coated on the microneedle array and delivered directly through the skin after the stratum corneum has been punctured.

[0005] Microneedle arrays can be used in conjunction with an injection and infusion apparatus (i.e., an "applicator" that applies the hollow microneedles to the skin and facilitates infusion of a substance through the hollow microneedles) capable of being used several times or as a single-use device. The microneedle arrays are generally used once and then discarded.

SUMMARY

[0006] It has now been found that an interaction between an article comprising a plurality of hollow microneedles and a skin surface against which the article is urged can result in undesirable effects on the penetration of at least one microneedle of the plurality into the skin. It has further been found that, when the article comprises an array of microneedles, one of the effects can be significant variability in the depth of penetration into the skin by one or more of the microneedles in the array. The present inventors recognized the consistency of penetration depth can be controlled by including several features into the design of the article. The inventive design features result in the ability to rapidly, effectively and consistently insert the needles to a desired depth in the skin and quickly deliver a pharmaceutically-effective dose in a variety of skin locations. In addition, certain features of the inventive design permit simpler, more robust processes to be used for the manufacture of the articles.

[0007] The present disclosure generally relates to articles comprising microneedles and their use to deliver materials through the surface of skin or remove biological fluids through the surface of skin. In particular, the present disclosure relates to an article comprising an array of a plurality of microneedles that is configured to provide consistent depths of penetration for each microneedle of the plurality of microneedles by facilitating the contact between microneedles and skin and by reducing the possibility of contact between skin and non-microneedle surfaces during the use of the articles.

[0008] ~~Some aspects of t~~The present disclosure provide~~s~~ an article. The article can comprise a first side, a second side opposite the first side, and at least three hollow microneedles. The first side can comprise a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion. The microneedles can extend from the platform portion in a first direction. The platform portion can substantially surround the central cavity portion and can comprise an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion. Each of the at least three microneedles comprises a body that comprises an outer surface; a base segment having a base and a first shape that is defined by a first section of the outer surface; a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape

is distinct from the first shape; a transition plane that delineates the base segment and the tip segment; and a central axis. A first angle, defined by the central axis of each of the at least three microneedles and a shortest line extending from the outer perimeter of the platform and through the transition plane of the at least one microneedle, is greater than 50˚ and less than or equal to about 85˚. Therefore, in one aspect, there is provided an article comprising: a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion; a second side opposite the first side; and at least three hollow microneedles extending from the platform portion in a first direction (A); wherein the platform portion substantially surrounds the central cavity portion; wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion; wherein the at least three hollow microneedles each comprise a body that comprises: an outer surface; a base segment having a base and a first shape that is defined by a first section of the outer surface; a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape; a transition plane that delineates the base segment and the tip segment; and a central axis; wherein a first angle, defined by the central axis of each of the at least three hollow microneedles and a shortest line extending from the outer perimeter of the platform and through the transition plane of the microneedle, is greater than 50˚ and less than or equal to about 85˚. In any ~~embodiment~~example, the first angle can be about 65˚ to about 75˚, inclusive. In any of the above ~~embodiments~~examples, the first angle can be about 70˚.

[0009] ~~Other aspects of t~~The present disclosure also provides an article. The article can comprise a first side, a second side opposite the first side, and at least three hollow microneedles. The first side can comprise a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion. The microneedles can extend from the platform portion in a first direction. The platform portion can substantially surround the central cavity portion and can comprise an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion. Each of the at least three microneedles comprises a body that comprises an outer surface; a base segment having a base and a first shape that is defined by a first section of the outer surface; a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape; a transition plane that delineates the base segment and the tip segment; and a central axis. Each of the at least three microneedles comprises a height measured from the base to the tip. The tip segment of each of the at least three microneedles can define at least about 45% of the height of the microneedle. In any embodiment, the tip segment of each of the at least three microneedles can define at least about 70-80% of the height of the microneedle.

[0010] The phrase "injection apparatus" refers to an integrated device capable of delivering or extracting a fluid over a certain period and is not limited to devices intended solely for an infusion. Accordingly, an injection apparatus may be used, for example, for injecting fluid into the dermis or extracting fluid from tissue. In another aspect, there is provided an injection and infusion apparatus, comprising: a hollow-microneedle array article as defined herein; a hollow-microneedle array article holder; a first stored energy component configured to move the hollow-microneedle array article from a first position to a second position; and a reservoir containing a fluid, the reservoir being in fluid communication with the hollow microneedles; wherein the apparatus is configured to propel the article in a predetermined direction at a predetermined velocity.

[0011] The term "transdermally" and variations thereof, is generally used to refer to any type of delivery of an active ingredient that crosses any portion of skin. That is, transdermally can generally include systemic delivery (i.e., where the active ingredient is transported across, or substantially through, the dermis such that the active ingredient is delivered into the bloodstream), as well as intradermal delivery (i.e., where the active ingredient is transported partially through the dermis, e.g., across the outer layer (stratum corneum) of the skin, where the active ingredient is delivered into the skin, e.g., for treating psoriasis or for local anesthetic delivery). That is, transdermal delivery as used herein includes delivery of an active ingredient that is transported across at least a portion of skin (but not necessarily all of the layers of skin), rather than merely being topically applied to an outer layer of the skin.

[0012] The phrase “hollow microneedle” refers to a specific microscopic structure that is designed for piercing the stratum corneum to facilitate the delivery of drugs through the skin. By way of example, microneedles can include needle or needle-like structures, as well as other structures capable of piercing the stratum corneum and delivering liquid drug formulations to skin or tissue layers beneath the stratum corneum.

[0013] The words “preferred” and “preferably” refer to embodiments of the invention that may afford certain benefits, under certain circumstances. However, other embodiments may also be preferred, under the same or other circumstances. Furthermore, the recitation of one or more preferred embodiments does not imply that other embodiments are not useful, and is not intended to exclude other embodiments from the scope of the invention.

[0014] The terms “comprises” and variations thereof do not have a limiting meaning where these terms appear in the description and claims.

[0015] As used herein, “a,” “an,” “the,” “at least one,” and “one or more” are used interchangeably. Thus, for example, a microneedle can be interpreted to mean “one or more” microneedles.

[0016] The term “and/or” means one or all of the listed elements or a combination of any two or more of the listed elements.

[0017] Also herein, the recitations of numerical ranges by endpoints include all numbers subsumed within that range (e.g., 1 to 5 includes 1, 1.5, 2, 2.75, 3, 3.80, 4, 5, etc.).

[0018] The above summary of the present ~~invention~~ disclosure is not intended to describe each disclosed embodiment or every implementation of the present disclosure~~invention~~. The description that follows more particularly exemplifies illustrative embodiments. In several places throughout the application, guidance is provided through lists of examples, which examples can be used in various combinations. In each instance, the recited list serves only as a representative group and should not be interpreted as an exclusive list.

[0019] Additional details of these and other embodiments are set forth in the accompanying drawings and the description below. Other features, objects and advantages will become apparent from the description and drawings, and from the claims.

BRIEF DESCRIPTION OF DRAWINGS

[0020] The present invention will be further explained with reference to the drawing figures listed below, where like structure is referenced by like numerals throughout the several views.

[0021] FIG. 1 is a perspective view showing one embodiment of an article comprising a plurality of microneedles according to the present disclosure.

[0022] FIG. 2 is a side view of the article of FIG. 1.

[0023] FIG. 2A is a detail view of a portion of the article of FIG. 2.

CLAIMS:

1. An article, comprising:

a first side comprising a central cavity portion and a platform portion that projects from the first side and that is not coplanar with the central cavity portion;

a second side opposite the first side; and

at least three hollow microneedles extending from the platform portion in a first direction (A);

wherein the platform portion substantially surrounds the central cavity portion;

wherein the platform portion comprises an inner perimeter proximate the central cavity portion and an outer perimeter distal the central cavity portion;

wherein the at least three hollow microneedles each comprise a body that comprises:

an outer surface;

a base segment having a base and a first shape that is defined by a first section of the outer surface;

a tip segment having a tip and a second shape that is defined by a second section of the outer surface, wherein the second shape is distinct from the first shape;

a transition plane that delineates the base segment and the tip segment; and

a central axis;

wherein a first angle, defined by the central axis of each of the at least three hollow microneedles and a shortest line extending from the outer perimeter of the platform and through the transition plane of the microneedle, is greater than 50˚ and less than or equal to about 85˚.

2. The article of claim 1, wherein the first angle is about 65˚ to about 75˚.

3. The article of any one of the preceding claims, wherein a second angle, defined by the central axis and a shortest line extending from the inner perimeter and through the transition plane, is greater than 50˚ and less than or equal to about 85˚.

4. The article of any one of the preceding claims, wherein the transition plane is disposed about 60 μm to about 490 μm away from the platform portion when measured along the central axis.

5. The article of any one of the preceding claims, wherein the first side further comprises a microneedle-free peripheral portion extending laterally from at least a part of the outer

perimeter of the platform portion, wherein the peripheral portion is canted away from the platform portion in a second direction opposite the first direction.

6. The article of any one of the preceding claims; wherein the article further comprises a side wall portion that extends from the platform portion or, if present, the peripheral portion; wherein the sidewall portion extends substantially opposite the first direction.

7. The article of any one of the preceding claims, wherein the central cavity is a closed cavity.

8. The article of any one of claims 1 through 6, wherein the central cavity is a through-hole extending from the first side through the second side.

9. The article of any one of the preceding claims, wherein a unitary body comprises the platform portion, the peripheral portion, and the central cavity portion.

10. The article of any one of the preceding claims, wherein at least one microneedle of the plurality comprises:

a base;

an elongated body having a central axis and a body diameter;

a tip portion comprising a tip, a first bevel face oriented diagonally with respect to the central axis and extending through at least 75% of the body diameter, a second bevel face oriented substantially perpendicular to the central axis and intersecting the first bevel face, a bevel opening defined by a first edge of the first bevel face and a second edge of the second bevel face; and

a hollow channel that extends axially into the body from the bevel opening.

11. The article of any one of the preceding claims, wherein at least one microneedle of the plurality comprises:

a base;

an elongated body having a central axis;

a tip portion comprising a tip, a beveled surface, and a bevel opening in the beveled surface;

a first channel that extends axially from the bevel opening through at least a portion of the elongated body, wherein the first channel has a first wall that is substantially aligned with the central axis; and

a second channel that extends radially from the first channel to the bevel opening, wherein the second channel has a second wall that is oriented substantially orthogonal to the central axis;

wherein the first channel and second channel merge to form the bevel opening.

12. The article of any one of the preceding claims, wherein the at least one microneedle comprises a hollow channel extending through the article from a first opening proximate the tip to a second opening in the second side of the article.

13. The use of the article, as claimed in any one of claims 1 through 11, for injecting fluid into a body.

14. The article, as claimed in any one of claims 1 through 11, for extracting fluid from a body.

15. An injection and infusion apparatus, comprising:

a hollow-microneedle array article according to any one of the preceding claims;

a hollow-microneedle array article holder;

a first stored energy component configured to move the hollow-microneedle array article from a first position to a second position; and

a reservoir containing a fluid, the reservoir being in fluid communication with the hollow microneedles;

wherein the apparatus is configured to propel the article in a predetermined direction at a predetermined velocity.

16. The apparatus of claim 15, wherein the predetermined velocity is about 2 m/second to about 20 m/second.

17. The apparatus of claim 15 or claim 16, further comprising an actuator that actuates movement of the hollow-microneedle array article from the first position to the second position.

18. The apparatus of any one of claims 15 through 17, further comprising a second stored energy component configured to provide a force that moves the fluid from the reservoir to and through the hollow microneedles.

19. The apparatus of claim 17 or claim 18~~A method, comprising:~~;

providing the injection and infusion apparatus of claim 17 or claim 18;

wherein the actuator is actuable actuating the actuator so as to insert the hollow microneedles through a surface of a skin.

20. The apparatus method of claim 19 as dependent upon claim 18, further comprising releasing at least a portion of the stored energy of the second stored energy component so as to move fluid from the reservoir through the hollow microneedles and into a tissue below the surface of the skin.