having a release layer and transferred to substrate **510**. Drug **514** can be suspended in a volatile solvent such as, for example, but not limited to, acetone or isopropanol to facilitate application. A volatile solvent can be removed at room temperature or at elevated temperature, with or without application of a vacuum. The solvent can comprise a pharmaceutically acceptable solvent. Residual solvent can be reduced to a pharmaceutically acceptable level.

**[0164]** Drug **514** can be disposed on substrate **510** in any appropriate form such as a solid, viscous liquid, liquid, crystalline solid, or powder. The film of drug can be crystallized after disposition on the substrate.

**[0165]** As shown in **Figs. 10A-10B**, a drug supply unit can comprise an igniter **520**. Igniter **520** can comprise an initiator composition **522** disposed on an electrically resistive heating element connected to electrical leads disposed between two strips of insulating materials (not shown). The electrical leads can be connected to a power source (not shown). Initiator composition **522** can comprise any of the initiator compositions or compositions described herein. The ignition temperature of initiator composition can range from 200 °C to 500 °C. The electrically resistive material can comprise a material capable of generating heat when electrical current is applied. For example, the electrically resistive material can be a metal such as nichrome, tungsten or graphite. An initiator composition can be disposed on the surface of the electrically resistive material such that when the electrically resistive material is heated to the ignition temperature of the initiator composition, the initiator composition can ignite to produce sparks. An initiator composition can be applied to the electrically resistive heating element by depositing a slurry comprising the initiator composition and drying. An initiator composition can be deposited on a solid fuel at a position such that when assembled, the initiator composition forming the igniter is adjacent to the initiator composition deposited on the solid fuel. Having initiator composition on at least a portion of the solid fuel can increase the speed of ignition and the reliability of the ignition process.

**[0166]** The electrically resistive heating element can be connected to electrical conductors. The heating element can be soldered or electrically connected to conductors, such as, Cu conductors or graphite ink traces, disposed on an electrically insulating substrate, such as a polyimide, polyester, or fluoropolymer. The conductors can be disposed between two opposing layers of the electrically insulating material such as flexible or rigid printed circuit board materials. The heating element on which an initiator composition is disposed can be exposed through an opening in the end of ignition assembly **520**.

**[0167]** Igniter **520** can be positioned with respect to solid fuel **512** such that sparks produced by initiator composition **522** can be directed toward solid fuel area **512**, causing solid fuel **512** to ignite and burn. Initiator composition **522** can be located in any position such that sparks produced by the initiator can cause solid fuel **512** to ignite. The location of initiator composition **522** with respect to solid fuel **512** can determine the direction in which solid fuel 5**12** burns. For example, initiator composition **522** can be located to cause solid fuel **512** to burn in any direction with respect to the airflow including in the same direction of airflow, opposite the direction of airflow, or normal the direction of airflow. The direction of solid fuel burn with respect to airflow can influence the average particle diameter of particulates comprising the thermally vaporized drug forming the aerosol. For example, solid fuel burn opposite the direction of airflow can produce smaller diameter particles than when the direction of solid fuel burn is in the same direction as the airflow. The dynamics of solid fuel burn can be influenced by other parameters such as the spatial and temporal characteristics of the surface temperature, and the extent to which vaporized drug is redeposited on the substrate and/or other surfaces such as a housing in which the drug supply unit is incorporated.

**[0168]** Thin film drug supply unit **500** can comprise more than one igniter **520** and/or each igniter **520** can comprise more than one initiator composition **522**.

**[0169]** It can be useful to minimize the amount of initiator composition used, so as to reduce the amount of gas and other reaction products potentially generated by the initiator composition during burn.

**[0170]** Igniter **520** can comprise a mechanism configured to direct transmitted radiation to an initiator composition capable of absorbing and being heated by the transmitted radiation, to produce sparks. For example, the radiation can be infrared, visible, or ultraviolet radiation such as produced by a diode laser, light emitting diode, or flashlamp. Radiation produced by a radiation source can be transmitted through a waveguide such as an optical fiber, and directed to an initiator or the radiation source can be incorporated into the ignition assembly **522** with electrical conductors for connecting to an external power source. The transmission device can include elements such as lenses for focusing the transmitted radiation onto the initiator composition. The radiation can be directed to an initiator composition disposed within the heating unit through a window. The transmitted radiation can be directed onto an absorber or a material capable of absorbing the radiation, which can be the initiator composition, or an element on which the initiator composition is disposed. The initiator composition can comprise at least one metal such as, but not limited to, zirconium, titanium, or aluminum, and at least one solid oxidizer such as, but not limited to, $MoO_3$, $KClO_4$, CuO, or $WO_3$. The initiator composition can comprise any of those disclosed herein.

**[0171]** As shown in **Fig 10A**, thin film drug supply unit **500** can have a spacer **518**. Spacer **518** can retain igniter **520**. Spacer **518** can provide a volume or space within the interior of thin film heating unit **500** to collect gases and byproducts generated during the burn of the initiator composition **522** and solid fuel **512**. The volume produced by spacer **518** can reduce the internal pressure within thin film drug supply unit **500** upon ignition of the fuel. The volume can comprise a porous or fibrous material such as a ceramic, or fiber mat in which the solid matrix component is a small fraction of the unfilled volume. The porous or fibrous material can provide a high surface area on which reaction products generated during the burning of the initiator composition and the solid fuel can be absorbed, adsorbed or reacted. The pressure produced during burn can in part depend on the composition and amount of initiator composition and solid fuel used. The spacer can be less than 0.7 cm (0.3 inches) thick or less than 0.5 cm (0.2 inches) thick. The maximum internal pressure during and following burn can be less than $3{,}5.10^5$ Pa (50 psig), less than $1{,}4.10^5$ Pa (20 psig), less than $0{,}7.10^5$ Pa (10 psig), or less than $0{,}4.10^5$ Pa (6 psig). The spacer can be a material capable of maintaining structural and chemical properties at the temperatures produced by the solid fuel burn. The spacer can be a material capable of maintaining structure and chemical properties up to a temperature of about 100°C. It can be useful that the material forming the spacer not produce and/or release or produce only a minimal amount of gases and/or reaction products at the temperatures to which it is exposed by the heating unit. Spacer **518** can comprise a metal, a thermoplastic, such as, for example, but not limitation, a polyimide, fluoropolymer, polyetherimide, polyether ketone, polyether sulfone, polycarbonate, other high temperature resistant thermoplastic polymers, or a thermoset, and which can optionally include a filler.

**[0172]** Spacer **518** can comprise a thermal insulator such that the spacer does not contribute to the thermal mass of the thin film drug supply unit thereby facilitating heat transfer to the substrate on which drug **514** is disposed. Thermal insulators or impulse absorbing materials such as mats of glass, silica, ceramic, carbon, or high temperature resistant polymer fibers can be used. Spacer **518** can be a thermal conductor such that the spacer functions as a thermal shunt to control the temperature of the substrate.

**[0173]** Substrates **510**, spacer **518** and igniter **520** can be sealed. Sealing can retain any reactants and reaction products released by burning of initiator composition **522** and solid fuel **514**, as well as provide a self-contained unit. As shown in **Fig. 10A**, substrates **510** can be sealed to spacer **518** using an adhesive **516**. Adhesive **516** can be a heat sensitive film capable of bonding substrates **510** and spacer **518** upon the application of heat and pressure. Substrates **510** and spacer **518** can be bonded using an adhesive applied to at least one of the surfaces to be bonded, the parts assembled, and the adhesive cured. The access in spacer **518** into which igniter **520** is inserted can also be sealed using an adhesive. Other methods for forming a seal can be used such as for example, welding soldering, or fastening.

**[0174]** The elements forming the thin film drug supply unit **500** can be assembled and sealed using thermoplastic or thermoset molding methods such as insert molding and transfer molding.

**[0175]** An appropriate sealing method can, at least in part be determined by the materials forming substrate **510** and spacer **518**. Drug supply unit **500** can be sealed to withstand a maximum pressure of less than $3{,}5.10^5$ Pa (50 psig), less than $1{,}4.10^5$ Pa (20 psig) or less than $0{,}7.10^5$ Pa (10 psig) The materials used to form the seal can maintain structural integrity at the temperature reached by the article. The materials used can exhibit minimal degradation and produce minimal gaseous reaction products at the temperature reached by the heating unit

## *MULTIDOSE DRUG SUPPLY UNITS*

**[0176]** A drug supply unit can be configured for use in single-use devices or in multi-use devices. **Figs. 9A-9B** illustrate drug supply units configured for use in a drug delivery device designed for multiple uses. As shown in **Fig. 9A**, a tape **406** in the form of a spool or reel **400** comprises a plurality of drug supply units **402**, **404**. The plurality of drug supply units **402**, **404** can comprise a heating unit on which is disposed a thin film of a drug to be thermally vaporized. Each of the plurality of drug supply units **402**, **404** can comprise the same features as those described herein, for example, in **Fig. 1A** and/or **Fig. 1B**. Tape **406** can comprise a plurality of heating units. Each heating unit can comprise a solid fuel, an initiator composition, and a substrate.

**[0177]** Thin film drug supply units are schematically illustrated in **Figs. 11A-11B**, **Figs. 11A-11B** illustrate certain arrangements wherein the thin film drug supply units **600** are in the form of a tape **650** comprising multiple layers. As shown in **Fig. 11A**, tape **650** comprises a first layer **601** having openings in which a drug to be thermally vaporized **610** is disposed. A second layer **602** underlying first layer **601** separates drug **610** from solid fuel **620** disposed within a third layer **603** underlying second layer **602**. Second layer **602** can be thermally conductive such that heat can be efficiently transferred from solid fuel **620** to compound **610**. Second layer **602** can be any of the metals described herein. Regions comprising solid fuel **620** underlie regions comprising drug **610**. The amount of solid fuel **620** can be an amount sufficient to thermally vaporize drug **610**. The dimensions and geometry of the region comprising solid fuel **620** can be any appropriate dimension. Third layer **603** can comprise a volume **640** to collect reaction products generated during burn of solid fuel **620** and thereby reduce the pressure within thin film drug supply unit **600**. Volume **640** can comprise a material capable of absorbing, adsorbing of reacting with reaction products produced during burning of the solid, such as a porous ceramic or fibrous material. Third layer **603** can comprise a material in which the mechanical properties are substantially maintained and which will not appreciably chemically degrade up to the temperatures reached by the drug supply unit **600**. Third layer **603** can comprise a metal or a polymer such as polyimide, fluoropolymer, polyetherimide, polyether ketone, polyether sulfone, polycarbonate, or other high temperature resistance polymers.

**[0178]** Tape **650** can comprise an upper and lower layer (not shown) configured to physically and/or environmentally protect compound **610** and solid fuel **620**. The upper and/or lower protective layers can comprise, for example, a metal foil, a polymer, or can comprise a multilayer comprising metal foil and polymers. In certain embodiments, protective layers can exhibit low permeability to oxygen, moisture, and/or corrosive gases. All or portions of a protective layer can be removed prior to use to expose compound **610** and solid fuel **620**. To vaporize compound **610**, solid fuel **620** can be ignited by energy from an external source (not shown) to generate heat that can be conducted through second layer **602** to thermally vaporize compound **610**. Examples of initiators include those discussed herein such as, but not limited to, sparks or electrical resistance heating, Use of a protective layer can facilitate use of drug **610** in the form of a powder or liquid.

**[0179]** **Fig. 11B** shows a cross-sectional view of a tape **670** comprising thin film drug supply units **600**, which in addition to the element recited for **Fig. 11A**, further comprise an initiator composition **630**. Tape **670** has multiple layers including first layer **601** within which compound **610** is disposed, second layer **602** separating first layer **601** and third layer 603. Layer **603** retains solid fuel **620** and in certain embodiments, a volume **640**. Openings in a fourth layer **604** define a gap separating solid fuel **620** disposed in third layer 603, and initiator composition **630** disposed within regions of a fifth layer **605**. Initiator composition **630** can comprise any of the initiator compositions disclosed herein. Initiator **630** can adjoin an electrically resistive heating element **682** disposed within a sixth layer **606** and connected to electrical conductors **680** also disposed within sixth layer 606. As shown, a seventh layer **607** overlies sixth layer 606 and comprises openings **617** to facilitate electrical connection between electrical conductors **680** and a power source (not shown).

**[0180]** In an exemplary operation, tape **670** can be advanced to locale at least one region comprising drug **610** within an airway (not shown) and to connect respective electrical contacts **680**, with a power source (not shown). Upon activation of the power source, the electrical current can heat resistive element **682** to ignite initiator composition **630** and produce sparks. Sparks directed across gap **645** can ignite solid fuel **620**. Heat generated by the ignition of solid fuel **620** can be conducted through second layer **602** thermally vaporizing compound **610** to form an aerosol comprising drug **610** within the airway.

**[0181]** Another drug supply article configured for the delivery of multiple doses is illustrated in **Fig 9B**. **Fig. 9B** shows a plurality of individual drug-supply units provided on a card **410**. Drug supply units **412**, **414**, **416**, each consist of a solid fuel contained between a backing member and a substrate, such as substrate **418** on unit **412**. A film of drug can be coated onto substrate **418**. Card **410** can be loaded into a suitable device configured to ignite at least one drug supply unit at a time. Ignition can be, for example by sparks, as disclosed herein. To provide a subsequent dose, card **410** can be rotated to advance a fresh drug supply unit.

**[0182]** **Fig. 9C** shows a cartridge **420** containing a plurality of cylindrically-shaped drug supply units **422**, **424**, **426**, **428**. The drug supply units can be as described herein, and comprise a solid fuel contained within an enclosure comprising a substrate. The external surface of the substrate can be coated with a film of drug. Each drug supply unit can be successively advanced into position in a drug delivery device chamber for ignition of the solid fuel, vaporization of the drug, and administration to a user.

## *DRUG DELIVERY DEVICES*

**[0183]** Drug delivery devices comprising a housing defining an airway, a heating unit as disclosed herein, a drug disposed on a portion of the exterior surface of a substrate of the heating unit, wherein the portion of the exterior surface comprising the drug is configured to be disposed within the airway, and an initiator configured to ignite the solid fuel are disclosed Drug delivery devices can incorporate the heating units and drug supply units disclosed herein. The drug delivery device comprises a housing defining an airway. The housing can define an airway having any appropriate shape or dimensions and can comprise at least one inlet and at least one outlet. The dimensions of an airway can at least in part be determined by the volume of air that can be inhaled through the mouth or the nostrils by a user in a single inhalation, the intended rate of airflow through the airway, and/or the intended airflow velocity at the surface of the substrate that is coupled to the airway and on which a drug is disposed. Airflow can be generated by a patient inhaling with the mouth on the outlet of the airway, and/or by inhaling with the nostrils on the outlet of the airway. Airflow can be generated by injecting air or a gas into the inlet such as for example, by mechanically compressing a flexible container filled with air and/or gas, or by releasing pressurized air and/or gas into the inlet of the airway. Generating an airflow by injecting air and/or gas into the airway can be useful in drug delivery devices intended for topical administration of an aerosol comprising a drug.

**[0184]** A housing can be dimensioned to provide an airflow velocity through the airway sufficient to produce an aerosol of a drug during thermal vaporization. The airflow velocity can be at least 1 m/sec in the vicinity of the substrate on which the drug is disposed.

**[0185]** A housing can be dimensioned to provide a certain airflow rate through the airway. The airflow rate through the airway can range from 10 L/min to 120 L/min. An airflow rate ranging from 10 L/min to 120 L/min can be produced during inhalation by a user when the outlet exhibits a cross-sectional area ranging from 0.1 $cm^2$ to 20 $cm^2$. The cross-sectional area of the outlet can range from 0.5 $cm^2$ to 5 $cm^2$, and in certain embodiments, from 1 $cm^2$ to 2 $cm^2$.

**[0186]** An airway can comprise one or more airflow control valves to control the airflow rate and airflow velocity in airway. An airflow control valve can comprise, but is not limited to, at least one valve such as an umbrella valve, a reed valve, a flapper valve, or a flapping valve that bends in response to a pressure differential, and the like. An airflow control valve can be located at the outlet of the airway, at the inlet of the airway, within the airway, and/or can be incorporated into the walls of housing defining the airway An airflow control valve can be actively controlled, for example can be activated electronically such that a signal provided by a transducer located within the airway can control the position of the valve; or passively controlled, such as, for example, by a pressure differential between the airway and the exterior of the device

**[0187]** Drug delivery devices configured for inhalation delivery of thermal vapor generated from a drug supply unit are illustrated in **Fig. 8**. Inhalation device **150** has an upper external housing member **152** and a lower external housing member **154** that snap fit together. The downstream end of each housing member can be gently tapered for insertion into a users mouth, as shown on upper housing member **152** at downstream end **156**. The upstream end of the upper and lower housing members can be Slotted **158**, as shown in the upper housing member **152**, to provide for air intake when a user inhales. When fitted together, upper and lower housing members **152**, **154** define a chamber **160**. A drug supply unit **162** can be positioned within chamber **160**. Drug supply unit **162** comprises a tapered, substantially cylindrical substrate **164** having an external surface **168** on which is disposed a film **166** of drug. The interior surface **170** of the substrate and a portion of the inner, cylindrical backing member **172** are shown in the cut-away section of drug supply unit **162**. Solid fuel **174** is located within the annular shell region defined by backing member **172** and interior substrate surface **170**. At least one initiator composition can be provided for the heating unit, and shown in **Fig. 8**, an initiator composition can be positioned (not shown) in the upstream end of the device where the air intake occurs. The initiator composition can be configured to ignite solid fuel **174** by the application of electrical current to an ohmic heating element connected to a battery (not shown) located in end piece **176**. Activation of the initiator composition can produce spans that are confined within a space defined by backing member **172** and thus can be directed toward the downstream end of the drug supply unit indicated at point **178**. Sparks reaching the tapered nose portion at downstream end **178** can ignite solid fuel **174**. Solid fuel **174** then burns in a downstream-to-upstream direction, *i.e.* from point **178** toward the air intake end of the device at point **158**, generating a wave of heat in the downstream-to-upstream direction that vaporizes drug film **166** disposed on exterior substrate surface **168**. Thus, the direction of solid fuel burn and the direction of thermal drug vapor generation are opposite the direction of airflow through chamber **160** of the inhalation device.

## *METHODS FOR PRODUCING AND USING AEROSOLS*

**[0188]** Methods of producing an aerosol of a compound using the heating units, drug supply units, and drug delivery devices disclosed herein are described. The aerosol produced by an apparatus can comprise a therapeutically effective amount of a drug. The temporal and spatial characteristics of the heat applied to thermally vaporize the compound disposed on the substrate and the air flow rate can be selected to produce an aerosol comprising a drug having certain characteristics. For example, for intrapulmonary delivery it is known that aerosol particles having a mean mass aerodynamic diameter ranging from 0.01 μm to 0.1 μm and ranging from 1 μm to 3.5 μm can facilitate efficient transfer of drugs from alveoli to the systemic circulation. In applications wherein the aerosol is applied topically, the aerosol can have the same or different characteristics.

**[0189]** Methods for producing an aerosol comprise: (i) providing an airflow over a drug disposed on a portion of an exterior surface of a substrate forming a drug supply unit, wherein the drug supply unit comprises a heating unit as disclosed herein and the drug disposed on a portion of the exterior surface of the substrate, wherein the portion of the exterior surface comprising the drug is disposed within the airway; and an initiator composition configured to ignite the solid chemical fuel; and (ii) thermally vaporizing and condensing the drug to form an aerosol of the drug in the airway. The drug may be disposed on the surface of the substrate as a thin film.

**[0190]** Methods of treating a disease in a patient in need of such treatment comprising administering to the patient an aerosol comprising a therapeutically effective amount of a drug, wherein the aerosol is produced by the methods and devices disclosed herein are described. The aerosol can be administered by inhalation through the mouth, by nasal ingestion, and/or by topical application.

**[0191]** Other embodiments will be apparent to those skilled in the art. It is intended that the specification and examples be considered as exemplary only.

## Examples

**[0192]** In the examples below, the following abbreviations have the following meanings. If an abbreviation is not defined, it has its generally accepted meaning.

| | |
|---|---|
| wt% | weight percent |
| psig | pounds per square inch, gauge |
| DI | deionized |
| mL | milliliters |
| msec | milliseconds |
| L/min | liters per minute |
| μm | micrometer |

## Example 1

### Preparation of Solid Fuel with Laponite

**[0193]** The following procedure was used to prepare solid fuel coatings comprising 76.16% Zr : 19.04% $MoO_3$: 4.8% Laponite® RDS.

**[0194]** To prepare wet Zirconium (Zr), the as-obtained suspension of Zr in DI water (Chemetall, Germany) was agitated on a roto-mixer for 30 minutes. Ten to 40 mL of the wet Zr was dispensed into a 50 mL centrifuge tube and centrifuged (Sorvall 6200RT) for 30 minutes at 3,200 rpm. The DI water was removed to leave a wet Zr pellet.

**[0195]** To prepare a 15% Laponite® RDS solution, 85 grams of DI water was added to a beaker. While stirring, 15 grams of Laponite® RDS (Southern Clay Products, Gonzalez, TX) was added, and the suspension stirred for 30 minutes.

**[0196]** The reactant slurry was prepared by first removing the wet Zr pellet as previously prepared from the centrifuge tube and placed in a beaker. Upon weighing the wet Zr pellet, the weight of dry Zr was determined from the following equation: Dry Zr (g) = 0.8234 (Wet Zr (g))- 0.1059.

**[0197]** The amount of molybdenum trioxide to provide a 80:20 ratio of Zr to $MoO_3$ was then determined, e.g, $MoO_3$ =Dry Zr (g) / 4, and the appropriate amount of $MoO_3$ powder (Accumet, NY) was added to the beaker containing the wet Zr to produce a wet Zr : $MoO_3$ slurry. The amount of Laponite® RDS to obtain a final weight percent ratio of dry components of 76.16% Zr : 19.04% $MoO_3$: 4.80% Laponite® RDS was determined. Excess water to obtain a reactant slurry comprising 40% DI water was added to the wet Zr and $MoO_3$ slurry. The reactant slurry was mixed for 5 minutes using an IKA Ultra-Turrax mixing motor with a S2SN-8G dispersing head (setting 4). The amount of 15% Laponite® RDS previously determined was then added to the reactant slurry, and mixed for an additional 5 minutes using the IKA Ultra-Turrax mixer. The reactant slurry was transferred to a syringe and stored for at least 30 minutes prior to coating.

**[0198]** The Zr : $MoO_3$: Lapomite® RDS reactant slurry was then coated onto stainless steel foils. Stainless steel foils were first cleaned by sonication for 5 minutes in a 3,2% bv solution of Ridoline 298 in DI water at 60°C. Stainless steel foils were masked with 0.546cm (0.215 inch) wide Mylar®such that the center portion of each 0.01cm (0.004 inch) thick 304 stainless steel foil was exposed. The foils were placed on a vacuum chuck having 0.008 inch thick shims at the edges. Two (2) mL of the reactant slurry was placed at one edge of the foil. Using a Sheen Auto-Draw Automatic Film Applicator 1137 (Sheen Instruments) the reactant slurry was coated onto the foils by drawing a #12 coating rod at an auto-draw coating speed of up to 50 mm/sec across the surface of the foils to deposit approximately an 0.075 cm (0.006 inch) thick layer of the Zr: $MoO_3$: Laponite® RDS reactant slurry. The coated foils were then placed in a 40 °C forced-air convection oven and dried for at least 2 hours. The masks were then removed from the foils to leave a coating of solid fuel on the center section of each foil

**[0199]** The solid fuel coatings comprising Laponite® RDS adhered to the stainless steel foil surface and maintained physical integrity following mechanical and environmental testing including temperature cycling (-25 °C↔40 °C), accelerated humidity exposure (40 °C /75% RH), drop testing impact testing, and flexure testing.

## Example 2

### Measurement of Internal Pressure

**[0200]** Thin film heating units were used to measure the peak internal pressure and the peak temperature of the exterior surface of the substrate following ignition of the solid fuel.

**[0201]** The thin film heating units were substantially as described in Example 9 below and as illustrated in Figs. 10A and 10B. Two 5.08 x 5.08 square cm (2 x 2 square inch), 0.01cm (0.004 inch) thick 304 stainless steel foils formed the substrates. A solid fuel comprising 76.16 wt% Zr, 19.04% $MoO_3$, 4.8% Laponite® RDS and water was coated onto the interior surface of the stainless steel substrates. The thickness of the solid fuel layer was 0.0045cm ± 0.00076cm (0.0018 ± 0.0003 inches). The layer of solid fuel covered an area of 10.9 $cm^2$ (1.69 $in^2$) and after drying, the weight of the solid fuel disposed on the interior surface of each substrate was 0.165 to 0.190 grams. The spacer comprised a 0.61cm (0.24 inch) thick section of polycarbonate (Makrolon). The ignition assembly comprised a FR-4 printed circuit board having a 0.076 cm (0.03 inch) diameter opening at the end to be disposed within an enclosure defined by the spacer and the substrates. A 0.002cm (0.0008 inch) diameter Nichrome wire was soldered to electrical conductors on the printed circuit board and positioned across the opening. An initiator composition comprising 26.5% Al, 51.4% $MoO_3$ 7.7%B and 143% Viton A500 weight percent was deposited onto the Nichrome wire and dried.

**[0202]** To assemble the thin film drug supply unit, the Nichrome wire comprising the initiator composition was positioned at one end of the solid fuel area. A bead of epoxy (Epo-Tek 353 ND; Epoxy Technology) was applied to both surfaces of the spacer, and the spacer, substrates and the ignition assembly positioned and compressed. The epoxy was cured at a temperature of 100 °C for 3 hours.

**[0203]** To ignite the solid fuel, a 0.4 amp current was applied to the electrical conductors connected to the Nichrome wire.

**[0204]** The peak internal pressure was measured using a pressure sensor (Motorola, MPXA42S0A). The external surface temperature was measured using IR camera (FLIR, Therma CAM SC3000).

## Example 3

### Thermal Images of Heating Unit

**[0205]** A solid fuel consisting of a mixture of zirconium (40.6 wt%), $MoO_3$ (21.9 wt%), and $KClO_3$ (1.9 wt%), nitrocellulose (0.6 wt%), and diatomaceous earth (35 wt%) was prepared. The solid fuel was placed in a 0.076cm (0.030-inch) gap between a stainless steel substrate (0.038cm (0.015 inch) wall thickness) and a stainless steel backing member (0.038cm (0.015 inch) wall thickness). The diameter of the substrate was 1.43cm (9/16inch). The fuel was ignited, and thermal images of the heating unit were taken as a function of time after ignition. The results are shown in **Figs. 4A-4F**.

## Example 4

### Thermal Images of Heating Units to Evaluate Surface Temperature Uniformity

**[0206]** A. A solid fuel consisting of a mixture of zirconium (53.8 wt%), $MoO_3$ (23.1 wt%), and $KClO_3$ (2.3 wt%), nitrocellulose (0.8 wt%) and diatomaceous earth (20 wt%), was prepared. The solid fuel mixture was placed in a 0.076cm (0.030-inch) gap between a stainless steel substrate (0.038cm (0.015 inch) wall thickness) and a stainless steel backing member (0.038cm (0.015 inch) wall thickness). The diameter of the substrate was 1.43cm (9/16 inch). The fuel was ignited, and a thermal image of the heating unit was taken 400 milliseconds after ignition. The image is shown in **Fig. 5A**.

**[0207]** B. A solid fuel consisting of a mixture of zirconium (46.9 wt%), $MoO_3$ (25.2 wt%), $KClO_3$ (2.2 wt%), nitrocellulose (0.7 wt%), and diatomaceous earth (25.0 wt%) was prepared. The solid fuel was placed in a 0.076cm (0.030-inch) gap between a stainless steel substrate (0.038cm (0.015 inch) wall thickness) and a stainless steel backing member (0.038cm (0.015 inch) wall thickness). The diameter of the substrate was 1.43cm (9/16 inch). The fuel was ignited, and a thermal image of the heating unit was taken 400 milliseconds after ignition. The image is shown in **Fig. 5B**.

## Example 5

### Exemplary Heating Unit

**[0208]** A solid fuel consisting of a mixture of zirconium (46.9 wt%), $MoO_3$ (25.2 wt%), and $KClO_3$ (2.2 wt%), grain size 100-325 mesh, along with nitrocellulose (0.7 wt%) and diatomaceous earth (25.0 wt%) was prepared. The solid fuel was placed in a 0.076cm (0.030-inch) gap between a stainless steel substrate (0.038cm (0.015 inch) wall thickness) and a stainless steel backing member (0.038cm (0.015 inch) wall thickness). The diameter of the substrate was 1.43cm (9/16 inch) The solid fuel was remotely ignited from the tip of the heating unit. During and after burn, the pressure in the cylindrical substrate was measured as described herein. The burn propagation speed and the surface temperature uniformity were evaluated by infrared imaging.

**[0209]** The internal pressure increased to 1.14 x $10^6$Pa (150 psig) during the reaction period of 0.3 seconds. The residual pressure was under 5.2 x $10^5$ Pa (60 psig). The burn propagation speed was 13 cm/sec. With respect to surface temperature uniformity, no obvious cold spots were observed.

### Example 6

### Exemplary Heating Unit

**[0210]** A solid fuel consisting of a mixture of zirconium (69.3 wt%) and $MoO_3$ (29.7 wt%), grain size 100-325 mesh, along with nitrocellulose (1.0 wt%) was prepared. The solid fuel mixture was placed in a 0.05cm (0.020-inch) gap between a stainless steel substrate (0.05cm (0.020 inch) wall thickness) and a stainless steel backing member (0.05cm (0.020 inch) wall thickness). The outside of the backing member was coated with initiator to increase burn propagation speed. The primary fuel was remotely ignited from the tip of the heating unit. During and after burn, the pressure in the cylindrical substrate was measured as described herein. The burn propagation speed and the surface temperature uniformity were evaluated by infrared imaging.

**[0211]** The internal pressure increased to 1.48 x $10^6$Pa (200 psig) during the reaction period of 0.25 seconds. The residual pressure was under 5.2 x $10^5$Pa (60 psig). The burn propagation speed was 15 cm/sec, With respect to surface temperature uniformity, no obvious cold spots were observed.

### Example7

### Exemplary Heating unit

**[0212]** A solid fuel consisting of a mixture of aluminium (49.5 wt%) and $MoO_3$ (49.5 wt%), grain size 100-325 mesh, along with nitrocellulose (1.0 wt%) was prepared, The solid fuel mixture was placed in a 0.05cm (0.020-inch) gap between a stainless steel substrate (0.05cm (0.020 inch) wall thickness) and a stainless steel backing member 0.05cm (0.020 inch) wall thickness). The primary fuel was directly ignited near the plug. During and after burn, the pressure in the cylindrical substrate was measured as described herein. The surface temperature uniformity was evaluated by infrared imaging.

**[0213]** The internal pressure increased to 2.17 x $10^6$Pa (300 psig) during the reaction period of less than 5 milliseconds. The residual pressure was under 5.2 x $10^5$Pa (60 psig). The exterior surface expanse was uniformly heated, with between 5-10 percent of the surface being 50 °C to 100°C cooler than the rest of the expanse.

### Example 8

### Wet Processing for Zirconium Fuel Slurry

**[0214]** The following procedure was used to prepare fuel compositions comprising Zr and $MoO_3$ for a thin film drug supply unit. Wet Zr particles, 46.7 wt%, having a 2 μm to 3 μm particle size were obtained from Chemetall, GmbH, Germany. The Zr particles were rinsed with DI water, following which the excess water was decanted. DI water, 5.1 wt%, was added to the Zr and the mixture centrifuged. Excess water was decanted. Dry $Mo\hat{O}_3$, 20 wt%, (Climax Molybdenum Co., AZ) and DI water was then added to the washed Zr, and the mixture homogenized for 2 minutes with a high shear mixer (IKA, Germany). A 15% aqueous solution of Laponite® RDS, 2.5 wt%, (Southern Clay Products, Inc., Texas) was added and the mixture homogenized with a high shear mixer for an additional 5 minutes. The Zr : $MO_3$ solid fuel slurry was transferred to a syringe or holding vessel for subsequent coating. The wet Zr included 8.5 wt% water and the Laponite® RDS gel included 14 wt% water. The weight percents represent the percent weight of the total wet composition.

### Example 9

### Exemplary Thin Film Drug Supply Unit

**[0215]** A thin film drug supply unit according to **Figs. 10A-10B** was fabricated and the performance evaluated, Two, 5.08 x 5.08 square cm, 0.01cm (2 x 2 square inch, 0.004 inch) thick 304 stainless steel foils formed the substrates. A solid fuel comprising 76.16 wt% Zr and 19.04% $MoO_3$ and 4.8% Laponite® RDS and water was coated onto the interior surface of the stainless steel substrates. The thickness of the solid fuel layer was 0.0046cm ± 0.00076cm (0.0018 ±

0.0003 inches). The layer of solid fuel covered an area 10.9cm$^2$ (1.69 in$^2$) and after drying, the weight of the solid fuel disposed on the interior surface of each substrate was 0.165 to 0.190 grams. An ~6 μm thick thin film of a drug was deposited onto a 7.81cm$^2$ (1.21 in$^2$) area of the exterior substrate surfaces using spray coating. The drug was dissolved in a 15 mg/ml solution of isopropanol or acetone to facilitate processing. The thin film of drug was dried at ambient conditions and 1.5 mg to 3.0 mg of drug was deposited on the exterior surface of each substrate. The spacer comprised a 0.61cm (0.24 inch) thick section of polycarbonate (Makronlon). The ignition assembly comprised a FR-4 printed circuit board having a 0.076cm (0.03 inch) diameter opening at the end to be disposed within an enclosure defined by the spacer and the substrates. A 0.002cm (0.0008 inch) diameter Nichrome wire was soldered to electrical conductors on the printed circuit board and positioned across the opening. An initiator composition comprising 26.5% Al, 51.4% $MoO_3$, 7.7%B and 14.3% Viton A500 weight percent was deposited onto the Nichrome wire and dried.

**[0216]** To assemble the thin film drug supply unit, the Nichrome wire comprising the initiator composition was positioned at one end of the solid fuel area A bead of epoxy (Epo-Tek 353 ND, Epoxy Technology) was applied to both surfaces of the spacer, and the spacer, substrates and the ignition assembly positioned and compressed. The epoxy was cured at a temperature of 100 °C for 3 hours.

**[0217]** To ignite the solid fuel, a 0.4 Amp current was applied to the electrical conductors connected to the Nichrome wire.

**[0218]** The airflow in the airway used for the measurements ranged from 14 L/min to 28 L/min corresponding to an airflow velocity of 1.5 m/sec and 3 m/sec, respectively.

**[0219]** Measurements an such drug supply units demonstrated that the exterior surface of the substrate reached temperatures in excess of 400 °C in less than 150 milliseconds following activation of the initiator at which time the drug was completely thermally vaporized. The maximum pressure within the enclosure was less than $0,7.10^5$ Pa (10 psig) In separate measurement, it was demonstrated that the enclosure was able to withstand a static pressure in excess of $4.10^5$ Pa (60 psig) at room temperature. The burn propagation speed across the expanse of solid fuel was measured to be 25 cm/sec. The particulates forming the aerosol comprised greater than 95% of the drug, and greater than 90% of the drug originally deposited on the substrates formed the aerosol.

### Example 10

### Measurement of Aerosol Purity and Yield

**[0220]** Drug supply units substantially as described in Example 9 and illustrated in **Figs. 10A and 10B** were used to measure the percent yield and percent purity of aerosols.

**[0221]** Two, 5.08x5.08 square cm, 0.01cm (2 x 2 square inch, 0.004 inch) thick 304 stainless steel foils formed the substrates. A solid fuel comprising 76.16 wt% Zr, 19.04% $MoO_3$, 4.8% Laponite® RDS and water was coated onto the interior surface of the stainless steel substrates. The thickness of the solid fuel layer was 0.0046cm ± 0.00076cm (0.0018 ± 0.0003 inches). The layer of solid fuel covered an area of 10.9cm$^2$ (1.69 in$^2$) and after drying, the weight of the solid fuel disposed on the interior surface of each substrate was 0.165 to 0.190 grams. An ~6 μm thick thin film of a drug was deposited onto a 7.81cm$^2$ (1.21 in$^2$) area of the exterior substrate surfaces using spray coating. The drug was dissolved in a 15 mg/ml solution of isopropanol or acetone to facilitate processing. The thin film of drug was dried at ambient conditions and 1.5 mg to 3.0 mg of drug was deposited on the exterior surface of each substrate. The spacer comprised a 0.61cm (0.24 inch) thick section of polycarbonate (Makronlon). The ignition assembly comprised a FR-4 printed circuit board having a 7.62cm (0.03 inch) diameter opening at the end to be disposed within an enclosure defined by the spacer and the substrates. A 0.002cm (0.0008 inch) diameter Nichrome wire was soldered to electrical conductors on the printed circuit board and positioned across the opening. An initiator composition comprising 26.5% Al, 51.4% $MoO_3$, 7.7%B and 14.3% Viton A500 weight percent was deposited onto the Nichrome wire and dried.

**[0222]** To assemble the thin film drug supply unit, the Nichrome wire comprising the initiator composition was positioned at one end of the solid fuel area. A bead of epoxy (Epo-Tek 353 ND, Epoxy Technology) was applied to both surfaces of the spacer, and the spacer, substrates and the ignition assembly positioned and compressed. The epoxy was cured at a temperature of 100 °C for 3 hours.

**[0223]** To ignite the solid fuel, a 0.4 Amp current was applied to the electrical conductors connected to the Nichrome wire.

**[0224]** The airflow in the airway used for the measurements ranged from 14 L/min to 28 L/min corresponding to an airflow velocity of 1.5 m/sec and 3 m/sec, respectively.

**[0225]** After volatilization, the aerosol was captured on a mat for quantification of yield and analysis of purity. The quantity of material recovered on the mat was used to determine a percent yield, based on the mass of drug coated onto the substrate. Any material deposited on the housing or the remaining on the substrate was also recovered and quantified to determine a percent total recovery ((mass of drug on the mat + mass of drug remaining on substrate and housing)/mass of drug coated onto substrate). For compounds without UV absorption GC/MS or LC/MS was used to quantify the recovery.

**[0226]** The percent purity was determined using HPLC UV absorption at 250 nm. However, as one of skill in the art recognizes, the purity of a drug-containing aerosol may be determined using a number of different methods. It should be noted that when the term "purity" is used, it refers to the percentage of aerosol minus the percent byproduct produced in its formation. Byproducts for example, are those unwanted products produced during vaporization. For example, byproducts include thermal degradation products as well as any unwanted metabolites of the active compound or compounds. Examples of suitable methods for determining aerosol purity are described in Sekine et al., Journal of Forensic Science 32:1271-1280 (1987) and in Martin et al., Journal of Analytic Toxicology 13:158-162 (1989).

**[0227]** One suitable method involves the use of a trap. In this method, the aerosol is collected in a trap in order to determine the percent or fraction of byproduct. Any suitable trap may be used. Suitable traps include mats, glass wool, impingers, solvent traps, cold traps, and the like. Mats are often most desirable. The trap is then typically extracted with a solvent, e.g. acetonitrile, and the extract subjected to analysis by any of a variety of analytical methods known in the art, for example, gas, liquid, and high performance liquid chromatography particularly useful.

**[0228]** The gas or liquid chromatography method typically includes a detector system, such as a mass spectrometry detector or an ultraviolet absorption detector. Ideally, the detector system allows determination of the quantity of the components of the drug composition and of the byproduct, by weight. This is achieved in practice by measuring the signal obtained upon analysis of one or more known mass(es) of components of the drug composition or byproduct (standards) and then comparing the signal obtained upon analysis of the aerosol to that obtained upon analysis of the standard(s), an approach well known in the art.

**[0229]** In many cases, the structure of a byproduct may not be known or a standard for it may not be available. In such cases, one may calculate the weight fraction of the byproduct by assuming it has an identical response coefficient (e.g. for ultraviolet absorption detection, identical extinction coefficient) to the drug component or components in the drug composition. When conducting such analysis, byproducts present in less than a very small fraction of the drug compound, e.g. less than 0.1 % or 0.03% of the drug compound, are typically excluded. Because of the frequent necessity to assume an identical response coefficient between drug and byproduct in calculating a weight percentage of byproduct, it is often more desirable to use an analytical approach in which such an assumption has a high probability of validity. In this respect, high performance liquid chromatography with detection by absorption of ultraviolet light at 225 nm is typically desirable. UV absorption at 250 nm may be used for detection of compounds in cases where the compound absorbs more strongly at 250 nm or for other reasons one skilled in the art would consider detection at 250 nm the most appropriate means of estimating purity by weight using HPLC analysis. In certain cases where analysis of the drug by UV are not viable, other analytical tools such as GC/MS or LC/MS may be used to determine purity.

## Claims

1. Use of a layer of an essentially homogenous slurry of a selected mass of a solid fuel (20, 316, 212, 114, 512, 174, 620), which comprises a metal-containing oxidizing agent and a metal which is a reducing agent in a defined ratio, that is coated on a portion of an interior surface of a substrate (12, 302, 210, 510, 170, 418) to be heated, wherein the thickness of the coated layer of solid fuel is in the range 0.00254 cm (0.001 inches) to 0.0762 cm (0.030 inches) in a method of controlling uniformity of temperature and peak temperature of an exterior surface of the substrate when rapidly heated, the method comprising igniting the solid fuel.

2. The use of claim 1, wherein the peak temperature of the substrate upon heating is controlled by using a mass of solid fuel determined to give that peak temperature.

3. The use of claim 1, wherein the substrate is selected from a metal, an alloy, and a ceramic.

4. The use of claim 3, wherein the substrate is a metal foil.

5. The use of claim 4, wherein the thickness of the metal foil is in the range 0.00254 cm (0.001 inches) to 0.0254 cm (0.010 inches).

6. The use of claim 1, wherein the layer of solid fuel exhibits a thickness ranging from 0.00254 cm (0.001 inches) to 0.0127 cm (0.005 inches).

7. The use of claim 1, wherein the metal containing oxidizing agent is selected from at least one of the following $MoO_3$, $KClO_4$, $KClO_3$, and $Fe_2O_3$.

8. The use of claim 1, wherein the metal which is a reducing agent is selected from at least one of the following: aluminum, zirconium, iron, and titanium.

**9.** The use of claim 1, wherein the amount of metal which is a reducing agent ranges from 60% by weight to 90% by weight of the total dry weight of the solid fuel.

**10.** The use of claim 1, wherein the amount of metal-containing oxidizing agent ranges from 10% by weight to 40% by weight of the total dry weight of the solid fuel.

**11.** The use of claim 1, wherein the solid fuel comprises at least one additive material.

**12.** The use of claim 11, wherein said additive material is an inorganic material.

**13.** The use of claim 12, wherein the inorganic material is selected from the group consisting of clays, metal alkoxides, sodium silicates, potassium silicates, aluminum silicates, alumina, silica based sol and inorganic sol-gel material.

**14.** The use of claim 11, wherein the additive material is a clay gelling agent.

**15.** A method for providing an essentially homogenous and uniform coating of dry solid fuel (20, 316, 212, 114, 512, 174, 620) on a surface of a substrate (12, 302, 210, 510, 170, 418) comprising:

a. mixing a solid fuel, comprising at least one metal-containing oxidizing agent and at least one metal which is a reducing agent, with an additive material in a solvent to form a homogenous slurry;
b. coating a thin layer of the slurry at a set thickness on a surface of a substrate; and
c. drying the coated slurry to form a layer of dry solid fuel on the substrate wherein the thickness of the layer of solid fuel is in the range 0.00254 cm (0.001 inches) to 0.0762 cm (0.030 inches).

**16.** The method of claim 15, wherein said coating is dip coating, spray coating, roller coating, gravure coating, reverse roll coating, gap coating, metering rod coating, slot die coating, curtain coating, or air knife coating.

**17.** The method of claim 16, wherein said gap coating is done with a wire wound coating rod in a bar coater.

**18.** The method of claim 15, wherein prior to coating a mask is positioned on a portion of the surface of the substrate to prevent deposition of the solid fuel on said portion.

**19.** The method of claim 15, wherein the substrate is a metal foil.

**20.** The method of claim 19, wherein the thickness of the metal foil is in the range 0.00254 cm (0.001 inches) to 0.0254 cm (0.010 inches).

**21.** The method of claim 15, wherein the layer of solid fuel exhibits a thickness ranging from 0.00254cm (0.001 inches) to 0.0127cm (0.005 inches).

**22.** The method of claim 15, wherein the oxidizing agent is selected from at least one of the following $MoO_3$, $KClO_4$, $KClO_3$. and $Fe_2O_3$.

**23.** The method of claim 15, wherein the reducing agent is selected from at least one of the following: aluminum, zirconium, iron, and titanium.

**24.** The method of claim 15, wherein said additive material is an inorganic material.

**25.** The method of claim 15, wherein the additive material is a clay gelling agent.

**26.** The method of claim 15, wherein said drying is in an oven for at least two hours.

**27.** The method of claim 15, wherein the substrate is a metal, an alloy, or a ceramic.

**28.** A heating unit (10, 300, 102, 530) that upon firing rapidly heats a defined area of an exterior surface of a substrate to a set peak temperature comprising:

a. an enclosure comprising at least one substrate having an exterior surface and an interior surface,

b. a layer of solid fuel (20, 80, 316, 212, 114, 514, 174, 620) which comprises a metal-containing oxidizing agent and a metal which is a reducing agent in a defined ratio, coated on the interior surface of the substrate (12, 302, 210, 510, 170, 418) corresponding to the defined area of the exterior surface of the substrate to be heated, wherein the thickness) of the layer of solid fuel is in the range 0.00254 cm (0.001 inches) to 0.0762 cm (0.030 inches); and
c. an igniter disposed within the enclosure for igniting the solid fuel.

**29.** The heating unit of claim 28, wherein the peak temperature is set by the mass of solid fuel coated on the interior surface of the substrate.

**30.** The heating unit of claim 28, wherein the layer of solid fuel exhibits a thickness ranging from 0.00254 cm (0.001 inches) to 0.0127 cm (0.005 inches).

**31.** The heating unit of claim 28, wherein the enclosure comprises more than one substrate.

**32.** The heating unit of claim 28, wherein the substrate is a metal foil.

**33.** The heating unit of claim 28, wherein the solid fuel comprises an oxidizing agent selected from at least one of the following $MoO_3$, $KClO_4$, $KClO_3$, and $Fe_2O_3$.

**34.** The heating unit of claim 28, wherein the solid fuel comprises a reducing agent selected from at least one of the following: aluminum, zirconium, iron, and titanium.

**35.** The heating unit of claim 28, wherein the solid fuel comprises at least one additive material.

**36.** The heating unit of claim 35, wherein the additive material is a clay gelling agent.

**37.** The heating unit of claim 28, wherein the substrate is a metal, an alloy, or a ceramic.

**38.** The heating unit of any one of claims 28 to 37 further comprising a resistive heating element to activate the igniter.

**39.** The heating unit of any one of claims 28 to 37 further comprising an electromagnetic radiation source to activate the igniter.

**40.** The heating unit of any one of claims 28 to 37 further comprising a mechanism for producing a percussive force to activate the igniter.

**41.** The heating unit of any one of claims 28 to 40 wherein the solid fuel layer is essentially homogeneous.

**42.** The use, method or heating unit of any one of the preceding claims wherein the solid fuel is configured to heat a portion of the exterior surface of the substrate to a temperature of at least 200° C in less than 1 second following ignition of the solid fuel.

**43.** A drug supply unit (500) comprising the heating unit (530) of any one of claims 28 to 42 and further comprising;

a drug (514) disposed on a portion of the exterior surface of the substrate (510).

**44.** A drug delivery device (150) comprising the drug supply unit of claim 43 and further comprising:

a housing (152, 154) defining an airway, wherein the portion of the exterior surface of the substrate comprising the drug is configured to be disposed within the airway.

## Patentansprüche

**1.** Verwendung einer Schicht einer im Wesentlichen homogenen Aufschlämmung einer ausgewählten Menge eines festen Brennstoffs (20, 316, 212, 114, 512, 174, 620), der ein metallhältiges Oxidationsmittel und ein Metall, das ein Reduktionsmittel ist, in einem definierten Verhältnis umfasst und auf einen Abschnitt einer Innenoberfläche eines

Substrats (12, 302, 210, 510, 170, 418) aufgebracht ist, um erhitzt zu werden, wobei die Dicke der aufgebrachten Schicht des festen Brennstoffs im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0762 cm (0,030 Zoll) liegt, in einem Verfahren zur Steuerung der Einheitlichkeit von Temperatur und des Temperaturhöchstwerts einer Außenoberfläche des Substrats, wenn dieses rasch erhitzt wird, wobei das Verfahren das Entzünden des festen Brennstoffs umfasst.

**2.** Verwendung nach Anspruch 1, worin der Temperaturhöchstwert des Substrats beim Erhitzen durch die Verwendung einer Menge des festen Brennstoffs gesteuert wird, die so bestimmt wurde, dass sie den Temperaturhöchstwert liefert.

**3.** Verwendung nach Anspruch 1, worin das Substrat aus einem Metall, einer Legierung und Keramik ausgewählt ist.

**4.** Verwendung nach Anspruch 3, worin das Substrat eine Metallfolie ist.

**5.** Verwendung nach Anspruch 4, worin die Dicke der Metallfolie im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0254 cm (0,010 Zoll) liegt.

**6.** Verwendung nach Anspruch 1, worin die Schicht des festen Brennstoffs eine Dicke aufweist, die im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0127 cm (0,005 Zoll) liegt.

**7.** Verwendung nach Anspruch 1, worin das metallhältige Oxidationsmittel aus zumindest einem der folgenden ausgewählt ist: $MoO_3$, $KClO_4$, $KClO_3$ und $Fe_2O_3$.

**8.** Verwendung nach Anspruch 1, worin das Metall, das ein Reduktionsmittel ist, aus zumindest einem der folgenden ausgewählt ist: Aluminium, Zirconium, Eisen und Titan.

**9.** Verwendung nach Anspruch 1, worin die Menge des Metalls, das ein Reduktionsmittel ist, im Bereich von 60 bis 90 Gew.-% des Gesamttrockengewichts des festen Brennstoffs liegt.

**10.** Verwendung nach Anspruch 1, worin die Menge des metallhältigen Oxidationsmittels im Bereich von 10 bis 40 Gew.-% des Gesamttrockengewichts des festen Brennstoffs liegt.

**11.** Verwendung nach Anspruch 1, worin der feste Brennstoff zumindest ein Additivmaterial umfasst.

**12.** Verwendung nach Anspruch 11, worin das Additivmaterial ein anorganisches Material ist.

**13.** Verwendung nach Anspruch 12, worin das anorganische Material aus der aus Tonen, Metallalkoxiden, Natriumsilicaten, Kaliumsilicaten, Aluminiumsilicaten, Aluminiumoxid, Sol auf Silicabasis und anorganischem Sol-Gel-Material bestehenden Gruppe ausgewählt ist.

**14.** Verwendung nach Anspruch 11, worin das Additivmaterial ein Tongelbildner ist.

**15.** Verfahren zur Bereitstellung einer im Wesentlichen homogenen und einheitlichen Beschichtung aus trockenem festem Brennstoff (20, 316, 212, 114, 512, 174, 620) auf einer Oberfläche eines Substrats (12, 302, 210, 510, 170, 418), das Folgendes umfasst:

a. das Mischen eines festen Brennstoffs, der zumindest ein metallhältiges Oxidationsmittel und zumindest ein Metall umfasst, das ein Reduktionsmittel ist, mit einem Additivmaterial in einem Lösungsmittel zur Ausbildung einer homogenen Aufschlämmung;
b. das Aufbringen einer dünnen Schicht der Aufschlämmung mit einer festgelegten Dicke auf eine Oberfläche eines Substrats und
c. das Trocknen der aufgebrachten Aufschlämmung zur Ausbildung einer Schicht von trockenem festem Brennstoff auf dem Substrat, wobei die Dicke der Schicht des festen Brennstoffs im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0762 cm (0,030 Zoll) liegt.

**16.** Verfahren nach Anspruch 15, worin das Beschichten durch Tauchbeschichten, Sprühbeschichten, ein Walzenstreichverfahren, ein Gravurstreichverfahren, Umkehr-Walzenbeschichtung, Spaltbeschichtung, Rollrakelbeschichtung, Schlitzdüsenbeschichtung, Vorhangbeschichtung oder ein Luftrakelverfahren erfolgt.

**17.** Verfahren nach Anspruch 16, worin die Spaltbeschichtung mit einem mit Draht umwickelten Beschichtungsstab in einer Vorstreichvorrichtung erfolgt.

**18.** Verfahren nach Anspruch 15, worin vor dem Beschichten eine Maske auf einem Abschnitt der Oberfläche des Substrats positioniert wird, um die Abscheidung des festen Brennstoffs auf diesem Abschnitt zu verhindern.

**19.** Verfahren nach Anspruch 15, worin das Substrat eine Metallfolie ist.

**20.** Verfahren nach Anspruch 19, worin die Dicke der Metallfolie im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0254 cm (0,010 Zoll) liegt.

**21.** Verfahren nach Anspruch 15, worin die Schicht des festen Brennstoffs eine Dicke aufweist, die im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0127 cm (0,005 Zoll) liegt.

**22.** Verfahren nach Anspruch 15, worin das metallhältige Oxidationsmittel aus zumindest einem der folgenden ausgewählt ist: $MoO_3$, $KClO_4$, $KCl_3$ und $Fe_2O_3$.

**23.** Verfahren nach Anspruch 15, worin das Metall, das ein Reduktionsmittel ist, aus zumindest einem der folgenden ausgewählt ist: Aluminium, Zirconium, Eisen und Titan.

**24.** Verfahren nach Anspruch 15, worin das Additivmaterial ein anorganisches Material ist.

**25.** Verfahren nach Anspruch 15, worin das Additivmaterial ein Tongelbildner ist.

**26.** Verfahren nach Anspruch 15, worin das Trocknen zumindest 2 h lang in einem Ofen erfolgt.

**27.** Verfahren nach Anspruch 15, worin das Substrat ein Metall, eine Legierung oder ein Keramikmaterial ist.

**28.** Heizeinheit (10, 300, 102, 530), die bei Zündung einen definierten Bereich einer Außenoberfläche eines Substrats rasch auf einen festgelegten Temperaturhöchstwert erhitzt und Folgendes umfasst:

a. eine Einfassung, die zumindest ein Substrat mit einer Außenoberfläche und einer Innenoberfläche umfasst,
b. eine Schicht aus festem Brennstoff (20, 80, 316, 212, 114, 514, 174, 620), der ein metallhältiges Oxidationsmittel und ein Metall, das ein Reduktionsmittel ist, in einem definierten Verhältnis umfasst, die auf die Innenoberfläche des Substrats (12, 302, 210, 510, 170, 418) aufgebracht ist, die dem definierten Bereich der Außenoberfläche des Substrats entspricht, der erhitzt werden soll, wobei die Dicke der Schicht des festen Brennstoffs im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0762 cm (0,030 Zoll) liegt; und
c. einen Zünder, der in der Einfassung angeordnet ist, um den festen Brennstoff zu entzünden.

**29.** Heizeinheit nach Anspruch 28, worin der Temperaturhöchstwert durch die Menge des festen Brennstoffs festgelegt wird, der auf die Innenoberfläche des Substrats aufgebracht ist.

**30.** Heizeinheit nach Anspruch 28, worin die Schicht des festen Brennstoffs eine Dicke aufweist, die im Bereich von 0,00254 cm (0,001 Zoll) bis 0,0127 cm (0,005 Zoll) liegt.

**31.** Heizeinheit nach Anspruch 28, worin die Einfassung mehr als ein Substrat umfasst.

**32.** Heizeinheit nach Anspruch 28, worin das Substrat eine Metallfolie ist.

**33.** Heizeinheit nach Anspruch 28, worin der feste Brennstoff ein Oxidationsmittel umfasst, das aus zumindest einem der folgenden ausgewählt ist: $MoO_3$, $KClO_4$, $KClO_3$ und $Fe_2O_3$.

**34.** Heizeinheit nach Anspruch 28, worin der feste Brennstoff ein Reduktionsmittel umfasst, das aus zumindest einem der folgenden ausgewählt ist: Aluminium, Zirconium, Eisen und Titan.

**35.** Heizeinheit nach Anspruch 28, worin der feste Brennstoff zumindest ein Additivmaterial umfasst.

**36.** Heizeinheit nach Anspruch 35, worin das Additivmaterial ein Tongelbildner ist.

**37.** Heizeinheit nach Anspruch 28, worin das Substrat ein Metall, eine Legierung oder ein Keramikmaterial ist.

**38.** Heizeinheit nach einem der Ansprüche 28 bis 37, die weiters ein Widerstandsheizelement umfasst, um den Zünder zu aktivieren.

**39.** Heizeinheit nach einem der Ansprüche 28 bis 37, die weiters eine elektromagnetische Strahlungsquelle umfasst, um den Zünder zu aktivieren.

**40.** Heizeinheit nach einem der Ansprüche 28 bis 37, die weiters einen Mechanismus zur Erzeugung einer Schlagkraft zur Aktivierung des Zünders umfasst.

**41.** Heizeinheit nach einem der Ansprüche 28 bis 40, worin die Schicht des festen Brennstoffs im Wesentlichen homogen ist.

**42.** Verwendung, Verfahren oder Heizeinheit nach einem der vorangegangenen Ansprüche, worin der feste Brennstoff konfiguriert ist, um einen Abschnitt der Außenoberfläche des Substrats in weniger als 1 s nach dem Entzünden des festen Brennstoffs auf eine Temperatur von zumindest 200 °C zu erhitzen.

**43.** Arzneimittelzufuhreinheit (500), die die Heizeinheit (530) nach einem der Ansprüche 28 bis 42 und weiters Folgendes umfasst:

ein Arzneimittel (514), das auf einem Abschnitt der Außenoberfläche des Substrats (510) vorliegt.

**44.** Arzneimittelzufuhrvorrichtung (150), die die Arzneimittelzufuhreinheit nach Anspruch 43 und weiters Folgendes umfasst:

ein Gehäuse (152, 154), das einen Luftkanal definiert, worin der Abschnitt der Außenoberfläche des Substrats, der das Arzneimittel umfasst, konfiguriert ist, um in dem Luftkanal angeordnet zu sein.

## Revendications

**1.** Utilisation d'une couche d'une boue essentiellement homogène d'une masse sélectionnée d'un combustible solide (20, 316, 212, 114, 51, 174, 620), qui comprend un agent d'oxydation contenant du métal et un métal qui est un agent réducteur en un rapport défini, qui est appliquée sur une portion d'une surface intérieure d'un substrat (12, 302, 210, 510, 170, 418) à chauffer, où l'épaisseur de la couche appliquée de combustible solide est dans la plage de 0,00254 cm (0,001 pouce) à 0,0762 cm (0,030 pouce) dans un procédé de contrôle de l'uniformité de la température et de la température de crête d'une surface extérieure du substrat lorsqu'il est chauffé rapidement, le procédé comprenant l'allumage du combustible solide.

**2.** Utilisation selon la revendication 1, où la température de crête du substrat lors du chauffage est contrôlée en utilisant une masse de combustible solide déterminée comme fournissant cette température de crête.

**3.** Utilisation selon la revendication 1, où le substrat est sélectionné parmi un métal, un alliage et une céramique.

**4.** Utilisation selon la revendication 3, où le substrat est une feuille métallique.

**5.** Utilisation selon la revendication 4, où l'épaisseur de la feuille métallique est dans la plage de 0,00254 cm (0,001 pouce) à 0,0254 cm (0,010 pouce).

**6.** Utilisation selon la revendication 1, où la couche de combustible solide présente une épaisseur de 0,00254 cm (0,001 pouce) à 0,0127 cm (0,005 pouce).

**7.** Utilisation selon la revendication 1, où le métal contenant l'agent d'oxydation est sélectionné parmi au moins un des suivants $MoO_3$, $KClO_4$, $KClO_3$ et $Fe_2O_3$.

**8.** Utilisation selon la revendication 1, où le métal qui est un agent réducteur est sélectionné parmi au moins un des suivants: aluminium, zirconium, fer et titane.

**9.** Utilisation selon la revendication 1, où la quantité de métal, qui est un agent réducteur, est de 60% en poids à 90% en poids du poids total sec du combustible solide.

**10.** Utilisation selon la revendication 1, où la quantité de l'agent d'oxydation contenant du métal est de 10% en poids à 40% en poids du poids total sec du combustible solide.

**11.** Utilisation selon la revendication 1, où le combustible solide comprend au moins un matériau additif.

**12.** Utilisation selon la revendication 11, où ledit matériau additif est un matériau inorganique.

**13.** Utilisation selon la revendication 12, où le matériau inorganique est sélectionné dans le groupe consistant en argiles, alcoxydes de métal, silicates de sodium, silicates de potassium, silicates d'aluminium, alumine, sol à base de silice et matériau sol-gel inorganique.

**14.** Utilisation selon la revendication 11, où le matériau additif est un agent de gélification d'argile.

**15.** Procédé de réalisation d'un revêtement essentiellement homogène et uniforme en combustible solide sec (20, 316, 212, 114, 51, 174, 620) sur une surface d'un substrat (12, 302, 210, 510, 170, 418) comprenant:

a. mélanger un combustible solide, comprenant au moins un agent d'oxydation contenant du métal et au moins un métal, qui est un agent réducteur, avec un matériau additif dans un solvant pour former une boue homogène;
b. appliquer une mince couche de la boue à une épaisseur réglée sur une surface d'un substrat; et
c. sécher la boue appliquée pour former une couche de combustible solide sec sur le substrat, où l'épaisseur de la couche de combustible solide est dans la plage de 0,00254 cm (0,001 pouce) à 0,0762 cm (0,030 pouce).

**16.** Procédé selon la revendication 15, où ledit revêtement est un dépôt par trempage, dépôt par pulvérisation, dépôt par rouleau, dépôt par gravure, dépôt par rouleau inverse, dépôt d'espace, dépôt à barre de calibrage, dépôt à filière plate, dépôt par voile ou dépôt à lame d'air.

**17.** Procédé selon la revendication 16, où ledit dépôt d'espace est exécuté avec une barre de calibrage enroulée de fil dans une coucheuse à lame.

**18.** Procédé selon la revendication 15, où avant le revêtement, un masque est positionné sur une portion de la surface du substrat pour empêcher un dépôt du combustible solide sur ladite portion.

**19.** Procédé selon la revendication 15, où le substrat est une feuille métallique.

**20.** Procédé selon la revendication 19, où l'épaisseur de la feuille métallique est dans la plage de 0,00254 cm (0,001 pouce) à 0,0254 cm (0,010 pouce).

**21.** Procédé selon la revendication 15, où la couche de combustible solide a une épaisseur de 0,00254 cm (0,001 pouce) à 0,0127 cm (0,005 pouce).

**22.** Procédé selon la revendication 15, où l'agent d'oxydation est sélectionné parmi au moins un des suivants $MoO_3$, $KCl0_4$, $KCl_3$ et $Fe_2O_3$.

**23.** Procédé selon la revendication 15, où l'agent réducteur est sélectionné parmi au moins un des suivants: aluminium, zirconium, fer et titane.

**24.** Procédé selon la revendication 15, où ledit matériau additif est un matériau inorganique.

**25.** Procédé selon la revendication 15, où le matériau additif est un agent de gélification d'argile.

**26.** Procédé selon la revendication 15, où ledit séchage a lieu dans un four pendant au moins deux heures.

**27.** Procédé selon la revendication 15, où le substrat est un métal, un alliage ou une céramique.

**28.** Unité de chauffage (10, 300, 102, 530) qui, lors de l'allumage, chauffe rapidement une zone définie d'une surface extérieure d'un substrat à une température de crête réglée comprenant:

a. une enceinte comprenant au moins un substrat ayant une surface extérieure et une surface intérieure,
b. une couche de combustible solide (20, 80, 316, 212, 114, 514, 174, 620) qui comprend un agent d'oxydation contenant du métal et un métal, qui est un agent réducteur, en un rapport défini, appliquée à la surface intérieure du substrat (12, 302, 210, 510, 170, 418) correspondant à la zone définie de la surface extérieure du substrat à chauffer, où l'épaisseur de la couche de combustible solide est dans la plage de 0,00254 cm (0,001 pouce) à 0,0762 cm (0,030 pouce); et
c. un allumeur disposé dans l'enceinte pour allumer le combustible solide.

**29.** Unité de chauffage selon la revendication 28, où la température de crête est réglée par la masse de combustible solide appliquée à la surface intérieure du substrat.

**30.** Unité de chauffage selon la revendication 28, où la couche de combustible solide a une épaisseur dans la plage de 0,00254 cm (0,001 pouce) à 0,0127 cm (0, 005 pouce).

**31.** Unité de chauffage selon la revendication 28, où l'enceinte comprend plus d'un substrat.

**32.** Unité de chauffage selon la revendication 28, où le substrat est une feuille métallique.

**33.** Unité de chauffage selon la revendication 28, où le combustible solide comprend un agent d'oxydation sélectionné parmi au moins un des suivants $MoO_3$, $KClO_4$, $KClO_3$ et $Fe_2O_3$.

**34.** Unité de chauffage selon la revendication 28, où le combustible solide comprend un agent réducteur sélectionné parmi au moins un des suivants: aluminium, zirconium, fer et titane.

**35.** Unité de chauffage selon la revendication 28, où le combustible solide comprend au moins un matériau additif.

**36.** Unité de chauffage selon la revendication 35, où le matériau additif est un agent de gélification d'argile.

**37.** Unité de chauffage selon la revendication 28, où le substrat est un métal, un alliage ou une céramique.

**38.** Unité de chauffage selon l'une quelconque des revendications 28 à 37 comprenant en outre un élément de chauffage par résistance pour activer l'allumeur.

**39.** Unité de chauffage selon l'une quelconque des revendications 28 à 37, comprenant en outre une source de rayonnement électromagnétique pour activer l'allumeur.

**40.** Unité de chauffage selon l'une quelconque des revendications 28 à 37, comprenant en outre un mécanisme pour produire une force de percussion pour activer l'allumeur.

**41.** Unité de chauffage selon l'une quelconque des revendications 28 à 40, où la couche de combustible solide est essentiellement homogène.

**42.** Utilisation, procédé ou unité de chauffage selon l'une quelconque des revendications précédentes, où le combustible solide est configuré pour chauffer une portion de la surface extérieure du substrat à une température d'au moins 200°C en moins de 1 seconde à la suite de l'allumage du combustible solide.

**43.** Unité d'amenée de médicament (500) comprenant l'unité de chauffage (530) selon l'une quelconque des revendications 28 à 42 et comprenant en outre:

un médicament (514) disposé sur une portion de la surface extérieure du substrat (510).

**44.** Dispositif de délivrance de médicament (150) comprenant l'unité d'amenée de médicament de la revendication 43 et comprenant en outre:

un boîtier (152, 154) définissant une voie d'air, où la portion de la surface extérieure du substrat comprenant le médicament est configurée pour être disposée dans la voie d'air.

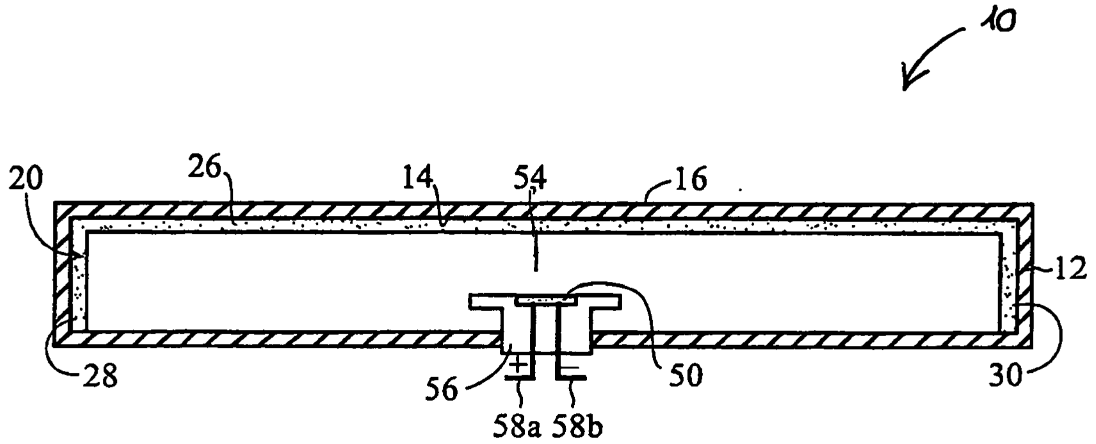


FIG. 1A

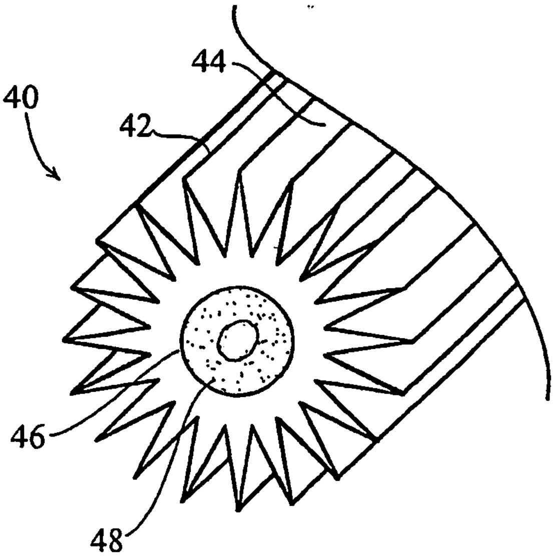


FIG. 1B

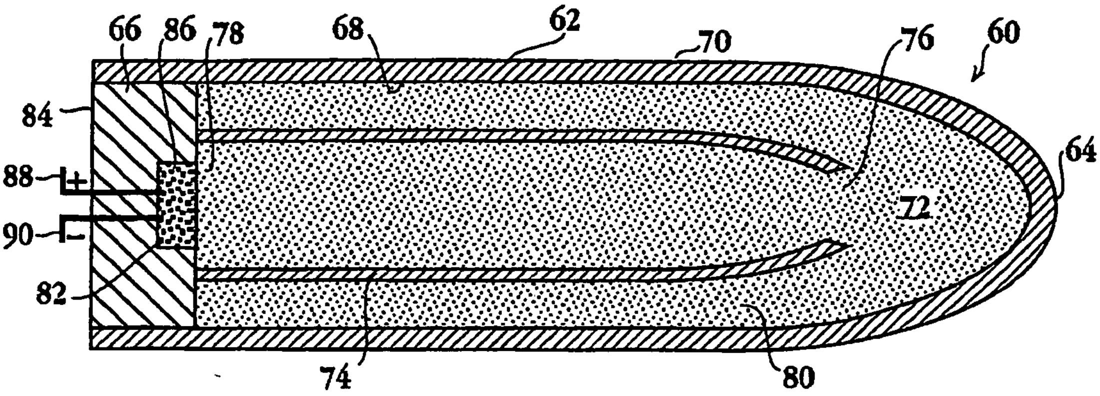


FIG. 2A

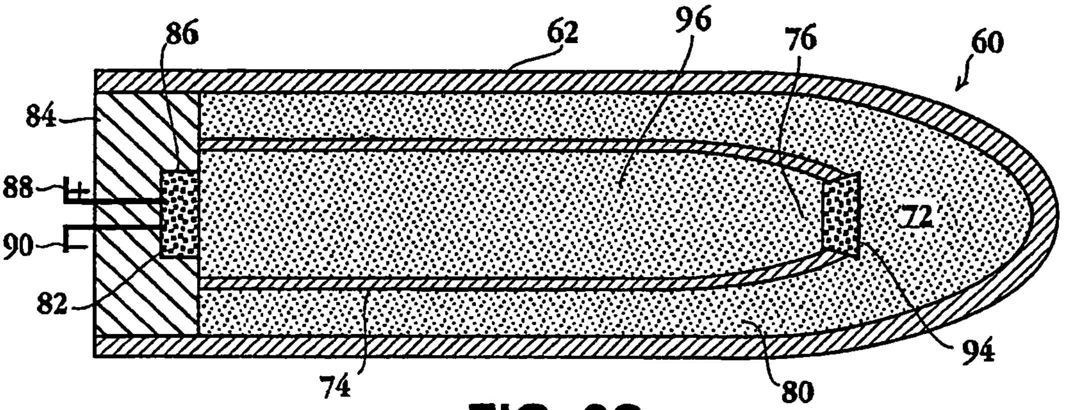


FIG. 2C

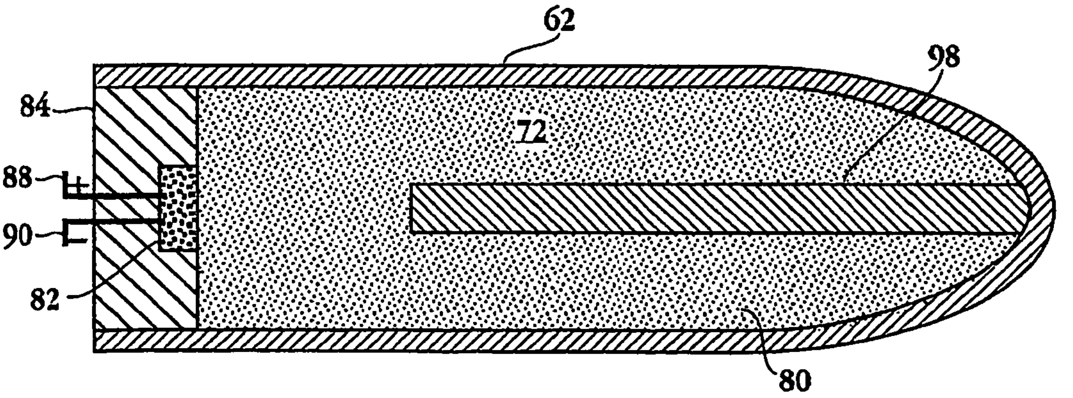


FIG. 2D

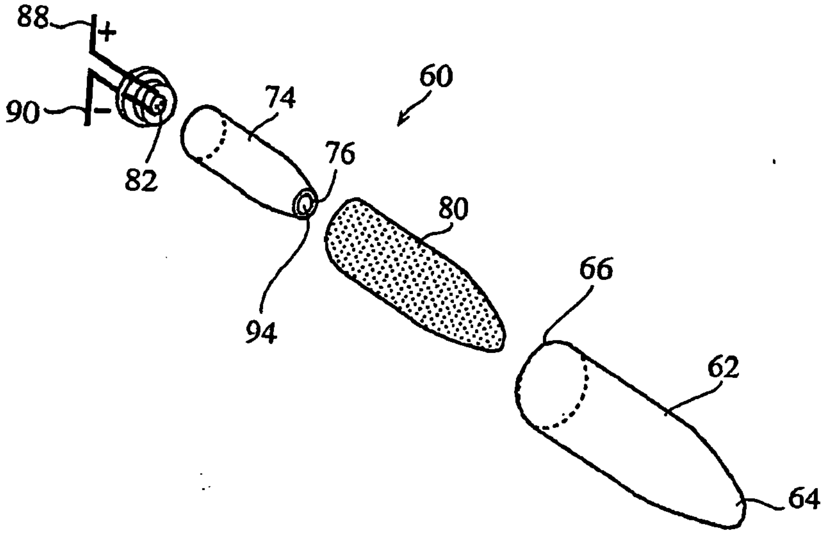


FIG. 2B

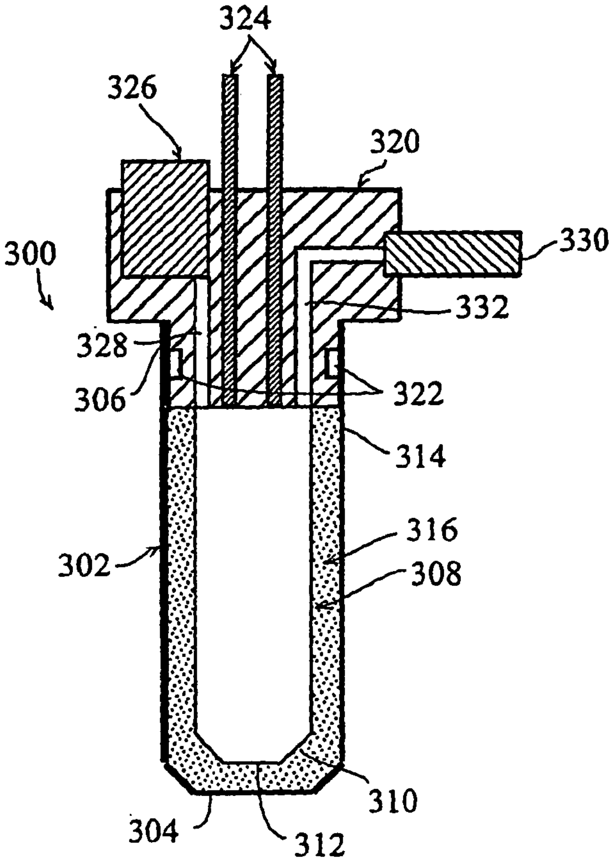


FIG. 3

FIG. 4A

FIG. 4B

FIG. 4C

FIG. 4D

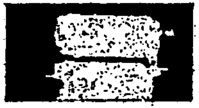


FIG. 4E

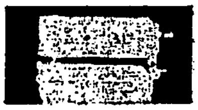


FIG. 4F

FIG. 5A

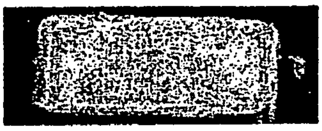
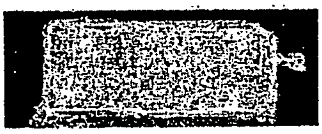


FIG. 5B



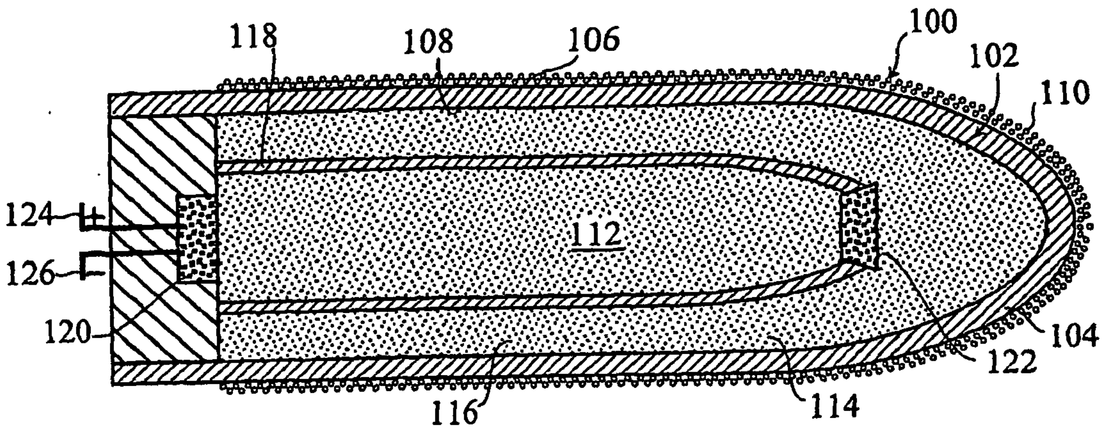


Fig. 6A

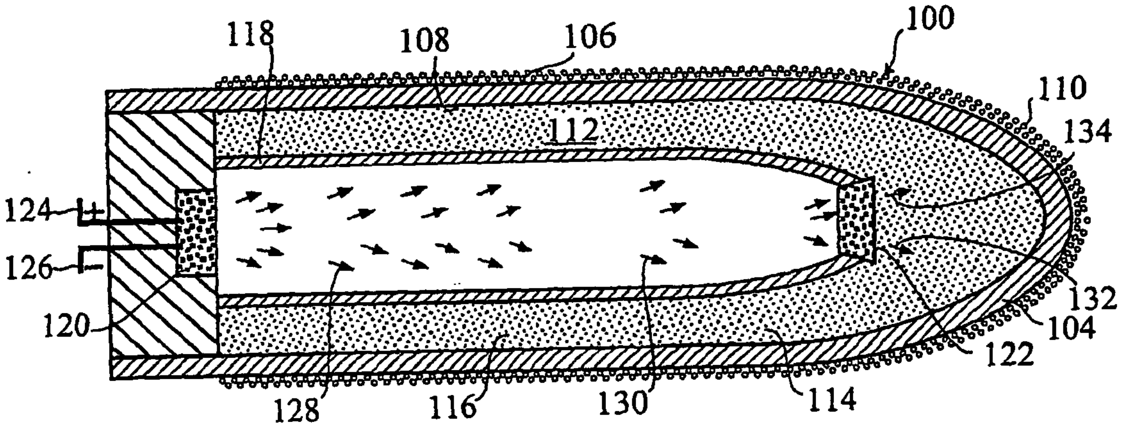


Fig. 6B

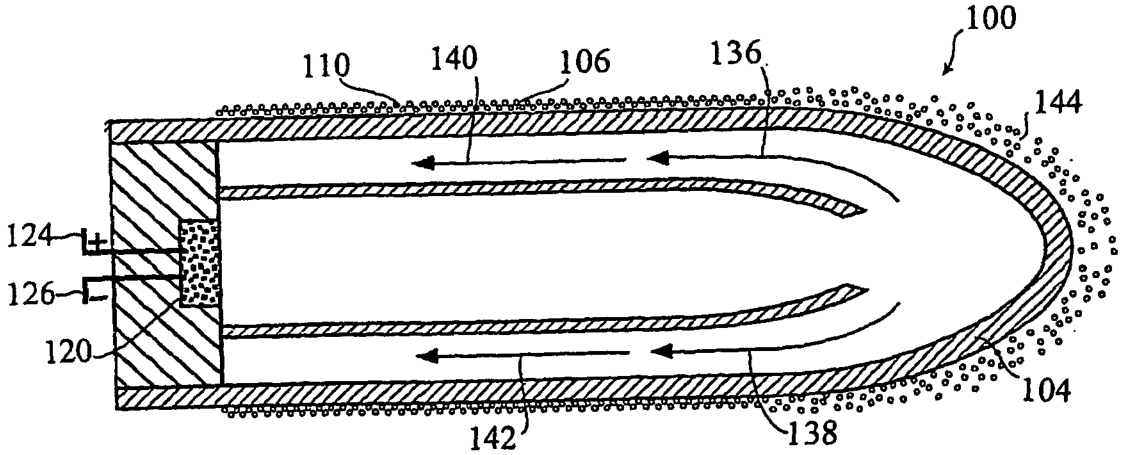


Fig. 6C

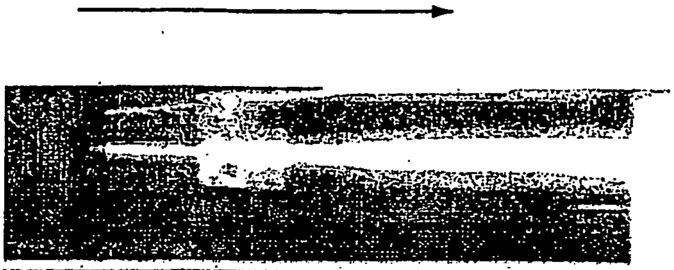


**FIG. 7A**

*t* = 0ms

**FIG. 7B**

*t* = 150ms

**FIG. 7C**

*t* = 250ms

**FIG. 7D**

*t* = 500ms

**FIG. 7E**

*t* = 1000ms

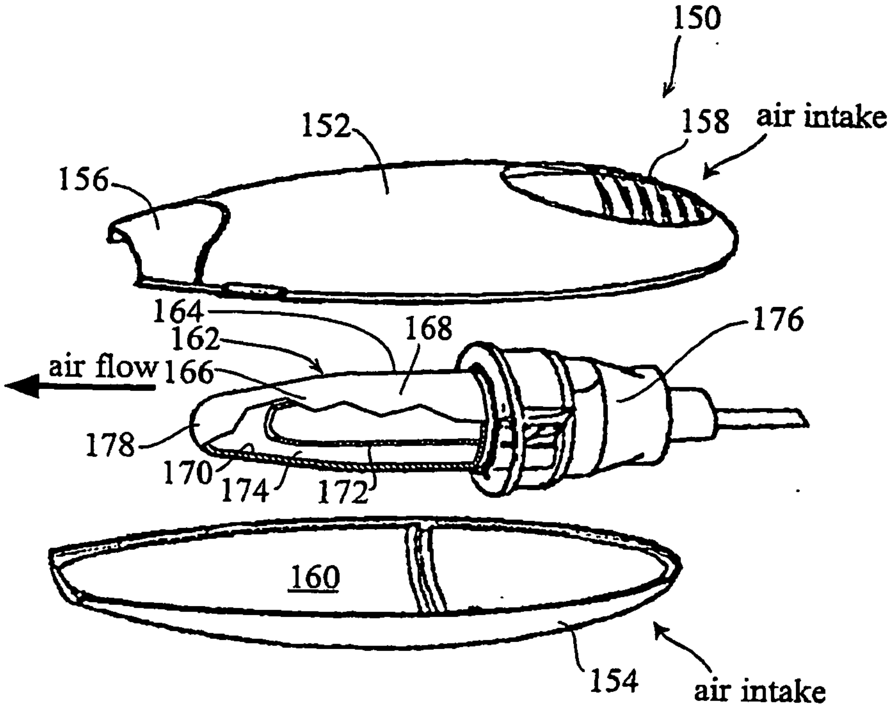

150
152
156
158
air intake
164
162
168
176
air flow
166
178
170
174
172
160
154
air intake

FIG. 8

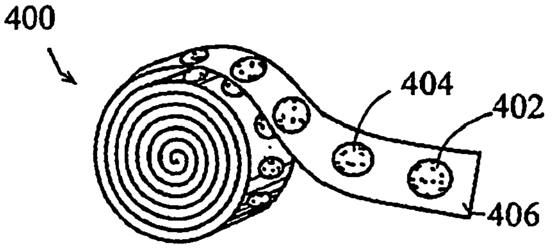


FIG. 9A

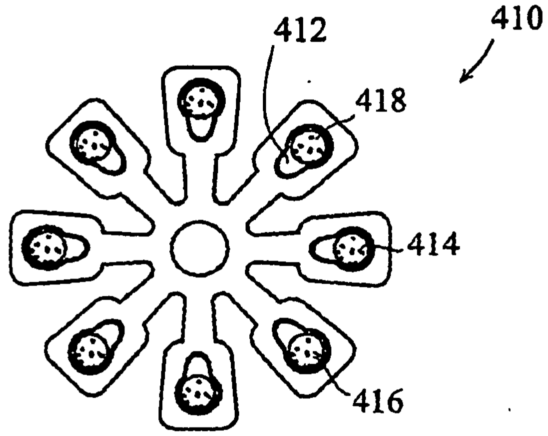


FIG. 9B

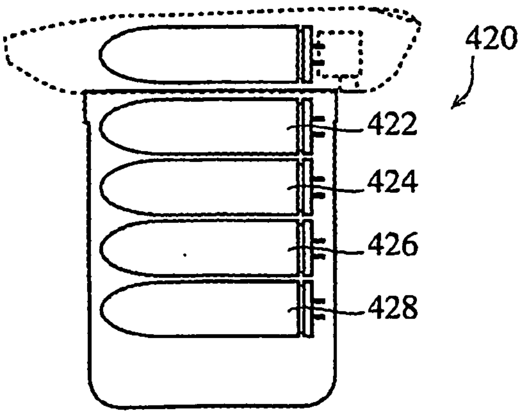


FIG. 9C

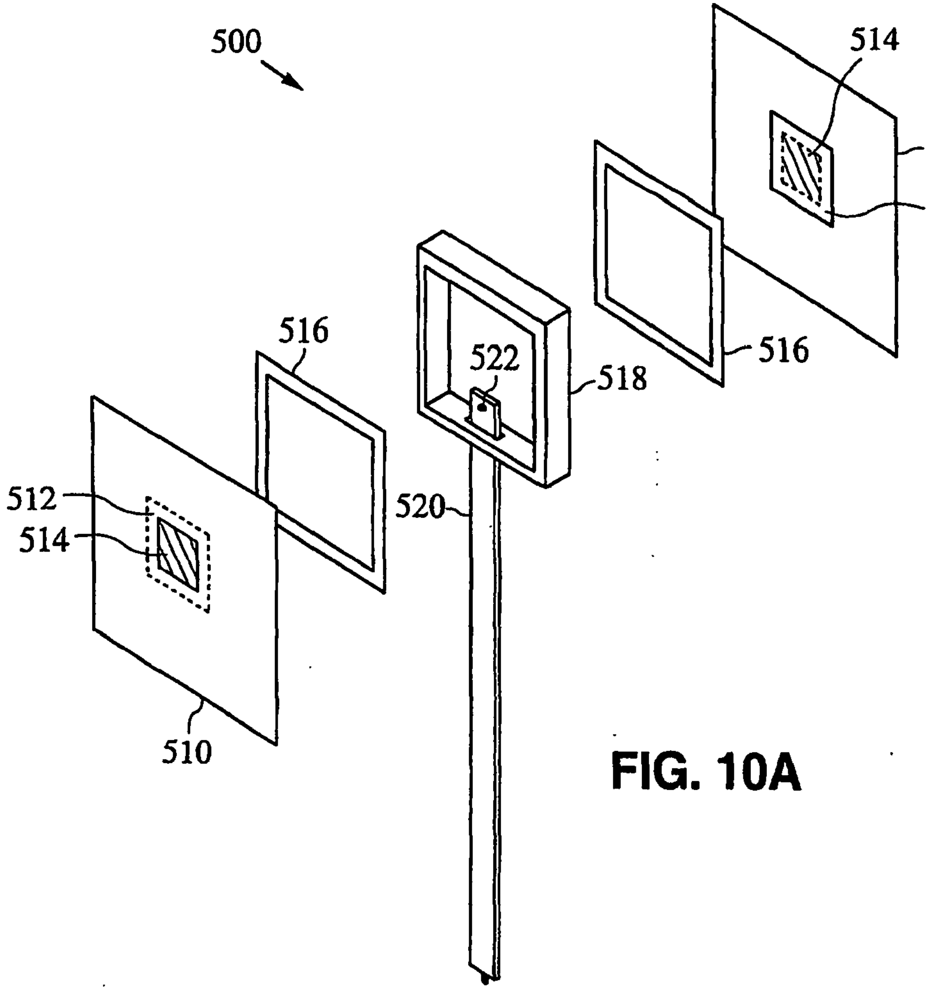


FIG. 10A

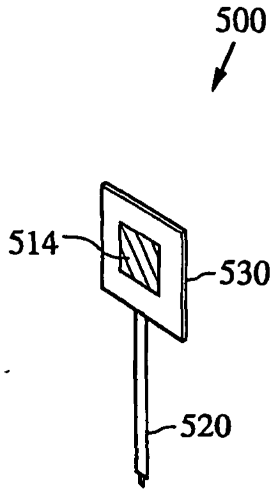


FIG. 10B

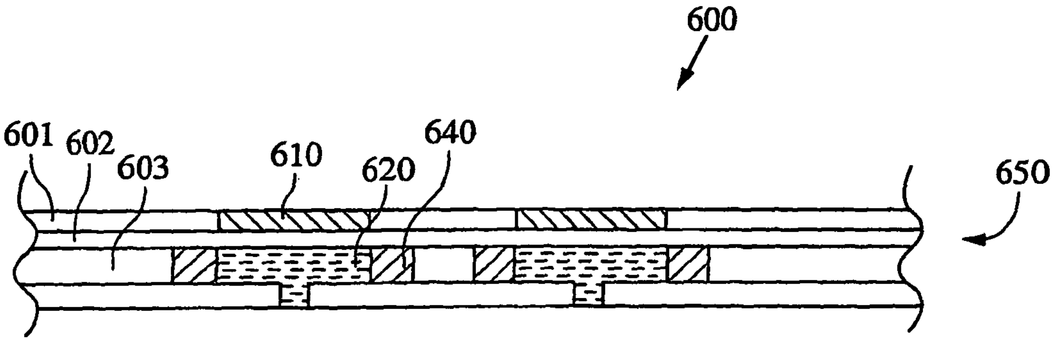


FIG. 11A

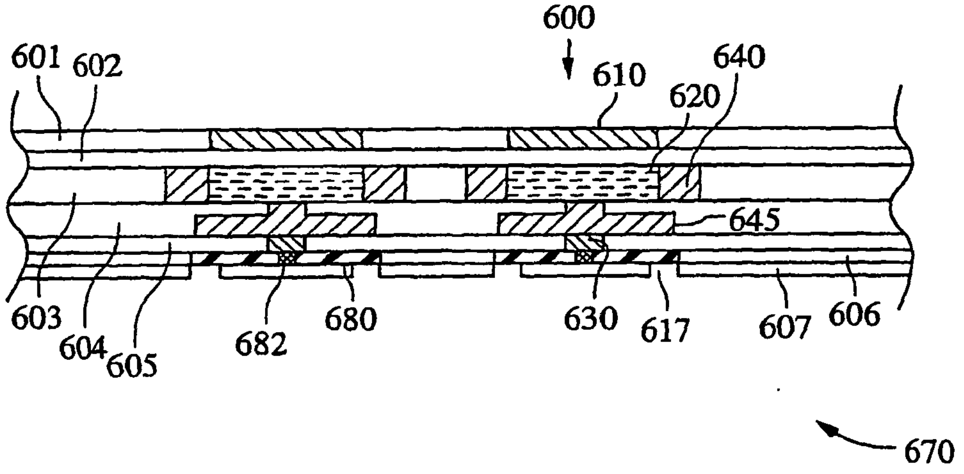


FIG. 11B

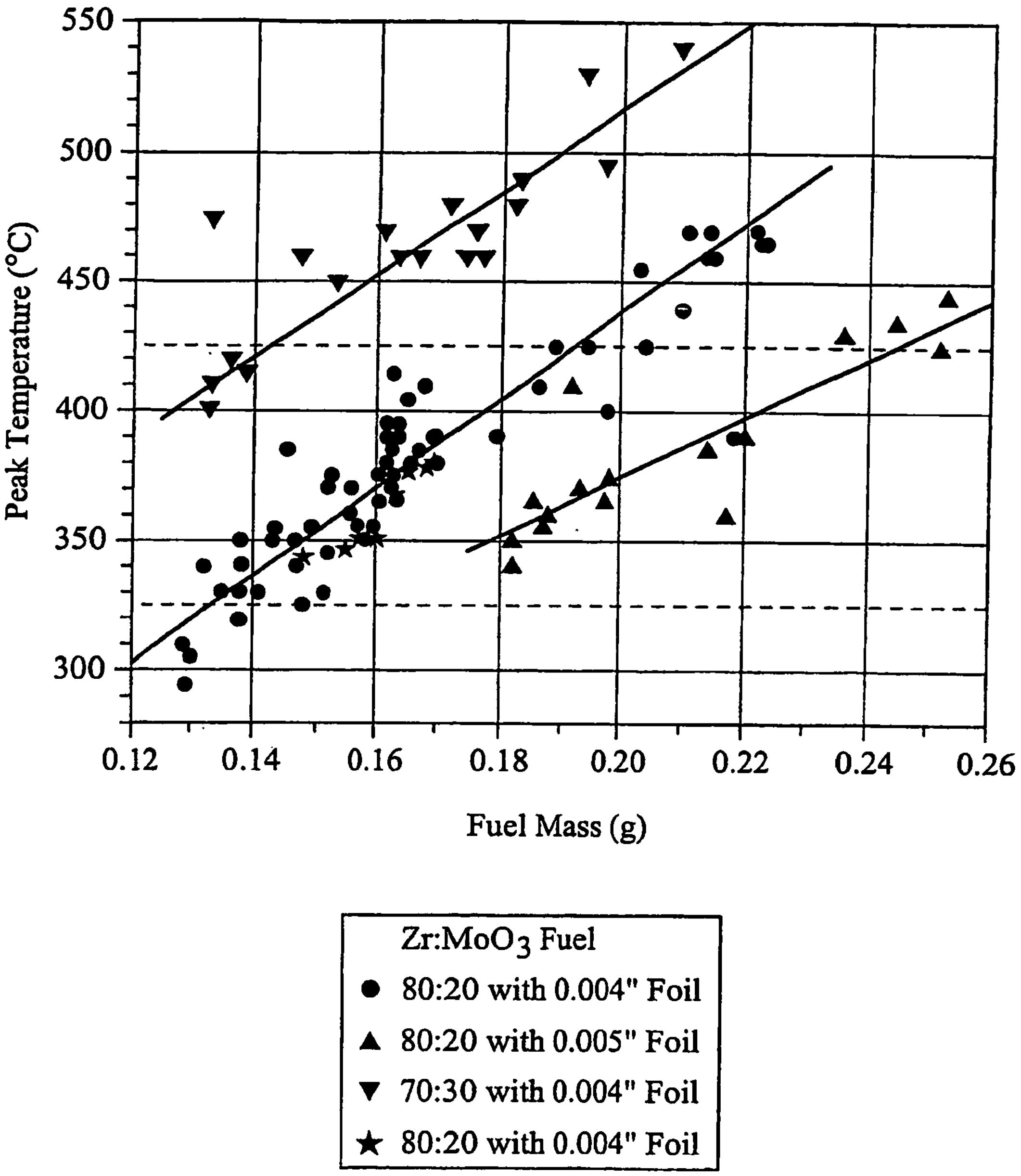

550
500
450
400
350
300
Peak Temperature (°C)
0.12
0.14
0.16
0.18
0.20
0.22
0.24
0.26
Fuel Mass (g)
Zr:MoO3 Fuel
● 80:20 with 0.004" Foil
▲ 80:20 with 0.005" Foil
▼ 70:30 with 0.004" Foil
★ 80:20 with 0.004" Foil

FIG. 12

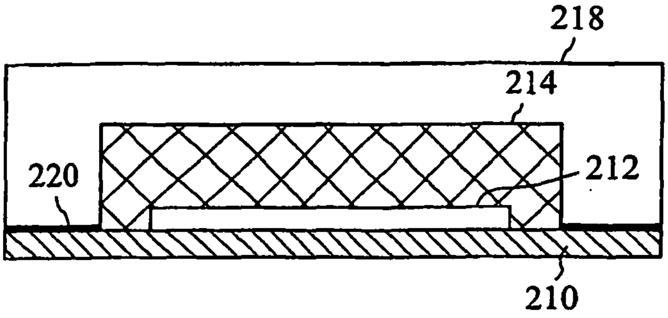


FIG. 13A

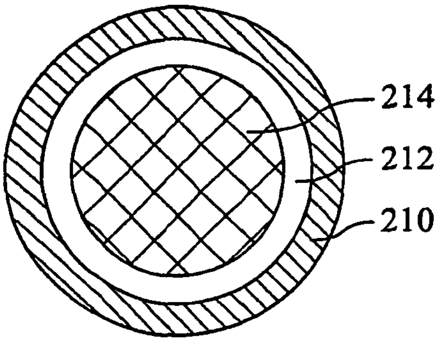


FIG. 13B

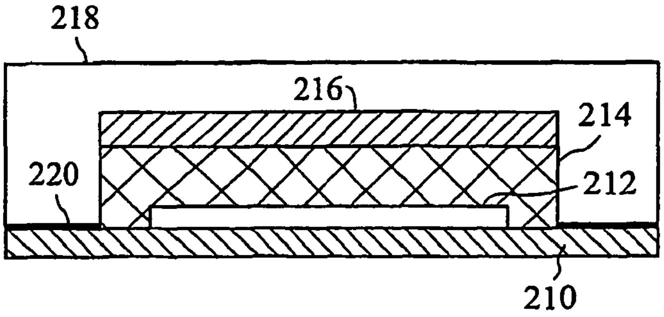


FIG. 13C

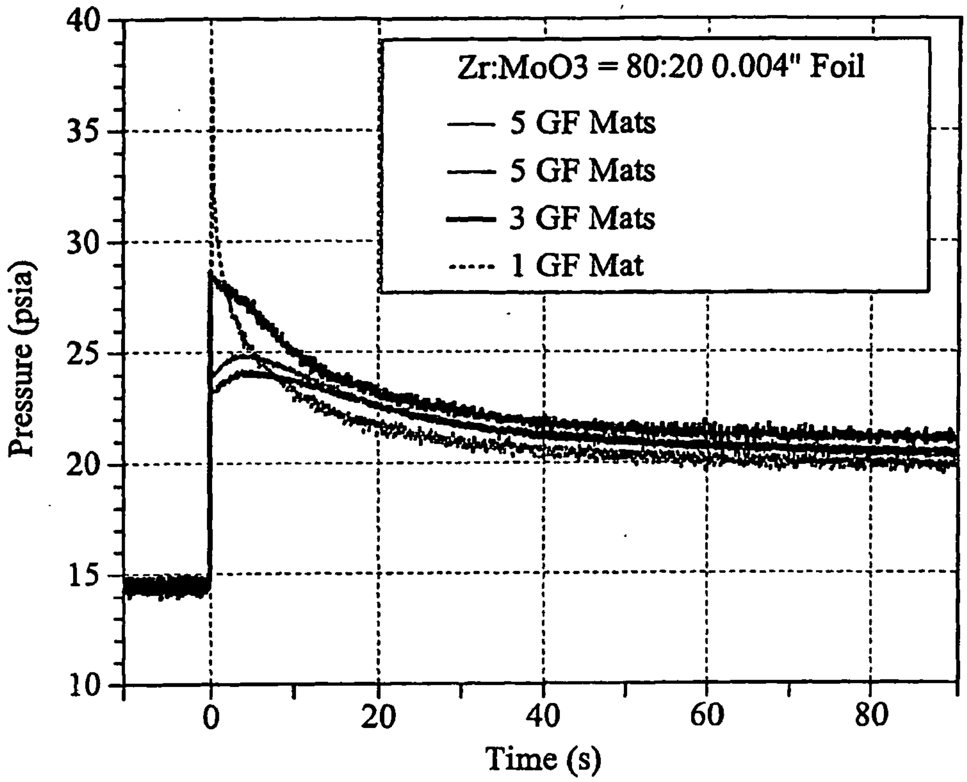

Zr:MoO3 = 80:20 0.004" Foil
5 GF Mats
5 GF Mats
3 GF Mats
1 GF Mat
Pressure (psia)
40
35
30
25
20
15
10
0
20
40
60
80
Time (s)

FIG. 14

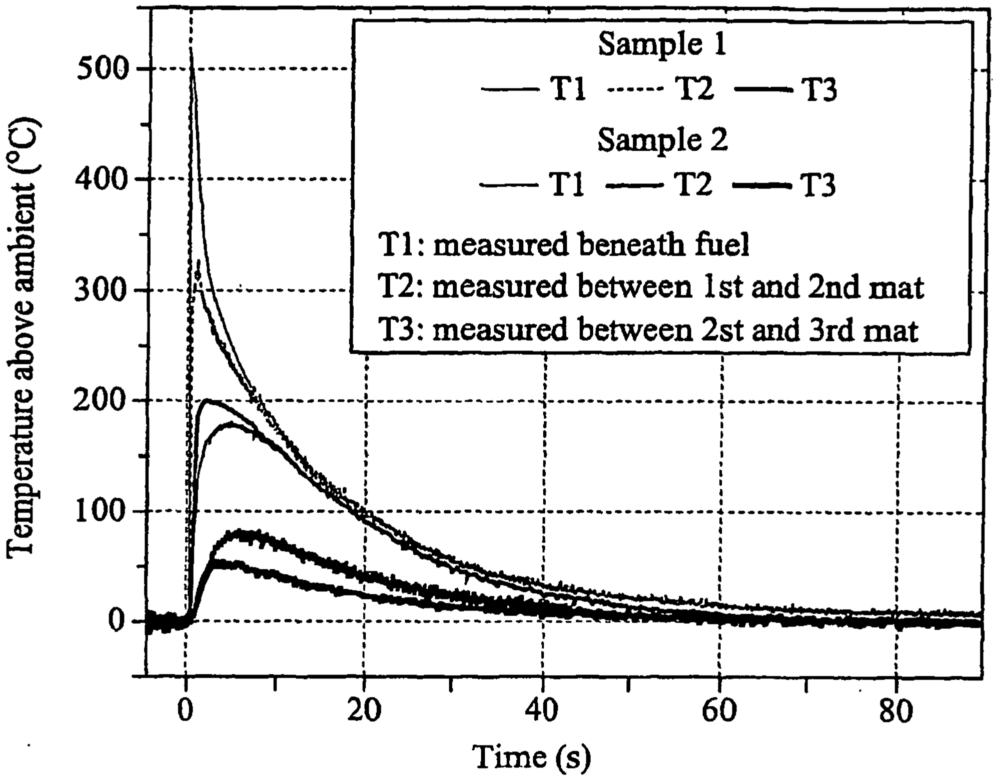

Sample 1
—— T1 ------ T2 —— T3
Sample 2
—— T1 —— T2 —— T3
T1: measured beneath fuel
T2: measured between 1st and 2nd mat
T3: measured between 2st and 3rd mat
Temperature above ambient (°C)
500
400
300
200
100
0
0
20
40
60
80
Time (s)

FIG. 15

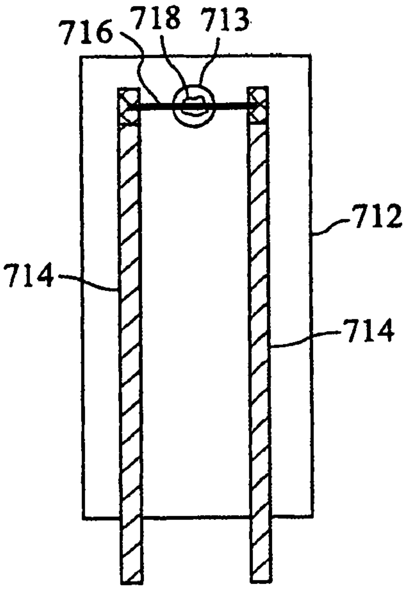


FIG. 16

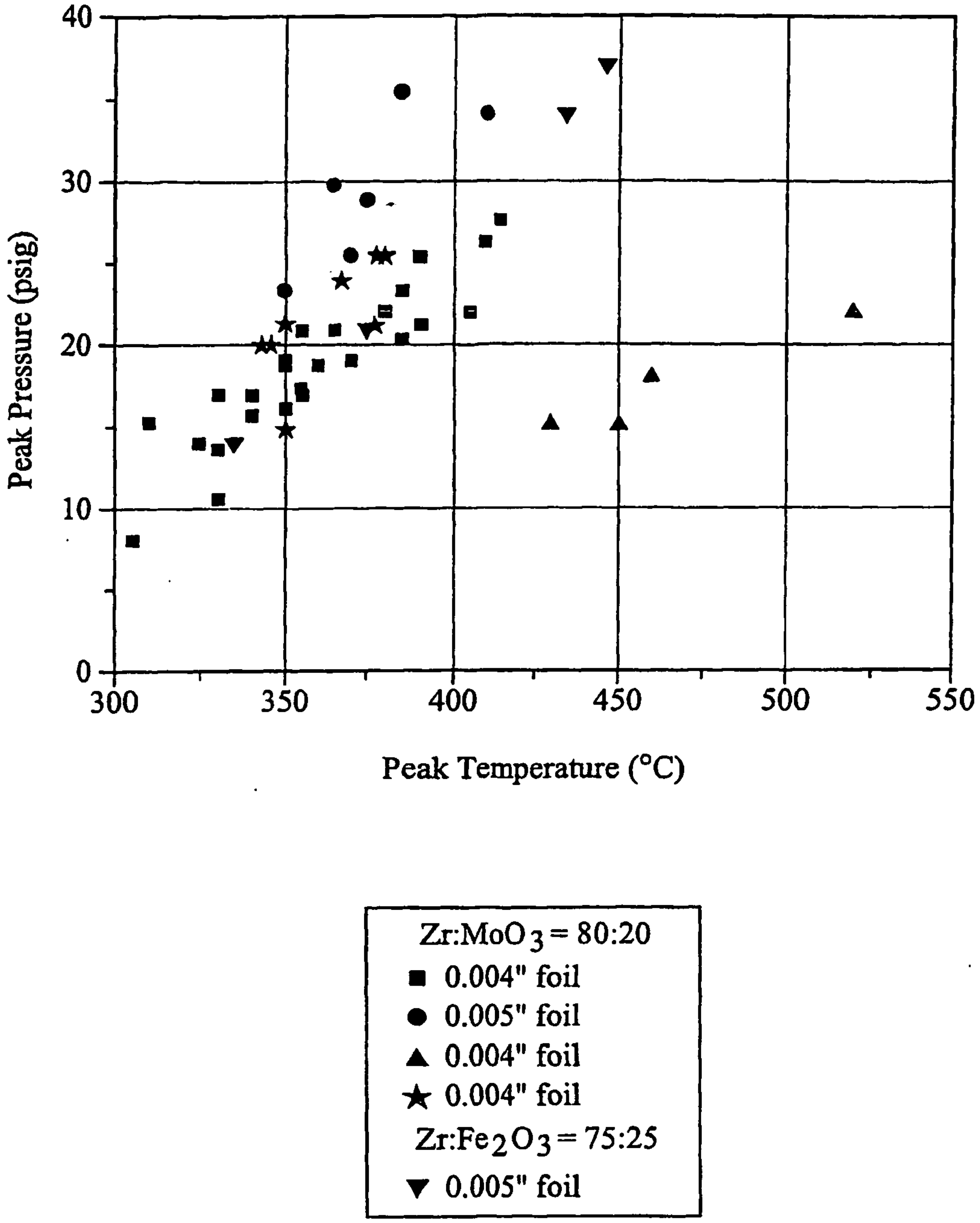

40
30
20
10
0
Peak Pressure (psig)
300
350
400
450
500
550
Peak Temperature (°C)
Zr:MoO3 = 80:20
■ 0.004" foil
● 0.005" foil
▲ 0.004" foil
★ 0.004" foil
Zr:Fe2O3 = 75:25
▼ 0.005" foil

FIG. 17

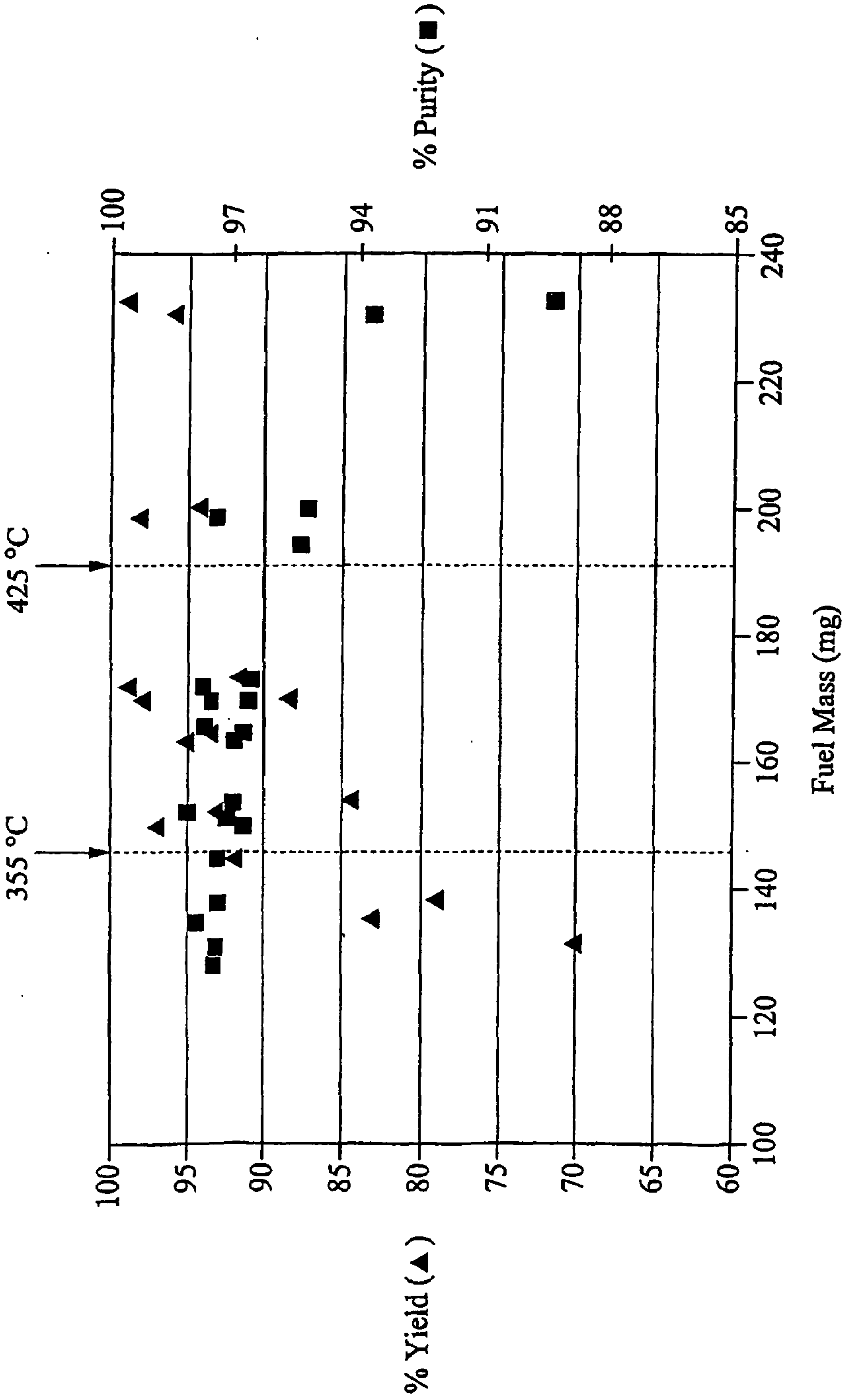

355 °C
425 °C
% Yield (▲)
100
95
90
85
80
75
70
65
60
% Purity (■)
100
97
94
91
88
85
Fuel Mass (mg)
100
120
140
160
180
200
220
240

FIG. 18

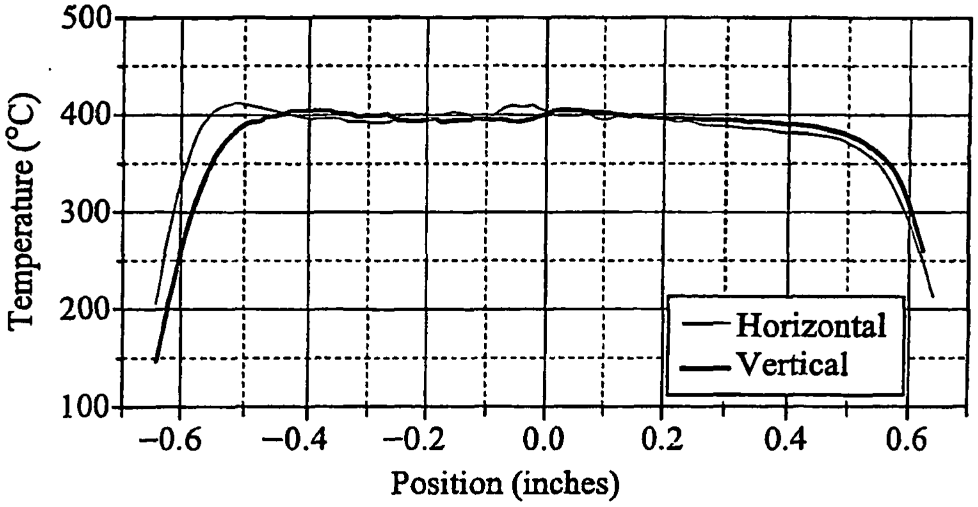

500
400
300
200
100
Temperature (°C)
−0.6
−0.4
−0.2
0.0
0.2
0.4
0.6
Position (inches)
Horizontal
Vertical

FIG. 19

## REFERENCES CITED IN THE DESCRIPTION

### Patent documents cited in the description

- US 5628304 A **[0002]**
- US 4773389 A **[0002]**
- US 6289889 B **[0002]**
- US 2104266 A **[0002]**
- US 4922901 A **[0002]**
- US 6095143 A **[0002]**
- WO 9409842 A **[0002]**
- US 5285798 A **[0003]**
- US 4941483 A **[0003]**
- US 5593792 A **[0003]**
- US 5322018 A **[0005]**
- US 4193388 A **[0006]**
- US 5603350 A **[0021]**
- US 5739460 A **[0054]**
- US 71898203 A **[0162]**

### Non-patent literature cited in the description

- **Sekine et al.** *Journal of Forensic Science,* 1987, vol. 32, 1271-1280 **[0226]**
- **Martin et al.** *Journal of Analytic Toxicology,* 1989, vol. 13, 158-162 **[0226]**