Furthermore, adding an additional step in the process after the filling involves extra resources in terms of capabilities (with dedicated equipment, room, human resources and conditions) and timing, extending the process and thus decreasing the overall yield.

[0005] Thus, a need exists for improved drug delivery vehicles that prevent moisture and vapor ingress.

SUMMARY

[0006] The present disclosure relates to capsules, enteric coatings for capsules, methods of producing capsules, and methods of coating capsules. The capsules described herein prevent moisture and vapor ingress into the capsule during delivery of the payload. For example, the capsule may include a moisture-barrier layer that prevents moisture from entering interior volume of the capsule until delivery in the gastrointestinal tract. The capsules described herein also include an enteric coating that leaves little or no residue when dissolved. The friability of the enteric coating of the capsule advantageously allows for mechanical actuators to effectively deploy from the interior volume of the capsule.

[0006a] In one aspect, the present disclosure refers to a method of producing a capsule, the method comprising:

providing a mold;

depositing parylene on the mold to form a parylene layer;

scoring the parylene layer, and

coating the parylene layer with a polymer to produce a capsule.

[0006b] In another aspect, the present disclosure refers to a capsule comprising:

a first layer comprising parylene;

a second layer adjacent the first layer, the second layer comrpising a polymer; and

a third layer adjacent the second layer, the hird layer comprising an enteric coating.

[0007] Examples of the present disclosure include a method of producing a capsule. The method includes providing a mold, depositing a parylene on the mold to form a parylene layer, scoring the parylene layer, and coating the parylene layer with a polymer to produce a capsule. In some examples, the method includes polishing a surface of the mold to ease release of the capsule. In some examples, the method includes applying a release agent on the mold before deposition of the parylene layer. In some examples, the release agent is Micro90. In some examples, scoring the parylene layer comprises cutting

the parylene to form a pattern on opposing sides of the capsule. In some examples, the method includes treating an outer surface of the parylene layer with oxygen plasma prior to coating with the polymer. In some examples, a thickness of the parylene layer ranges from 0.5 μm to 30 μm. In some examples, a thickness of the parylene layer ranges from 5 μm to 10 μm. In some examples, depositing the parylene layer comprises chemical vapor deposition of parylene on the mold. In some examples, depositing the parylene layer comprises depositing, in a first deposition step, parylene on the mold to produce a primer layer, treating the primer layer with a release agent, and depositing, in a second deposition step, parylene on the primer layer to produce the parylene layer. In some examples, wherein the polymer is polyvinyl alcohol. In some examples, coating the parylene

layer with the polymer comprises a plurality of coating steps. In some examples, a thickness of the polymer layer ranges from 100 μm to 250 μm. In some examples, the method further comprises applying an enteric coating on the polymer layer. In some examples, the enteric coating comprises anionic methacrylate copolymer, talc, and plasticizer. In some examples, the method further comprises encapsulating a needle delivery system in the capsule.

[0008] Examples of the present disclosure include a capsule. The capsule includes a first layer comprising parylene. The capsule includes a second layer adjacent the first layer. The second layer comprises a polymer. The coating includes a third layer adjacent the second layer. The third layer comprises an enteric coating. In some embodiments, wherein the first layer is scored. In some examples, the first layer is scored to form a bi-fold pattern on opposing sides of the capsule. In some examples, a thickness of the parylene layer ranges from 0.5 μm to 30 μm. In some examples, the second layer comprises a plurality of layers, wherein at least one of the plurality of layers comprises polyvinyl alcohol. In some examples, the polymer comprises one or more of hydroxypropyl methylcellulose, pullulan, polyvinyl alcohol, or polyvinylpyrrolidone. In some examples, the second layer has a thickness from 100 μm to 250 μm. In some examples, the enteric coating comprises anionic methacrylate copolymer, talc, and plasticizer. In some examples, talc comprises 40 wt. % to 80 wt. % of the enteric coating, based on the total weight of the enteric coating. In some examples, anionic methacrylate copolymer comprises 20 wt. % to 60 wt. % of the enteric coating, based on the total weight of the enteric coating. In some examples, the first layer is surface treated with oxygen plasma. In some examples, the capsule does not comprise pullulan or hydroxypropyl methylcellulose. In some examples, the capsule comprises a fourth layer comprising anionic methacrylate copolymer and plasticizer. In some examples, the polymer of the second layer comprises polyvinyl alcohol, the enteric coating comprises anionic methacrylate copolymer, talc, and plasticizer, and a fourth layer comprises anionic methacrylate copolymer and plasticizer.

[0009] Examples of the present disclosure include an enteric coating composition. The enteric coating composition may comprise an anionic methacrylate copolymer, talc, and plasticizer. In some examples, the enteric coating composition comprises 20 wt. % to 60 wt. % anionic methacrylate copolymer, based on

the total weight of the composition. In some examples, the enteric coating composition comprises 40 wt. %

to 80 wt. % of talc, based on the total weight of the composition. In some examples, a weight ratio of talc to anionic methacrylate copolymer ranges from 0.5:1 to 10:1. In some examples, a weight ratio of talc to anionic methacrylate copolymer ranges from 1:1 to 3:1. In some examples, the plasticizer is present in an amount from 5 wt. % to 25 wt. %, based on the total weight of the anionic methacrylate copolymer. In some examples, the plasticizer is hydrophobic. In some examples, the plasticizer comprises dibutyl sebacate. In some examples, a capsule comprising the enteric coating composition described herein.

[0010] Examples of the present disclosure include a method of producing a coating composition. The method includes providing a solvent comprising a plasticizer, adding anionic methacrylate copolymer to the solvent, adding talc to the solvent, and mixing the anionic methacrylate copolymer and talc in the solvent to produce the coating composition. In some examples, the plasticizer is hydrophobic. In some embodiments, the plasticizer comprises dibutyl sebacate. In some examples, the solvent comprises one or more of acetone, isopropyl alcohol, and water. In some examples, the plasticizer is present in an amount from 5 wt. % to 25 wt. %, based on the weight of the anionic methacrylate copolymer. In some examples, a weight ratio of talc to anionic methacrylate copolymer ranges from 0.5:1 to 10:1. In some examples, a weight ratio of talc to anionic methacrylate copolymer ranges from 1:1 to 3:1. In some examples, providing the solvent comprises mixing the plasticizer in the solvent prior to adding the enteric composition.

[0011] Examples of the present disclosure include a method of coating a capsule. The method includes providing an enteric solution comprising a solvent, a plasticizer, anionic methacrylate copolymer, and talc, coating a capsule with the enteric solution, and drying the enteric solution on the capsule to produce an enteric coating. In some examples, coating the capsule comprises dip coating the capsule in the enteric solution. In some examples, the enteric coating comprises 20 wt. % to 60 wt. % of anionic methacrylate copolymer, based on the total weight of the enteric coating. In some examples, the enteric coating comprises 40 wt. % to 80 wt. % of talc, based on the total weight of the enteric coating. In some examples, the method includes overcoating the capsule with a second enteric solution comprising anionic methacrylate copolymer and plasticizer. In some

examples, the method includes coating one or more additional polymer layers on the capsule. In some examples, drying the enteric solution on the capsule comprises a first drying step comprising rotating the capsule in a

rotisserie at ambient conditions, a second drying step comprising rotating the capsule in a rotisserie at ambient conditions with forced air, and a third drying step comprising drying the enteric solution in an oven.

[0012] Further examples, objects, and advantages will become apparent upon consideration of the detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] FIG. 1 provides a flow diagram of a method of producing a capsule according to some embodiments of the present disclosure.

[0014] FIG. 2A illustrates a capsule according to some embodiments of the present disclosure.

[0015] FIG. 2B illustrates a capsule including a needle delivery system according to some embodiments of the present disclosure.

[0016] FIGS. 3A and 3B illustrate an embodiment of a scored parylene layer of the capsule according to some embodiments of the present disclosure.

[0017] FIG. 4 illustrates a scoring pattern on the parylene layer of the capsule according to some embodiments of the present disclosure.

[0018] FIG. 5 provides a graph of the polymer thickness of the capsule according to some embodiments of the present disclosure.

[0019] FIGS. 6A-6C illustrate deploying a microneedle system from a capsule according to some embodiments of the present disclosure.

[0020] FIG. 7 provides a flow diagram of a method of coating a capsule with an enteric solution according to some embodiments of the present disclosure.

[0021] FIGS. 8A-8D illustrate a manufacturing process for producing a capsule according to some embodiments of the present disclosure.

[0022] FIG. 9 provides a qualitative graph of the dissolution rates and gastric protection for various HPMC capsules.

[0023] FIG. 10A-H provide images showing the residue of the capsule after dissolution according to some embodiments of the present disclosure.

[0024] FIG. 11A-F provide visibility tests showing moisture ingress in the capsules in simulated gastric fluid according to some embodiments of the present disclosure.

[0025] FIGS. 12A-12F show a process of producing capsules by melting and reflowing a polymer according to some embodiments of the present disclosure.