[0006] It has been reported that in order to deliver a powder directly into the lower respiratory regions the powder should generally have a particle size of less than 5 μm. Further, powders in the 5-10 μm range have been found not to penetrate as deeply and instead tend to stimulate the upper respiratory tract regions.

[0007] When manufacturing drug formulations for dry powder inhalers (DPIs), the medicament must first be milled to obtain an acceptable particle size for pulmonary delivery. This micronization step can cause problems during manufacture. For example, the heat produced during milling can cause degradation of the medicament. Additionally, metal can rub off some mills and contaminate the medicament. Furthermore, due to the small size of the particles, dry powder formulations tend to agglomerate, especially in the presence of moisture.

[0008] Agglomeration results in low flowability of the particles which diminishes the efficacy of the dry powder formulation. As a result, careful supervision is required during milling, blending, powder flow, filling and even administration to ensure that the dry powder aerosols are properly delivered.

[0009] Thus, there is a need for new methods to prepare aerosols for medicament delivery. The present disclosure describes in part a method for combining nicotine or other medicaments with a delivery enhancing compound in a gaseous stream to generate an aerosol for pulmonary delivery, without the need for excipients or other additives including solvents.

DISCLOSURE OF INVENTION

Brief Summary ~~of the Invention~~

[0010] In some embodiments, the disclosure relates to a method of delivering nicotine to a subject by inhalation, the method comprising the steps of:

a) first placing a gaseous carrier comprising a delivery enhancing compound in communication with a nicotine source comprising the nicotine, and

b) second providing the gaseous carrier comprising the nicotine to a subject.

[0011] In some embodiments, the disclosure relates to the method of paragraph [0010], further comprising the step of placing the gaseous carrier in communication with a delivery enhancing compound source comprising the delivery enhancing compound.

[0035a] In an aspect, there is provided a device for delivering nicotine to a subject, the device comprising a housing, the housing comprising: a) an inlet and an outlet in communication with each other and adapted so that a gaseous carrier may pass into the housing through the inlet, through the housing and out of the housing through the outlet, the device comprising in series from inlet to outlet: b) a first internal area in communication with the inlet, the first internal area comprising a delivery enhancing compound source, c) a second internal area in communication with the first internal area, the second internal area comprising a nicotine source, i) the nicotine source comprising the nicotine and an electrolyte forming compound, both in an aqueous solution, wherein the electrolyte forming compound is an Alkali metal hydroxide or oxide; an Alkaline earth metal oxide; or a salt, and d) optionally, a third internal area in communication with the second internal area and the outlet.

[0035b] In another aspect, there is provided a device for delivering nicotine to a subject, the device comprising a housing, the housing comprising: a) an inlet and an outlet in communication with each other and adapted so that a gaseous carrier may pass into the housing through the inlet, through the housing and out of the housing through the outlet, the device comprising in series from inlet to outlet: b) a first internal area in communication with the inlet, the first internal area comprising a delivery enhancing compound source, c) a second internal area in communication with the first internal area, the second internal area comprising a nicotine source, i) the nicotine source comprising the nicotine and an electrolyte forming compound, both in an aqueous solution, wherein the electrolyte forming compound is an Alkali metal hydroxide or oxide; an Alkaline earth metal oxide; or a salt, and d) optionally, a third internal area in communication with the second internal area and the outlet wherein the delivery enhancing compound source comprises an inorganic acid or a carboxylic acid.

[0035c] In yet another aspect, there is provided a device for delivering nicotine to a subject, the device comprising a housing, the housing comprising: a) an inlet and an outlet in communication with each other and adapted so that a gaseous carrier may pass into the housing through the inlet, through the housing and out of the housing through the outlet, the device comprising in series from inlet to outlet: b) a first internal area in communication with the inlet, the first internal area comprising a delivery enhancing compound source, c) a second internal area in communication with the first internal area, the second internal area comprising a nicotine source, i) the nicotine source comprising the nicotine and an electrolyte forming compound, both in an aqueous solution, wherein the electrolyte forming compound is an Alkali metal hydroxide or oxide; an Alkaline earth metal oxide; or a salt, and d) optionally, a third internal area in communication with the second internal area and the outlet wherein the delivery enhancing compound source comprises a 2-keto carboxylic acid.

[0036] In some embodiments, the disclosure relates to the device of [0035] wherein a partial vacuum at the outlet is capable of pulling the gaseous carrier through the inlet, the first compartment, the second compartment, the third compartment, when present, and then through the outlet.

[0037] In some embodiments, the disclosure relates to the device of [0035] or [0036] wherein the delivery enhancing compound source comprises an adsorption element with the delivery enhancing compound adsorbed thereon and/or wherein the nicotine source comprises an adsorption element with the nicotine adsorbed thereon.

[0038] In some embodiments, the disclosure relates to the device of [0037] wherein the adsorption element or elements comprises at least one of glass, aluminum, Polyethylene Terephthalate (PET), Polybutylene Terephthalate (PBT), Polytetrafluoroethylene (PTFE or TEFLON®), Expanded Polytetrafluoroethylene (ePTFE) (ePTFE is described for example in U.S. Patent No. 4,830,643), and BAREX®.

[0039] In some embodiments, the disclosure relates to the devices of [0035]-[0037], or [0038], further comprising a first reservoir in communication with the first internal area, the first reservoir comprising the delivery enhancing compound.

[0040] In some embodiments, the disclosure relates to the devices of [0035]-[0038], or [0039], further comprising a second reservoir in communication with the second internal area, the second reservoir comprising nicotine.

[0041] In some embodiments, the disclosure relates to the devices of [0035]-[0039], or [0040], comprising the third internal area, the third internal area comprising a third internal area element.

[0042] In some embodiments, the disclosure relates to the device of [0041], wherein the third internal area element comprises a purifying agent.

[0043] In some embodiments, the disclosure relates to the device of [0042], wherein the purifying agent comprises activated charcoal.

[0044] In some embodiments, the disclosure relates to the devices of [0041], [0042], or [0043], wherein the third internal area element comprises a flavoring agent.

[0045] In some embodiments, the disclosure relates to the devices of [0041]-[0043], or [0044], where the third internal area element comprises a medicament.

[0046] In some embodiments, the disclosure relates to the device of [0045], wherein the medicament comprises nicotine.

[0047] In some embodiments, the disclosure relates to the devices of [0035]-[0045], or [0046], wherein the housing simulates a tobacco smoking product.

[0048] In some embodiments, the disclosure relates to the device of [0047], wherein the tobacco smoking product is a cigarette.

[0049] In some embodiments, the disclosure relates to the devices of [0035]-[0045], or [0046], wherein the housing simulates a pharmaceutical inhalation device.

[0050] In some embodiments, the disclosure relates to the device of [0049], wherein the simulated pharmaceutical inhalation device is selected from the group consisting of a metered dose inhaler, a pressurized metered dose inhaler, a dry powder inhaler, a nebulizer, and a liquid based inhaler.

[0051] In some embodiments, the disclosure relates to a method of increasing a nicotine concentration in a gaseous carrier comprising a step of placing the gaseous carrier comprising a delivery enhancing compound in communication with a nicotine source comprising the nicotine.

[0051a] In an aspect, there is provided a method of increasing a nicotine concentration in a gaseous carrier, the method comprising the step of: placing the gaseous carrier comprising a delivery enhancing compound in communication with a nicotine source comprising the nicotine and an electrolyte forming compound, both in an aqueous solution, wherein the electrolyte forming compound is an Alkali metal hydroxide or oxide; an Alkaline earth metal oxide; or a salt.

[0052] In some embodiments, the disclosure relates to the method of [0051], further comprising the step of placing the gaseous carrier in communication with a delivery enhancing compound source comprising the delivery enhancing compound.

[0053] In some embodiments, the disclosure relates to the method of [0052], wherein the step of placing the gaseous carrier in communication with the delivery enhancing compound source precedes the step of placing the gaseous carrier comprising the delivery enhancing compound in communication with the nicotine source.

[0054] In some embodiments, the disclosure relates to the method of [0051], [0052], or [0053], wherein the delivery enhancing compound source comprises a plurality of compartments comprising two or more precursor compounds.

[0116] In embodiments of the method of [0110]-[0114] or [0115],wherein the electrolyte forming compound is KOH, the ratio of KOH to nicotine base (or base equivalents) is 10:40, 10:60, 10:80 or 10:100 with 10:60 preferred. These points also form the boundaries of various exemplary ranges within the present ~~invention~~ disclosure such as the range 10:40 to 10:100.

[0117] In some embodiments of the method of [0110]-[0113] or [0114], the method further comprises the step of mixing the electrolyte forming compound with the nicotine in an aqueous solution.

[0118] In some embodiments of the method of [0117], the electrolyte forming compound is exothermic when dissolved into the aqueous solution, and is preferably added in sufficient amount to elevate the temperature of the aqueous solution of nicotine, such as to about 80 degrees C or higher.

[0119] The foregoing has outlined rather broadly the features and technical advantages of the present disclosure~~invention~~ in order that the detailed description of the present disclosure~~invention~~ that follows may be better understood. Additional features and advantages of the present disclosure~~invention~~ will be described hereinafter which form the subject of the claims of the present disclosure~~invention~~. It should be appreciated by those skilled in the art that the conception and specific embodiment disclosed may be readily utilized as a basis for modifying or designing other structures for carrying out the same purposes of the present disclosure~~invention~~. It should also be realized by those skilled in the art that such equivalent constructions do not depart from the spirit and scope of the present disclosure~~invention~~ as set forth in the appended claims. The novel features which are believed to be characteristic of the present disclosure~~invention~~, both as to its organization and method of operation, together with further objects and advantages will be better understood from the following description when considered in connection with the accompanying figures. It is to be expressly understood, however, that each of the figures is provided for the purpose of illustration and description only and is not intended as a definition of the limits of the present disclosure~~invention~~.

BRIEF DESCRIPTION OF DRAWINGS

[0120] For a more complete understanding of the present invention, reference is now made to the following descriptions taken in conjunction with the accompanying drawing, in which: