(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 February 2012 (23.02.2012)

PCT

(10) International Publication Number
WO 2012/023030 A2

(51) International Patent Classification:
B65D 81/20 (2006.01)

(21) International Application Number:
PCT/IB2011/001901

(22) International Filing Date:
17 August 2011 (17.08.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/374,649 18 August 2010 (18.08.2010) US

(71) Applicant *(for all designated States except US)*: **PURDUE PHARMA L.P.** [US/US]; One Stamford Forum, 201 Tresser Boulevard, Stamford, CT 06901-3431 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **MCKENNA, William** [US/US]; 10 Longmeadow Road, Yonkers, NY 10704 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: VACUUM AVOIDING PACKAGING SYSTEMS AND METHODS THEREOF

(57) Abstract: Disclosed in certain embodiments is a packaging system comprising a container having an inner cavity; a product subject to degradation; a gas removing material; and a gas releasing material, wherein the gas releasing material is capable of liberating an effective amount of gas to replace at least a portion of the gas removed by the gas removing material in order to minimize buckling of the container.

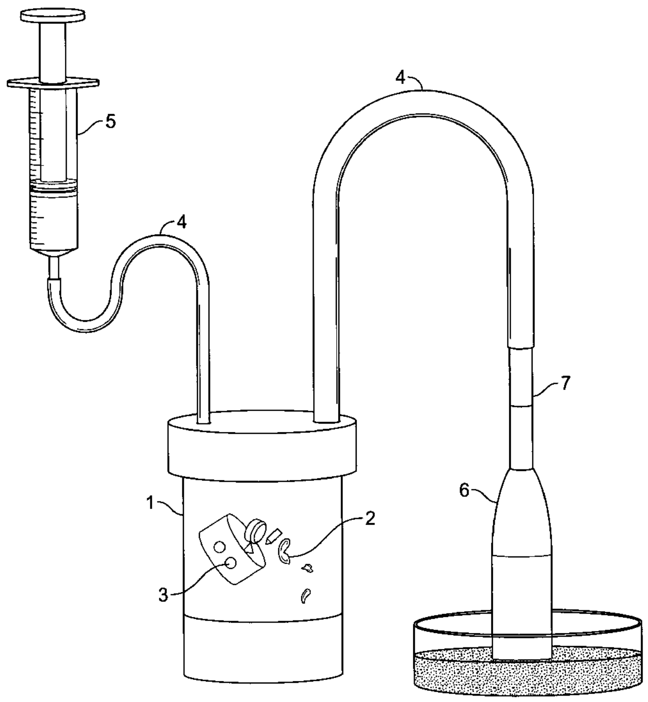

FIG. 1

WO 2012/023030 A2

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

VACUUM AVOIDING PACKAGING SYSTEMS AND METHODS THEREOF

FIELD OF THE INVENTION

[0001] The present invention is directed to systems and methods for avoiding the creation of a vacuum in packaged containers. The avoidance in creating the vacuum helps prevent buckling of the package and improves shelf life of the packaged material.

BACKGROUND OF THE INVENTION

[0002] The packaging and distribution of consumer products present many challenges, especially when the product is subject to degradation and has a limited shelf-life. This is especially true when the product is a pharmaceutical drug subject to testing under storage conditions in order to obtain regulatory approval. Many degradation issues of such packaged products are associated with the presence of oxygen in the headspace of the container.

[0003] Oxygen exists in two allotropic forms: as an invisible gas composed of two oxygen atoms (O_2); and as a perceptibly blue form composed of three oxygen atoms (O_3 or ozone). Unlike nitrogen or carbon dioxide, oxygen is paramagnetic wherein two electrons in the molecule are not paired to each other. These “free unpaired” electrons can interact with and cause degradation of many packaged products to create “free radicals”. The typical reaction is by hydrogen abstraction and formation of peroxides, which decompose to free radicals. The presence of peroxides causes further degradation of the packaged products.

[0004] In the case of pharmaceutical drugs, the degradation due to oxidation has the potential to reduce the amount of active agent so that the dosage form no longer contains the labeled amount of active agent. In certain cases, the inadequate stability of an active agent could result in an otherwise safe and efficacious pharmaceutical drug becoming non-approvable and therefore not available to provide benefit to the intended patient population.

[0005] The issue of air (and thus oxygen) in the headspace of packaging may be addressed by packaging the product with an inert gas (e.g., nitrogen) in place of air in the headspace. Procedures to carry this out may utilize liquid nitrogen, but this creates safety concerns, including the possibility of freeze burns when converting the liquid nitrogen to a gas, and the propensity of nitrogen to crowd out oxygen in confined spaces. Inert gas replacement procedures, equipment, and required maintenance can also significantly increase the cost of goods, which may have an adverse effect on distribution and marketing.

[0006] Another method to address degradation issues related to oxygen degradation is to add an oxygen scavenger inside the packaging prior to sealing. The oxygen scavenger (e.g., iron oxide based) reacts with the oxygen and thereby reduces its contact with the packaged material.

[0007] Atmospheric air, which is typically included in the headspace of packaging, is approximately 21% oxygen. The removal of oxygen from a sealed container using an oxygen scavenger can create a partial vacuum inside the container, which can lead to puckering of the package walls, package seal failure, and an increased permeation of gases through the package walls. Such package failure can lead to decreased shelf life and a product that is unsuitable for standard distribution channels.

[0008] One method to reduce buckling and package failure due to vacuum creation would be to increase the thickness of the container walls. However, this would result in a heavier product for distribution that could add significantly to the cost of goods. In addition, increasing the thickness of the container walls might not prevent package seal failure.

[0009] Accordingly, there exists a need in the art to address problems associated with the packaging of consumer products.

[0010] All references described herein are incorporated by reference in their entireties for all purposes.

SUMMARY OF THE INVENTION

[0011] It is an object of the present invention to provide a packaging system for a product, which packaging system avoids or reduces the creation of an inner vacuum.

[0012] It is a further object of certain embodiments of the present invention to provide a packaging system that maintains the shelf life and stability of a product that might otherwise be susceptible to oxidative degradation. In certain embodiments, the product is a pharmaceutical drug product. In other embodiments, the product is an industrial chemical. In alternative embodiments, the product is a foodstuff.

[0013] It is a further object of certain embodiments of the present invention to provide a packaging system that maintains its integrity within distribution channels and during periods of storage.

[0014] It is a further object of certain embodiments of the present invention to provide a method of packaging a product to avoid or reduce the creation of an inner vacuum that might otherwise result from incorporating an oxygen scavenger in the packaged product.

[0015] It is a further object of certain embodiments of the present invention to provide a method of packaging a product that maintains the shelf life and stability of the product.

[0016] It is a further object of certain embodiments of the present invention to provide a method of packaging a product that maintains its integrity within distribution channels and during periods of storage.

[0017] It is a further object of certain embodiments of the present invention to provide a gas releasing material that can be utilized in a packaging system to avoid or reduce the creation of an inner vacuum that might otherwise result from incorporating an oxygen scavenger therein.

[0018] It is a further object of certain embodiments of the present invention to provide a gas releasing material for use in a packaging system in conjunction with an oxygen scavenger that will help maintain the shelf life and stability of the packaged product.

[0019] It is a further object of certain embodiments of the present invention to provide a gas releasing material for use in a packaging system that will help maintain the integrity of the packaging system within distribution channels.

[0020] In one embodiment, the present invention provides a packaging system comprising: (i) a sealable container having an inner cavity; (ii) a product (e.g., a consumer or industrial product); (iii) a gas removing material; and (iv) a gas releasing material.

[0021] In another embodiment, the present invention provides a packaging system comprising: (i) a sealable container having an inner cavity; (iii) a gas removing material; and (iv) a gas releasing material. The packaging system is adapted to receive a product (ii) as described above, and is then sealed for distribution and marketing.

[0022] In another embodiment, the present invention provides a packaging system comprising: (i) a sealable container having an inner cavity; (ii) a product (e.g., a consumer or industrial product); and (iii) a gas releasing material. The container is adapted to contain the product and the gas releasing material as described above, and is then sealed for distribution and marketing.

[0023] In another embodiment, the present invention provides a packaging system comprising: (i) a sealable container having an inner cavity; and (iii) a gas releasing material. The packaging system is adapted to receive a product (ii) as described above, and is then sealed for distribution and marketing.

[0024] In certain embodiments, the product can be a pharmaceutical drug, a foodstuff or a commercial or industrial chemical. In particular embodiments, the product is subject to oxidative degradation.

[0025] In certain embodiments, the gas removing material is an oxygen scavenger, an oxygen adsorbent or a combination thereof.

[0026] In certain embodiments, gas liberated from the gas releasing material serves to replace the gas removed by the gas removing material, e.g. the oxygen removed by an oxygen scavenger. By replacing the scavenged (or adsorbed) oxygen with gas liberated from the gas releasing material, the packaging system avoids or reduces the creation of an inner vacuum, thereby preventing buckling of the container or package seal failure.

[0027] In another embodiment, the present invention provides a packaging system comprising: (i) a sealable container having an inner cavity; (ii) a product (e.g., a consumer or industrial product); (iii) an oxygen scavenger or adsorbent; and (iv) a gas releasing material, wherein gas liberated from the gas releasing material serves to replace the oxygen removed by the oxygen scavenger. By replacing the scavenged (or adsorbed) oxygen with gas liberated from the gas releasing material, the packaging system avoids or reduces the creation of an inner vacuum, thereby preventing or minimizing buckling of the container or package seal failure.

[0028] In another embodiment, the gas liberated from the gas releasing material is an inert gas (such as nitrogen). By replacing the scavenged (or adsorbed) oxygen with an inert gas liberated from the gas releasing material, the likelihood of oxidative degradation of the product is substantially reduced.

[0029] The sealable container can be any container that can be used for and/or is approved for storing, shipping, distributing and/or marketing a particular product, whether that product is an active pharmaceutical ingredients (API), a pharmaceutical dosage form in finished form, or any industrial chemical or other material that needs to be stored, shipped or distributed. The sealable container can be any such container that can be sealed against the passage of gases, and for which oxygen scavenging would help improve the stability of the material contained therein. Other than practical considerations, there is no lower or higher limit to the size or capacity of the sealable container for which the present invention may be used. Non-limiting examples of sealable containers for pharmaceutical use include drug bottles, vials or other sealable drug-containing packages provided directly to consumers; bulk containers (e.g., bottles) of drugs distributed by pharmaceutical manufacturers and pharmaceutical distributors to pharmacy chains, outlets and hospitals; and industrial size bins, drums and bags used by pharmaceutical companies to store large quantities of drug intermediates, API or finished dosage forms.

[0030] Non-limiting examples of sealable containers for non-pharmaceutical chemicals include bottles, vials or other sealable chemical-containing packages provided directly to academic or research laboratories; bulk containers (e.g., bottles) of chemicals distributed by chemical manufacturers and chemical distributors to chemical clearinghouses; and industrial size bins, drums and bags used by chemical companies for storing, shipping, distributing or marketing industrial chemicals.

[0031] The sealable container is adapted to contain the product, the gas removing material and the gas releasing material, and then to be sealed for storage, distribution and/or marketing. The gas removing material and the gas releasing material are preferably maintained away from the product within the sealable container so as to prevent them from intermixing with the product, but so as to allow them to achieve their intended purposes of protecting the product by oxygen scavenging and liberation of the replacement gas. Thus, the gas-removing material and the gas releasing material are preferably maintained in one or more separate sub-containers within the sealable container, such as in one or more pouches or sachets, perforated vials, or other appropriate sub-containers that are sufficiently permeable to the passage of gases so as to allow them to achieve their intended purposes. In one embodiment, the gas removing material and the gas releasing material are maintained away from each other in separate sub-containers within the sealable container. In another embodiment, the gas-removing material and the gas releasing material are maintained together in the same sub-container within the sealable container.

[0032] The gas releasing material may be selected from a saccharide, a sugar alcohol, a starch, a dextrin, a gelatin, a gum, a protein and a combination thereof.

[0033] The present invention further provides a method of packaging a product subject to oxidative degradation, comprising combining the product with an oxygen scavenger and gas releasing material in a sealable container, and sealing the container. The different recited components can be added in any order prior to sealing of the container.

[0034] The present invention further provides specific gas releasing materials that can be utilized in the packaging systems and methods disclosed herein.

[0035] As used herein, the term "air" means atmospheric air that contains by volume approximately 78% nitrogen, 21% oxygen, 0.9% argon, 0.04% carbon dioxide, small amounts of other gases and a variable amount of water vapor.

[0036] The term "consumer product" means any article, or component part thereof, produced or distributed for sale to a consumer for use in or around a residence, a school, in recreation, or otherwise. Non-limiting examples of consumer products are foodstuffs, pharmaceuticals, household chemicals and lawn and gardening products.

[0037] The term "industrial product" means any article, or component part thereof, produced or distributed for sale to a business for use in or around a workplace, industrial setting, or agricultural setting. Non-limiting examples of industrial products are bulk foodstuffs or components, bulk pharmaceuticals or components, industrial chemicals and agricultural products.

[0038] The term "fluid communication" means the free transfer of a gas, fluid, or other substance from one area to another.

[0039] The term "adsorbent" means a material, typically porous and with a high surface area, that can adsorb substances onto its surface by intermolecular forces.

[0040] The term "gas releasing material" means a substance that can keep a gas under increased pressure.

[0041] The term "scavenger" means any material that is capable of reacting with a target material in order to reduce or minimize the presence of the target material in an environment of use.

BRIEF DESCRIPTION OF THE DRAWING

[0042] Figure 1 is a depiction of an apparatus to measure the amount of gas in gas releasing materials before or after exposure to controlled conditions.

DETAILED DESCRIPTION

[0043] The present invention addresses the issue of package disruption (e.g., puckering, buckling, seal breakage) due to the creation of an inner vacuum. The inner vacuum can be caused by a variety of factors, including but not limited to the use of adsorbents or scavengers to maintain or improve stability of the packaged product by the removal of oxygen from the sealed container. Other causes of inner vacuum and package disruption include cooling of packaged goods after being subject to heat, e.g., in sterilization processes, and removal of water or reactive gases by suitable scavengers from the sealed container..

[0044] The present invention utilizes a gas releasing material in order to avoid or reduce the creation of a vacuum in the packaging system, and to thereby minimize or prevent the disruption of the package seal. The gas releasing material is designed to liberate gas upon activation (e.g., by an external stimulus) or spontaneously over time.

[0045] In certain embodiments, the packaging system of the present invention comprises: (i) a sealable container having an inner cavity; (ii) a product subject to degradation by a gas, e.g., to oxidative degradation; (iii) a gas removing material; and (iv) a gas releasing material capable of liberating an effective amount of gas to replace at least a portion of the gas removed by the gas removing material (e.g., scavenger or adsorbent) in order to avoid or reduce the formation of a vacuum in the sealable container.

[0046] In certain embodiments, the gas releasing material is in the form of a solid matrix containing a compressed gas. The gas releasing material can be prepared, e.g., in accordance with the description of US Patent No. 3,012,893, US Patent No. 4,001,457 and US Patent No. 4,289,794, which are generally directed to preparing a gas releasing confection or candy. Such gas releasing candy is commercially available under the tradename PopRocks®.

[0047] The gas releasing material is prepared in certain embodiments by contacting a gas (e.g., any combination of nitrogen, inert gases like helium, carbon dioxide, air, etc.) with the matrix material (e.g., a saccharide) in a molten or semi-molten state. In this process, the gas is pressurized (e.g., at about 50 to 1000 psig) and is contacted with the molten matrix material for a sufficient time to permit adsorption of the gas therein. The gas can be in an amount of about 0.5 to about 25 mL per gram of matrix material. During processing, the matrix material is maintained in a molten or semi-molten state and when the desired concentration of gas is achieved, the gas-infused material is cooled and solidified to obtain the gas releasing material. The gas releasing material can then be processed into a desired shape and size, e.g., in the form of multiparticulates with a mean size from about 500 μm to about 3 mm, from about 0.1 mm to about 2 mm or from about 0.5 mm to about 1 mm.

[0048] The processing of the gas releasing material into a desired shape and size can be performed, e.g., by milling and an optional sieving step. The milling can be performed, e.g., with a batch ball mill, continuous ball mill, vibrating ball mill, cage mill, colloid mill, fluid energy mill, hammer mill, pebble batch mill, pellet mill, or air classifying mill. Commercially available equipment that can be utilized in the milling process is a Frewitt Mill, Comil, or Fitzmill. If necessary, the milled material can be sieved to obtain a desired size range of particles, e.g., with a Sweco vibratory separator, Russell sieve or a simple hand sieve.

[0049] In other embodiments, the gas releasing material can be prepared utilizing methods comprising hot melt extrusion or injection molding. In these processes, the gas can be added to the melted material in the extruder and the extruded material can be injected into a mold and quickly cooled to shape. After release from the mold, the gas releasing material may retain the shape of the mold or may spontaneously crack into smaller particles. Further milling and sieving may optionally be performed on the molded material. Examples of extrusion equipment that can be utilized in such processes include a single or twin screw extruder such as a Brabender or a Leistritz. An example of an injection molding apparatus is a B-Side Crane NW, 3-Ton, 12' High, Model Yale KEL3-15RT1053. The addition of a gear pump between the extruder and the mold may facilitate the process.

[0050] In other embodiments the gas releasing material can be extruded into a strand and be cut or chopped into a desired size. The strand can be extruded into a cooling media (such as chilled air or oil) to facilitate the size reduction. In certain embodiments, the process is performed above atmospheric pressure to reduce "die swell", which is the expansion of the extrudate to a size larger than the extruder orifice.

[0051] The gas which is contained in the gas releasing material can be any gas, but is typically a gas which contains no amount or reduced amounts (in comparison to air) of gaseous compounds (e.g., oxygen) which could be detrimental for the packaged product. It is in one embodiment not air. In certain embodiments, the gas is selected from the group consisting of nitrogen, carbon dioxide and inert gases, and more preferably is nitrogen or carbon dioxide.

[0052] The matrix material that is the basis of the gas releasing material can include but is not limited to a material selected from the group consisting of a carbohydrate (e.g., a saccharide, a starch or dextrin), a gelatin, a gum, a protein and a combination thereof.

[0053] As used herein, the term "carbohydrate" refers to a monosaccharide; disaccharide; oligosaccharide; digestible, partially digestible and non-digestible polysaccharide; and sugar alcohol.

[0054] Monosaccharides that can be utilized in the present invention include but are not limited to glucose, fructose, mannose, idose, galactose, allose, gulose, altrose, talose, fucose, erythrose, threose, lyxose, erythrulose, ribulose, xylulose, ribose, arabinose, xylose, psicose, sorbose, tagatose, glyceraldehyde, dihydroxyacetone, rhamnose and mixtures thereof.

[0055] Disaccharides that can be utilized in the present invention include but are not limited to sucrose, maltose, lactose, trehalose, cellobiose, invert sugar and mixtures thereof.

[0056] Oligosaccharides that can be utilized in the present invention include but are not limited to maltotriose, raffinose, cellotriose, manninotriose, fructooligosaccharide, stachyose, corn syrup solids and mixtures thereof.

[0057] Polysaccharides that can be utilized in the present invention include, but are not limited to digestible polysaccharides and non-digestible polysaccharides. Non-limiting examples of digestible polysaccharides include starches that are isolated or derived from cereal grains, legumes, tubers and roots; maltodextrins; glycogen; native, unmodified starches; pre-gelatinized starches; chemically modified starches; high amylose starches; waxy starches; and mixtures thereof.

[0058] Non-digestible polysaccharides may be water-soluble or water-insoluble. Non-limiting examples of water-soluble or predominately water-soluble, non-digestible polysaccharides include: oat bran; barley bran; psyllium; pentosans; plant extracts such as pectins, inulin, and beta-glucan soluble fiber; seed galactomannans such as guar gum, and locust bean gum; plant exudates such as gum arabic, gum tragacanth, and gum karaya; seaweed extracts such as agar, carrageenans, alginates, and furcellaran; cellulose derivatives such as carboxymethylcellulose, hydroxypropylmethylcellulose and methylcellulose; microbial gums such as xanthan gum and gellan gum; hemicellulose; polydextrose; and mixtures thereof. Non-limiting examples of water-insoluble, and predominately water-insoluble, non-digestible polysaccharides include cellulose; microcrystalline cellulose; brans; resistant starch; and mixtures thereof.

[0059] The polysaccharides of the present invention can also include chitosan and derivatives thereof such as trimethylchitosan.

[0060] Sugar alcohols that can be utilized in the present invention include, but are not limited to glycerol, sorbitol, xylitol, mannitol, maltitol, propylene glycol, erythritol and mixtures thereof.

[0061] The gas releasing material of the present invention can be prepared in order to liberate gas upon activation or spontaneously over time.

[0062] The gas releasing material will typically liberate gas spontaneously over a period of time without the need for any external stimulus or activation. The rate at which the material releases gas can be determined during the manufacturing process by varying factors such as the volume of gas per weight of matrix material and the pressure of the gas contained in the material. Accordingly, in certain embodiments, depending on the rate of spontaneous release of gas from the gas releasing material, a sufficient amount of gas releasing material can be incorporated into a packaging system to counteract the formation and negative effects of an inner vacuum.

[0063] In packaging systems utilizing oxygen scavengers, the inner vacuum resulting from the removal of gas by scavengers may reach a maximum within 2-3 days after sealing or more. The rate of spontaneous release of gas by the gas releasing material may not be sufficient during that initial time period to prevent package failure. Therefore, in certain embodiments of the present invention, the gas releasing material is designed to release the desired amount of gas upon activation, e.g., by an external or internal stimulus.

[0064] The activation method can include a pressure change, temperature change, moisture change, or application of a magnetic field, radiation or a combination thereof. The radiation can comprise electromagnetic radiation including ultraviolet radiation, microwave radiation, IR radiation, an induction field or a combination thereof. When a heat source is utilized as the stimulus, the gas releasing material preferably liberates gas at a temperature below the melting point of the gas releasing material as to maintain the integrity of the system. However, if the gas releasing material has sufficient viscosity above the melting point, the liberation temperature may be higher

[0065] A susceptor, i.e., a system that converts electromagnetic radiation to heat can be utilized in embodiments that rely on activation of the gas releasing material. The susceptor material can be packaged with the gas releasing material such that the gas is liberated by the heat or IR radiation resulting from exposure of the system to electromagnetic radiation (e.g., a change in magnetic field). The use of susceptors could be used in order to minimize exposure (amount and duration) of the total system to external heat. In this embodiment, the temperature of the packaged product would not be significantly affected and would not have a significant adverse effect on stability and shelf life. In certain embodiments, one material such as elemental iron or aluminum can have both scavenger and susceptor properties in order to reduce the number of components in the system.

[0066] In certain embodiments, the stimulus that activates the liberation of gas from the gas releasing material is internal and does not require the use of an external stimulant. For example, in certain embodiments, the heat generated by the reaction of oxygen with an oxygen scavenger (e.g., iron) could be sufficient to activate the liberation of gas from the gas releasing material. In such an embodiment, the scavenger and the gas releasing material must be in sufficient proximity or contact to effect the activation. In another embodiment, the gas releasing material can be packaged at a low temperature such that gas is liberated after a specific period at room temperature or at a different humidity within the interior of the container.

[0067] In certain embodiments, the gas releasing material has the ability to liberate gas upon the introduction of moisture to the material. In such embodiments, the packaging system of the invention can utilize a scavenger that has desiccant properties (i.e., the ability to absorb moisture) or include a separate desiccant component in the packaging system. The absorbed moisture by the scavenger (or desiccant) could then be utilized as an activator for the gas releasing material to release gas and reduce or minimize the inner vacuum. In such an embodiment, the scavenger and the gas releasing material must be in sufficient proximity or contact to effect the activation. Iron is an example of a scavenger that can be designed to release moisture upon introduction to the packaging system.

[0068] The scavenger can be selected from those that can be activated either during or after the packaging process. This is particularly an advantage for scavengers that have a limited duration of action so as to ensure they are within the packaging system for the majority or entire duration of their activity. In certain embodiments, the same stimulus can activate both the scavenger and the gas releasing material. In other embodiments, there can be a cascade wherein a stimulus activates the scavenger which results in heat generation to activate the gas releasing material.

[0069] In certain embodiments, the external activation can utilize existing equipment (such as heat generated by an induction sealer) in order to avoid the need for a separate activation step and the necessity of additional equipment. In one embodiment, the scavenger, gas releasing material or both, are included in the liner of a container cap, where it can readily be exposed to heat generated by the induction sealer. The inclusion in the cap, or elsewhere in the container, would reduce the need to introduce a separate processing step for the insertion of the scavenger and/or gas releasing material.

[0070] Additionally, many carbohydrates that can be utilized as the matrix for the gas releasing material will act as humectants by absorbing and holding moisture. Therefore, the gas releasing material can serve a dual purpose to avoid or reduce the creation of an inner vacuum and to act as a desiccant to further improve the stability of the packaged goods. In such an embodiment, the ability of the gas releasing material to absorb moisture acts as a self-contained stimulus to liberate gas, without the need for a separate stimulus or desiccant.

[0071] In certain embodiments, after the product is packaged with an oxygen scavenger and a gas releasing material and sealed, the sealed package can be subject to the external stimulus (e.g., heat, radiation) before, during or after the development of any internal vacuum. Preferably, the external stimulus to liberate gas from the gas releasing material will be within a sufficient time to prevent package failure. In certain embodiments, the external stimulus will be before or during the creation of any inner vacuum, which may result in a package having increased internal pressure until the scavenger has reacted with and removed the intended gas. Such embodiments are suitable for the purposes of the present invention provided that the integrity of the package and/or the seal is maintained during the time of increased pressure.

[0072] In certain embodiments, the gas removing material (i.e., the scavenger or adsorbent) is contained in a sub-container comprising a housing having at least one internal compartment in fluid communication with the exterior of the housing. The gas removing material and the gas releasing material can both be contained in the device, either separately or interdispersed. The materials can be contained in the device in different compartments or in the same compartment. The housing material can comprise a material selected from the group consisting of plastic, paper, fabric, metal and a combination thereof. The inclusion of both the gas removing material and the gas releasing material in the same device would streamline and facilitate packaging processes.

[0073] The gas releasing material in the packaging system of the present invention preferably liberates an effective amount of gas to replace at least a portion of the gas (e.g., oxygen) removed by the gas removing material. Preferably, the volume of gas that is liberated is the same or substantially the same as the volume of gas removed by the scavenger. In some embodiments, the volume of liberated gas is higher or lower than the volume of removed gas. Preferably, the volume of liberated gas minimizes or eliminates vacuum buckling or seal breaking of the container due to the activity of the scavenger. The volume of liberated gas should also not exceed the amount of removed gas to an extent that the integrity of the package and/or seal is compromised.

[0074] By way of example, a 75 cc bottle filled with pharmaceutical tablets could contain about 50 cm^3 of head space. The oxygen in 50 cm^3 would be approximately 10 cm^3. In such an embodiment, the packaging system could include approximately 2 grams of gas releasing material containing about 5 cm^3 of gas/gram.

[0075] The oxygen scavengers utilized in the present invention can include metal-based scavengers such as iron. In metal based systems, a finely powdered activated metal enters the oxide state when exposed to the proper moisture, effectively binding oxygen in the process.

[0076] The powdered scavengers can be contained by any suitable means, e.g., in a permeable housing or sachet. The scavenger can also be included in the packaging systems as an inner coating or directly within the container material, e.g., by way of an extrusion additive.

[0077] Oxygen scavengers that can be utilized in the present invention include those based on metal, catechol, oxidative enzymes, unsaturated hydrocarbons or polyamides.

The oxygen scavengers utilized in the present invention can also be, e.g., low molecular weight organic compounds such as ascorbic acid or sodium ascorbate, which bind oxygen by oxidizing carbon-carbon double bonds, and/or a polymeric based oxygen scavenging resin with a catalyst, which binds oxygen through oxidation of the polymers. Commercially available oxygen scavengers that can be utilized in the present invention include Ageless® products available from Mitsubishi Gas Chemical Co.

[0078] Adsorbents (e.g., oxygen adsorbents) utilized in the present invention may be based on, e.g., zeolite, charcoal, silica or combinations thereof. Commercially available adsorbents are supplied by Multisorb Technologies Inc. and Süd-Chemie, among other companies.

[0079] In certain embodiments, a gas removing material and/or a susceptor can be directly incorporated into the gas releasing material. For example, these materials can be added to the gas releasing material in its molten or semi-molten state, either before, during or after contact with pressurized gas. In other embodiments, these materials can be infused into the gas releasing material during the cooling process or after solidification of the molten matrix material.

[0080] The packaging material of the present invention can be a plastic that is substantially impermeable to gas. However, these materials still are susceptible to leaching of outside gas into the container. There is typically a greater ability to leach into the inner container when the vacuum is internally created, which results in the buckling and puckering of the container due to the pressure difference. Although materials with decreased permeability (e.g., glass, metal and thicker plastics) may be resistant to buckling and puckering, the present invention can still be useful when utilizing these container materials by minimizing or eliminating seal failure, which can be caused by the same factors which result in buckling and puckering of the container itself.

[0081] The avoidance or reduction of inner vacuum by the present invention can decrease the influx of outside air into the container. Therefore, the present invention may have the benefit of lowering the amount of scavenger material needed in the packaging system or decreasing the time necessary for the scavenger to become effective. This may also enable the use of thinner walled and/or more permeable packaging to decrease the net weight and costs of manufacture and distribution.

[0082] Products that can be packaged in the systems of the present invention include any product which may degrade in the presence of oxygen or other reactive gases, e.g., certain pharmaceutical drugs, foodstuffs, and industrial chemicals.

[0083] Non-limiting examples of food products that can be packaged according to the present invention include but are not limited to coffee, tea, milk, yogurt, ice cream, cheeses, stews, soups, meat products (e.g., hot dogs, cold cuts, chicken and beef jerky), single-serving pre-cooked meals and side dishes, homemade pasta, spaghetti sauce, condiments (e.g., barbecue sauce, ketchup, mustard and mayonnaise), beverages (e.g., fruit juice, wine and beer); dried fruits, dried vegetables, breakfast cereals, baked goods (e.g., bread, crackers, pastries, cookies, and muffins), snack foods (e.g., candy, potato chips, pretzels and cheese-filled snacks), peanut butter, jelly, peanut butter and jelly combinations, jams, dried or fresh seasonings, pet and animal foods and the like.

[0084] Non-limiting examples of pharmaceutical active agents generally susceptible to oxidation include those containing amine, hydroxyl, and thiol groups. A particular class of active agents that can be utilized in the present invention are opioid agonists which include, but are not limited to, alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, desomorphine, dextromoramide, dezocine, diampromide, diamorphone, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, eptazocine, ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene fentanyl, heroin, hydrocodone, hydromorphone, hydroxypethidine, isomethadone, ketobemidone, levorphanol, levophenacylmorphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, narceine, nicomorphine, norlevorphanol, normethadone, nalorphine, normorphine, norpipanone, opium, oxycodone, oxymorphone, papaveretum, pentazocine, phenadoxone, phenomorphan, phenazocine, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tilidine, tramadol, pharmaceutically acceptable salts thereof, and mixtures thereof.

[0085] In certain embodiments, the opioid agonist is selected from codeine, hydromorphone, hydrocodone, oxycodone, dihydrocodeine, dihydromorphine, morphine, tramadol, oxymorphone, pharmaceutically acceptable salts thereof, and mixtures thereof.

[0086] Other pharmaceutical active agents that can be included in the packaging systems of the present invention include non opioid analgesics. Examples of non opioid analgesics include, but are not limited to, non steroidal anti-inflammatory agents, such as aspirin, ibuprofen, diclofenac, naproxen, benoxaprofen, flurbiprofen, fenoprofen, flubufen, ketoprofen, indoprofen, piroprofen, carprofen, oxaprozin, pramoprofen, muroprofen, trioxaprofen, suprofen, aminoprofen, tiaprofenic acid, fluprofen, bucloxic acid, indomethacin, sulindac, tolmetin, zomepirac, tiopinac, zidometacin, acemetacin, fentiazac, clidanac, oxpinac, mefenamic acid, meclofenamic acid, flufenamic acid, niflumic acid, tolfenamic acid, diflurisal, flufenisal, piroxicam, sudoxicam, isoxicam, and pharmaceutically acceptable salts thereof, and mixtures thereof. Examples of other suitable non opioid analgesics include the following, non limiting, chemical classes of analgesic, antipyretic, nonsteroidal antiinflammatory drugs: salicylic acid derivatives, including aspirin, sodium salicylate, choline magnesium trisalicylate, salsalate, diflunisal, salicylsalicylic acid, sulfasalazine, and olsalazin; para aminophennol derivatives including acetaminophen and phenacetin; indole and indene acetic acids, including indomethacin, sulindac, and etodolac; heteroaryl acetic acids, including tolmetin, diclofenac, and ketorolac; anthranilic acids (fenamates), including mefenamic acid, and meclofenamic acid; enolic acids, including oxicams (piroxicam, tenoxicam), and pyrazolidinediones (phenylbutazone, oxyphenthartazone); alkanones, including nabumetone and Cox-II inhibitors, including rofecoxib and celecoxib.

[0087] The gas releasing material of the present invention can be utilized for different purposes other than to avoid or reduce creation of a vacuum in a packaging system. For example, the gas liberated from the gas releasing material can be utilized as an indicator that the particular package has been exposed to unwanted conditions such as heat or moisture during its storage or distribution. In such embodiments, the liberated gas upon exposure to these conditions could activate an indicator, such as the protrusion of a seal.

[0088] The following examples are set forth to assist in understanding the invention and should not, of course, be construed as specifically limiting the invention described and claimed herein. Such variations of the invention, including the substitution of all equivalents now known or later developed, which would be within the purview of those skilled in the art, and changes in formulation or minor changes in experimental design, are to be considered to fall within the scope of the invention incorporated herein.

EXAMPLE 1 (Prophetic)

[0089] Following the teachings of U.S. Patent No. 4,289,794, 1000 grams of sucrose, lactose and corn syrup in a weight ratio of 52:27:21 are dissolved in water and evaporated at a temperature of 320° F at atmospheric pressure to produce a melt having a moisture content of about 3%. This melt is placed in a pre-heated Parr bomb (a small pressure vessel equipped with a mixer). The bomb is placed in a controlled temperature bath (e.g., between 300 and 400° F) and pressurized with CO_2 at 750 psig for five minutes during which time the sugar melt is mixed vigorously. Following the carbonation, the pressure is maintained while the vessel is cooled to room temperature as to solidify the sugar melt. Rapidly releasing the pressure, e.g., with a screw valve that releases pressure over about 5 seconds, fractures the solidified carbonated material to produce multiple pieces of various sizes of gas releasing material.

[0090] A sufficient amount of the resultant gas releasing material is incorporated into a sealed container with a pharmaceutical product susceptible to oxidative degradation and an iron based oxygen scavenger.

EXAMPLE 2 (Prophetic)

[0091] Commercially available PopRocks® are obtained and a sufficient amount is incorporated into a sealed container with a pharmaceutical product susceptible to oxidative degradation and an iron based oxygen scavenger.

GENERAL PROCEDURES

[0092] For Examples 1 and 2, the characteristics of the gas releasing material can be measured by subjecting the gas releasing material to a variety of conditions/times and testing for the amount of remaining gas in the material. For example, an amount of gas releasing material can be placed in an open dish in a vacuum oven as a function of: pressure (0.8 atm -1 atm), temperature (RT- ~60°C), time (1 or 2 days), and %RH (0%-

~100%). The remaining gas in the gas releasing material can be tested against an established baseline. One method to measure the amount of remaining gas is to place the gas releasing material in water to liberate all of the remaining gas and take a measurement with an apparatus depicted in Figure 1. The baseline can be established using the same procedure.

[0093] Figure 1 shows a container (1) containing a gas releasing material (2) placed in a cup with magnets (3). The container is attached with tubes (4) to a syringe (5) and a pipette (6). The pipette is modified by having the fat end cut and immersed in water. The container is sealed and water is drawn up to a measurement line (7) on the pipette with the syringe. The syringe is detached and the plunger is depressed and decompressed without changing the water level. The cup is rotated from the outside with the magnets and the gas releasing material falls into the water and gas is evolved. The evolved gas will lower the water volume from the measurement line on the pipette. The plunger on the syringe is withdrawn until the water returns to the water level line. The volume on the syringe will represents the volume of gas evolved from the gas releasing material.

[0094] One method to maintain a desired humidity level is to utilize particular saturated salts which maintain specific humidities as a function of temperature. Examples of saturated salts which can be utilized include potassium hydroxide, lithium chloride, potassium acetate, magnesium chloride, potassium carbonate, magnesium nitrate, sodium dichromate, ammonium nitrate, sodium nitrite, sodium chloride, ammonium sulphate, potassium chloride, potassium nitrate, and potassium sulphate. The temperature and humidity can be measured by a temperature/humidity logger.

[0095] Another method to measure the amount of remaining gas and/or to establish a baseline is to use a grab sampling tube that is filled with small granules of a special chemical that has a very high ability to absorb the gas that is being measured. This chemical is called a sorbent. For example, hydrazine hydrate or sodium hydroxide coated silica (e.g., ASCARITE II®) can be used as a sorbent for carbon dioxide.

EXAMPLE 3

Objective:

[0096] To test the ability of a gas releasing material to relieve the partial vacuum in a pharmaceutical package created by a contained O_2 scavenger.

Materials:

[0097] - 33-400 C/R click loc caps commercially available from Drug Plastics and Glass Co. (Boyertown, PA.)

- 75 cc HDPE Bottles commercially available from Drug Plastics and Glass Co.
- PopRocks (1) 0.24 oz (6.8 g) Package Watermelon Flavor. The number 112 printed on back
- Multisorb DF-100 H42 O_2 absorbing canisters commercially available from Multisorb Technologies (Buffalo, NY)
- Foil (Aluminum) Strip: 1 inch (2.54 cm) x 3 inches (7.62 cm) cut from 0.024 mm thick sheet
- Lepak Jr. Induction Sealer commercially available from Lepel (Waukesha, WI)
- Marathon Digital Caliper commercially available from Marathon Watch Co., Ltd. (Richmond Hill, Ontario)

[0098] HDPE Bottles were chosen to be 36.3 mm thick (front to back) and 46.6 mm (side to side) and were packaged and labeled in the following configuration:

Bottle 1:	4 g Pop Rock; O_2 absorbing canister; foil strip.
Bottle 2:	Empty
Bottle 3:	O_2 absorbing canister

[0099] All three bottles were induction sealed at 0.70 seconds.

[00100] Approximately six days later (after the above induction sealing), the face to face distance was measured for each bottle. Small magnets (3 mm diameter, 1.5 mm thick) were placed on the jaws of the caliper to enable measurement of the concave faces. The measurements are set forth in Table 1 below:

Table 1

Bottle	Front to Back (mm)	Side to Side
1	32.7 mm	45.9 mm
2	36.3 mm	46.6 mm
3	31.5 mm	45.5 mm

[00101] Bottles 1 and 3 were concave front to back and remained convex side to side Bottle 2 remained convex at all sides. The dimensional changes in the bottles from the initial measurements to the measurements in Table 1 are set forth in Table 2 below:

Table 2

Bottle	Front to Back (mm)	Side to Side
1	3.6 mm (10%)	0.7 mm
2	0 mm	0 mm
3	4.8 mm (13%)	1.1 mm

[00102] The difference between Bottle 1 and Bottle 3 indicates that some of the gas was released from the Pop Rocks spontaneously without the necessity to provide an activation step.

[00103] Thereafter, Bottle 1 was placed in an inverted induction sealer. The sealer was set to 2.00 seconds and activated. This was done 4 times for each bottom corner of the bottle. Popping was heard on the first 3 corners, but not the fourth. The popping sound indicates that the induction sealer heated the foil which activated the gas releasing material to release an amount of gas. The system was allowed to cool for about 4 hours and measurements were repeated as set forth in Table 3 below:

Table 3

Bottle	**Front to Back (mm)**	**Side to Side**
1 (before induction)	32.7 mm	45.9 mm
1 (after induction)	34.2 mm	46.1 mm

[00104] After induction, 1.5 mm of the 3.6 mm was regained and 0.2 of the 0.7 mm was regained.

[00105] The present invention is not to be limited in scope by the specific embodiments disclosed in the examples which are intended as illustrations of a few aspects of the invention and any embodiments that are functionally equivalent are within the scope of this invention. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art and are intended to fall within the scope of the appended claims.

Claims

1. A packaging system comprising:
a container having an inner cavity;
a gas removing material; and
a gas releasing material.

2. The packaging system of claim 1, further comprising a consumer or industrial product.

3. The packaging system of claim 1 or 2, wherein the gas removing material comprises an adsorbent, a scavenger, or a combination thereof.

4. The packaged system of claim 3, wherein the gas removing scavenger comprises an oxygen scavenger, a carbon dioxide scavenger or a combination thereof and the adsorbent comprises zeolite, charcoal, silica or a combination thereof.

5. The packaged system of claim 4, wherein the oxygen scavenger is based on iron, catechol, ascorbic acid, oxidative enzymes, unsaturated hydrocarbons or polyamides.

6. The packaging system of any one of claims 1 to 5, wherein the container is permeable or substantially impermeable to gas.

7. The packaging system of any one of claims 1 to 6, wherein the container is sealed and holds the product, the gas removing material and the gas releasing material in the inner cavity.

8. The packaging system of any one of claims 1 to 7, wherein the container is a bottle, a bag, a vial, an envelope, a canister or a jar.

9. The packaging system of any one of claims 1 to 8, wherein the container has a removable seal.

10. The packaging system of any one of claims 2 to 9, which contains a consumer or industrial product and wherein the product is subject to degradation.

11. The packaging system of claim 10, wherein the product is subject to oxidation.

12. The packaging system of claim 10 or 11, wherein the product subject to degradation is selected from the group consisting of a pharmaceutical, a foodstuff, and a chemical.

13. The packaging system of claim 12, wherein the product is a pharmaceutical.

14. The packaging system of claim 13, wherein the pharmaceutical is an opioid analgesic.

15. The packaging system of claim 14, wherein the opioid analgesic is selected from the group consisting of codeine, hydromorphone, hydrocodone, oxycodone, dihydrocodeine, dihydromorphine, morphine, tramadol, oxymorphone, pharmaceutically acceptable salts thereof, and mixtures thereof.

16. The packaging system of claim 15, wherein the opioid analgesic is oxycodone or a pharmaceutically acceptable salt thereof.

17. The packaging system of any one of claims 1 to 16, wherein the gas releasing material contains compressed gas.

18. The packaging system of claim 17, wherein at least a portion of the compressed gas is in liquid form, solid form or a combination thereof.

19. The packaging system of any one of claims 1 to 18, wherein the gas releasing material contains from about 0.5 ml to about 25 ml gas per gram of material.

20. The packaging system of any one of claims 1 to 19, wherein the gas contained in the gas releasing material is selected from the group consisting of nitrogen, carbon dioxide, inert gases, air and a combination thereof.

21. The packaging system of any one of claims 1 to 20, wherein the gas releasing material liberates gas upon activation.

22. The packaging system of claim 21, wherein the activation is by an external or internal heat source.

23. The packaging system of claim 21 or 22, wherein the activation method comprises pressure change, temperature change, moisture change, magnetic field change, electromagnetic radiation or a combination thereof.

24. The packaging system of claim 23, wherein the electromagnetic radiation comprises visual light, ultraviolet radiation, microwave radiation, IR radiation and induction fields.

25. The packaging system of any one of claims 1 to 24, wherein the gas releasing material liberates gas at a temperature below the melting point of the material.

26. The packaging system of any of claims 1 to 20, wherein the gas releasing material liberates gas spontaneously over time.

27. The packaging system of any one of claims 1 to 26, wherein the gas releasing material comprises a carbohydrate.

28. The packaging system of any one of claims 1 to 26, wherein the gas releasing material comprises a material selected from the group consisting of a saccharide, a sugar alcohol, a starch, a dextrin, a gelatin, a gum, a protein and a combination thereof.

29. The packaging system of claim 28, wherein the saccharide is selected from the group consisting of a monosaccharide, a disaccharide, an oligosaccharide, a polysaccharide and a combination thereof.

30. The packaging system of claim 29, wherein the polysaccharide is chitosan.

31. The packaging system of claim 28, wherein the gum is selected from the group consisting of agar, carrageenan, alginate, pectin, xanthan, locust bean, guar and combinations thereof.

32. The packaging system of any one of claims 1 to 31, which contains an oxygen scavenger in an effective amount to remove oxygen from the sealed container.

33. The packaging system of claim 32, wherein the gas releasing material is capable of liberating an effective amount of gas to replace at least a portion of the oxygen removed by the oxygen scavenger.

34. The packaging system of any one of claims 1 to 33, wherein the gas releasing material has desiccant properties.

35. The packaging system of any one of claims 1 to 34, further comprising a susceptor.

36. A method of packaging a product subject to degradation comprising:
including a gas releasing material in a container with (i) the product subject to degradation and (ii) a gas removing material.

37. The method of claim 36, further comprising sealing the container.

38. The method of claim 36 or 37, wherein the container is permeable or substantially impermeable to gas.

39. The method of any one of claims 36 to 38, wherein the product is subject to oxidation.

40. The method of any one of claims 36 to 39, wherein the product subject to degradation is selected from the group consisting of a pharmaceutical, a foodstuff and a chemical.

41. The method of any one of claims 36 to 40, wherein the product is a pharmaceutical.

42. The method of claim 41, wherein the pharmaceutical is an opioid analgesic.

43. The method of claim 42, wherein the opioid analgesic is selected from the group consisting of codeine, hydromorphone, hydrocodone, oxycodone, dihydrocodeine, dihydromorphine, morphine, tramadol, oxymorphone, pharmaceutically acceptable salts thereof, and mixtures thereof.

44. The method of claim 42 or 43, wherein the opioid analgesic is oxycodone or a pharmaceutically acceptable salt thereof.

45. The method of any one of claims 36 to 44, wherein the gas removing material comprises an adsorbent, a scavenger or a combination thereof.

46. The method of any one of claims 36 to 45, wherein the gas releasing material contains compressed gas.

47. The method of any one of claims 36 to 46, wherein the gas releasing material contains from about 0.5 ml to about 25 ml gas per gram of material.

48. The method of any one of claims 36 to 47, wherein the gas contained in the gas releasing material is selected from the group consisting of nitrogen, carbon dioxide, inert gases, air and a combination thereof.

49. The method of any one of claims 36 to 48, wherein the gas releasing material liberates gas upon activation or spontaneously over time.

50. A device comprising:
a housing having at least one internal compartment in fluid communication with the exterior of the housing;
a gas removing material; and
a gas releasing material.

51. The device of claim 50, wherein the gas removing material and the gas releasing material are contained in the same internal compartment.

52. The device of claim 50 or 51, wherein the gas removing material and the gas releasing material are at least partially interdispersed.

53. The device of any one of claims 50 to 52, wherein the gas removing material and the gas releasing material are contained in different internal compartments.

54. The device of any one of claims 50 to 53, wherein the gas releasing material contains compressed gas.

55. The device of any one of claims 50 to 54, wherein the gas releasing material contains from about 0.5 ml to about 25 ml gas per gram of material.

56. The device of any one of claims 50 to 55, wherein the housing comprises a material selected from the group consisting of plastic, paper, fabric and metal.

57. The device of any one of claims 50 to 56, wherein the housing comprises a sachet.

58. The device of claim 57, wherein the sachet comprises the gas releasing material and/or the gas removing material.

59. Use of a gas releasing material to suppress or reduce a vacuum in a container.

60. The use of claim 59, wherein the vacuum in the container is caused by the presence of a gas removing material in the container.

61. A packaging system comprising:
a container having an inner cavity;
a consumer or industrial product; and
a gas releasing material.

62. The packaging system of claim 61, wherein the product is a pharmaceutical.

63. A method of packaging a product subject to degradation comprising:
including a gas releasing material in a container with a product subject to degradation.

64. The method of claim 63, wherein the product is a pharmaceutical.

65. A method of increasing the stability of a consumer or industrial product comprising preparing a packaging system according to any of claims 1-35, 61 or 62.

66. A method of decreasing package failure comprising preparing a packaging system according to any of claims 1-35, 61 or 62.

.

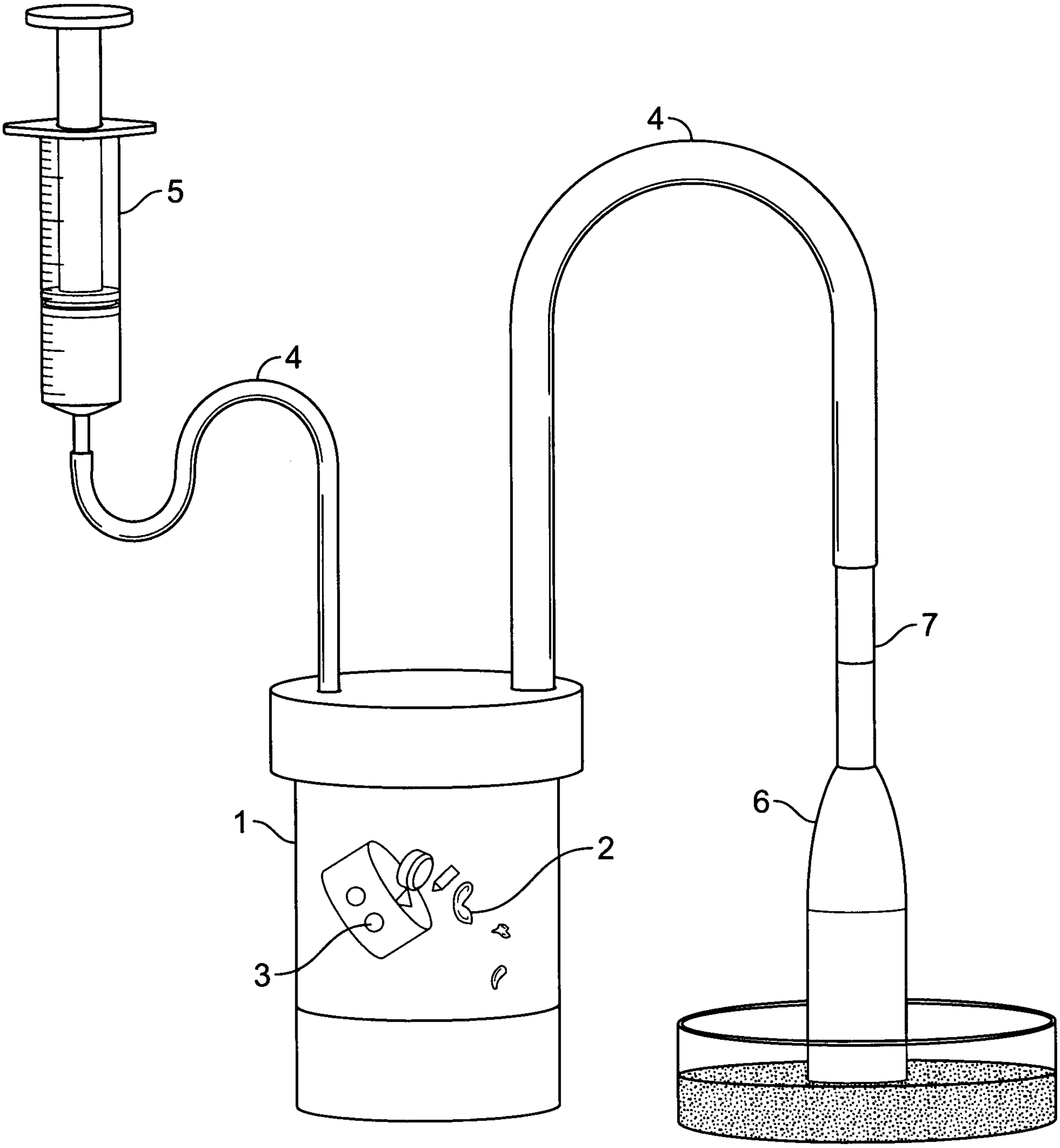

FIG. 1