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(54) **Title:** MULTI-COMPONENT PHARMACEUTICAL SINGLE DOSAGE FORMS AND METHODS EMPLOYED THEREOF

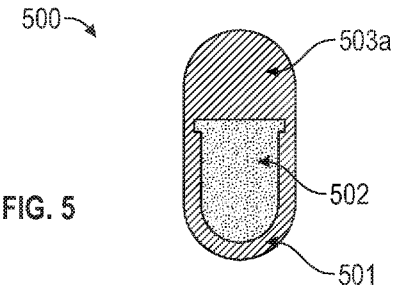


FIG. 5

(57) **Abstract:** Exemplary embodiments of the present disclosure are directed towards multi-component pharmaceutical single dosage forms and methods employed thereof. The multi-component pharmaceutical single dosage form comprising: a plurality of sub-units comprising a body piece and a cap piece, wherein the body piece is a capsule shaped or cup shaped tablet piece filled with a powder selected from an active drug substance blend, and the cap piece compressed in pre-determined dimensions with suitable punches to provide the multi- component pharmaceutical single dosage form. The advantage of the dosage form disclosed herein is that the active ingredient blend is not subjected to compression forces of tablet. Also lubricant, binder or disintegrant concentrations required in the blend is lower compared to conventional tablet dosage forms. These provide better scale up process with less quality issues.

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# "MULTI-COMPONENT PHARMACEUTICAL SINGLE DOSAGE FORMS AND METHODS EMPLOYED THEREOF"

## TECHNICAL FIELD

[001] The present disclosure relates generally to the field of tablet formulations In particular, the present disclosure is related to multi-component pharmaceutical single dosage forms and methods employed thereof. More particularly, the multi-component pharmaceutical single dosage forms disclosed herein comprise a plurality of tablet sub-units, a body piece and a cap.

## BACKGROUND

[002] Many oral dosage forms have been developed over the years and the more popular oral dosage forms are tablets, capsules and gelcaps. Tablets are compressed or molded solid dosage forms of various sizes or various shapes. Oblong-shaped tablets may sometimes be referred to as caplets. Tablets remain popular with consumers, however uncoated tablets suffer from drawbacks such as medicinal taste, a tendency to powder or flake (i.e., physical disintegration) when packaged in bottles, and/or the perception by consumers that they are not easy to swallow. These limitations are overcome by coating the tablets with a polymeric coating.

[003] Hard gelatin capsules are popular dosage forms consisting of two halves, a body and a cap. Over the years these hard gelatin capsules are used to deliver medicament in the form of powder, liquid or suspension form. Soft gelatin capsules are the dosage forms made of gelatin films and are used to deliver medicament in liquid or suspension form.

[004] Enrobed tablets are the dosage forms wherein solid tablet core is enrobed in soft elastic film material such as a gelatin film has significant advantages like tamper evident and ease of swallowing making it one of the most desired dosage form. The enrobed tablets can be further processed to have enteric coatings for acid resistant properties and also the enrobed tablet can be enrobed to have significantly more strength and resistance to breakage during handling.

[005] Several times while formulating some APIs in tablet dosage form we come across several challenges like variation in dissolution, drug stability and bioavailability issues. Further, tablets require very high compaction forces for formation. Hard gelatin capsules offer distinct advantages over tablets like the powder containing active substance can be filled into capsules with very little compaction or un-compacted, compared to tablet. Also pellets or mini tablets can be filled into the capsules. Capsules require lesser amounts of disintegrants and lubricants compared to tablets due to lower compacted powder mass. Many times direct mixing and filling into capsules minimize scale up issues in commercial production. Often capsule dosage form can offer better bioavailability and less scale up issues.

[006] There is a need to deliver powder with active substance/blend in un-compacted or with very little compaction in a stabilized multi-component pharmaceutical single dosage forms. Based on the aforementioned discussion, there still remains an unmet need in the art to ameliorate or overcome the lacunae in development of stabilized multi-component pharmaceutical single dosage forms and methods of preparing the same. The above discussion of documents is included solely for the purpose of providing a context for the present invention.

## BRIEF SUMMARY

[007] The following presents a simplified summary of the disclosure in order to provide a basic understanding to the reader. This summary is not an extensive overview of the disclosure and it does not identify key/critical elements of the invention or delineate the scope of the invention. Its sole purpose is to present some concepts disclosed herein in a simplified form as a prelude to the more detailed description that is presented later. A more complete appreciation of the present invention and the scope thereof can be obtained from the accompanying drawings which are briefly summarized below and the following detailed description of the presently preferred embodiments.

[008] An objective of the present disclosure is directed towards providing a multi-component pharmaceutical actives in a single unit of dosage form i.e., multi-component pharmaceutical single dosage forms.

[009] An objective of the present disclosure is directed towards providing a method of preparing multi-component pharmaceutical single dosage forms wherein the multi-

component pharmaceutical single dosage forms comprise at least two tablet sub-units, a body and a cap

[010] An objective of the present disclosure is directed towards providing various possible methods of sealing a body filled with powder with active drug substance and various forms of medicament (pellets, mini tablets, granules etc) incorporated in the dosage form of invention. Use of sealing agents to improve sealing is also disclosed herein.

[011] Another objective of the present disclosure is directed towards machines used for manufacturing of the multi-component pharmaceutical single dosage forms containing atleast two pieces comprising a body and a cap

[012] Another objective of the present disclosure is directed towards different capsule like multi-component pharmaceutical single dosage form offering advantages of capsule formulations.

[013] Another objective of the present disclosure is directed towards multi-component pharmaceutical single dosage form comprising placebo blend for body piece compressed in a tablet press with suitable punches and subsequently filled with powder form of active drug substances into the placebo body piece. The pre-compressed placebo cap piece is placed over body. Cap and body pieces are joined by pressing. A sealing agent having adhesive properties such as polymer or non-polymer in solvent can be applied to the cap surfaces coming in contact with placebo body piece to improve sealing strength.

[014] Another objective of the present disclosure is directed towards multi-component pharmaceutical single dosage form providing advantages like improving patient compliance by masking taste and odour.

[015] Another objective of the present disclosure is directed towards multi-component pharmaceutical single dosage form eliminating need of film coating for the dosage form. Further, stability of active drug substance is improved by adding antioxidants in placebo body piece and cap piece.

[016] Another objective of the present disclosure is directed towards multi-component pharmaceutical single dosage form wherein the active drug substance incorporated is in the form of pellets or mini tablets or tablets.

[017] In another aspect of the present disclosure, the multi-component pharmaceutical single dosage form may be extended release or immediate release tablets.

[018] According to an exemplary embodiment of the present disclosure, a multi-component pharmaceutical single dosage form comprising: a plurality of sub-units comprising a body piece and a cap piece, wherein the body piece is a capsule shaped tablet piece filled with an active drug substance blend, and the cap piece compressed in pre-determined dimensions with suitable punches and attached to provide the multi-component pharmaceutical single dosage form.

[019] Furthermore, the objects and advantages of this invention will become apparent from the following description.

## BRIEF DESCRIPTION OF THE DRAWINGS

[020] Other objects and advantages of the present invention will become apparent to those skilled in the art upon reading the following detailed description of the preferred embodiments, in conjunction with the accompanying drawings, wherein like reference numerals have been used to designate like elements, and wherein:

[021] FIG. 1 is a diagram 100 depicting a pictorial representation of multi-component pharmaceutical single dosage form comprising compression of placebo body piece, in accordance with one or more exemplary embodiments.

[022] FIG. 2 is a diagram 200 depicting a multi-component pharmaceutical single dosage form related to filling of powder with active drug substance into placebo body piece, in accordance with one or more exemplary embodiments.

[023] FIG. 3 is a diagram 300 depicting compression of placebo cap piece for a multi-component pharmaceutical single dosage form, in accordance with one or more exemplary embodiments.

[024] FIG. 4 is a diagram 400 depicting placing of placebo cap onto placebo body filled with powder with active drug substance, in accordance with one or more exemplary embodiments.

[025] FIG. 5 is a diagram 500 depicting a sealing of cap and body to form a multi-component pharmaceutical single dosage form, in accordance with one or more exemplary embodiments.

[026] FIG. 6 is a diagram 600 depicting different placebo cap designs for multi-component pharmaceutical single dosage form, in accordance with one or more exemplary embodiments.

## DETAILED DESCRIPTION

[027] It is to be understood that the present disclosure is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The present disclosure is capable of other embodiments and of being practiced or of being carried out in various ways. Also, it is to be understood that the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting.

[028] The use of "including", "comprising" or "having" and variations thereof herein is meant to encompass the items listed thereafter and equivalents thereof as well as additional items. The terms "a" and "an" herein do not denote a limitation of quantity, but rather denote the presence of at least one of the referenced item. Further, the use of terms "first", "second", and "third", and the like, herein do not denote any order, quantity, or importance, but rather are used to distinguish one element from another.

[029] All publications herein are incorporated by reference to the same extent as that clearly to be included by reference if each individual publication or patent application, and individually indicated. The following description includes information that may be useful for understanding the present invention. This does not admitted that any of the information is prior art, or to be or being specifically related to the invention claimed herein or implicit any prior art publication is referred to as provided herein.

[030] The term tablet unit/tablet sub-units refer to the tablet units that comprise the multi-component pharmaceutical single dosage form. As disclosed herein sub-units/units or table subunits, a body piece and a cap comprise the multi-component pharmaceutical single dosage form.

[031] Referring to FIG.1 represented by 100 is the placebo blend for body piece of the multi-component pharmaceutical single dosage form compressed with punches and specifically designed to form a capsule body shaped tablet piece as shown in FIG. 1. A capsule body shaped tablet piece can be prepared in various shapes and sizes. Example capsule body, cup etc. Placebo blend used for compression of body piece 101 comprises of at least one pharmaceutical diluent and a lubricant. The placebo blend optionally may comprise of a disintegrant, colorant, antiadherent. The placebo for body piece comprise of a lubricant to facilitate compression process. The placebo blend for body piece may also comprise other ingredients such as a disintegrant to facilitate disintegration of the dosage form such as Crospovidone, Croscarmellose sodium, Sodium starch glycolate, a lubricant such as Magnesium stearate, Sodium stearyl fumarate, stearic acid, and calcium stearate. Further optionally excipients such as binders, glidants, and wetting agents may be incorporated into the body piece. Diluent such as Lactose, microcrystalline cellulose, starch or dicalcium phosphate can be used.

[032] Referring to FIG. 2 is a diagram 200 depicting a multi-component pharmaceutical single dosage form related to filling of powder with active drug substance into placebo body piece, in accordance with one or more exemplary embodiments. Once the placebo body piece is formed the placebo body piece is filled with a powder with active drug substance 202 as shown in FIG. 2. The powder with active drug substance 202 may comprise of an active drug substance and at least one pharmaceutical excipient.

[033] Referring to FIG. 3 is a diagram 300 depicting compression of placebo cap piece for a multi-component pharmaceutical single dosage form, in accordance with one or more exemplary embodiments. A placebo cap is compressed in pre-determined dimensions with suitable punches in another tablet press as shown in FIG. 3. The cap portions coming in contact with body portion can be applied with sealing agent. A sealing agent may comprise of polymer or non-polymer substance having adhesive properties and dispersed or dissolved in solvent. The cap is then transported and placed over the body piece filled with powder with

active substance. 303a and 303b represents placebo caps while 304 represent the adhesive layer.

[034] Referring to FIG.S 4 and FIG.5 are diagrams 400 and 500 respectively; FIG.4 represented by 400 depicts placing of placebo cap onto placebo body filled with powder with active drug substance. 401 is the placebo body, 402 is the powder with active and 403a is placebo cap. While FIG.5 represented by 500 represents sealing of a cap and a body to form multi-component pharmaceutical single dosage form. 501 is the placebo body, 502 is the powder with active and 503a is placebo cap. The cap is pressed so that body and cap is tightly held as shown in FIG. 4 and FIG. 5. The cap may be compressed in various sizes and shapes suitable for the body piece. Excipients used for compression of placebo body piece can be used for compression of cap piece.

[035] FIG. 6 is a diagram 600 depicting different placebo cap designs for multi-component pharmaceutical single dosage form, in accordance with one or more exemplary embodiments. 601 is placebo body, 602 is powder with active, 603a, 603b and 604 represent placebo caps in different shapes/configurations.

[036] In another embodiment, alternatively a pre-formed placebo cap can also be used to seal the body piece which contains at least one pharmaceutical excipient. The pre-formed placebo cap can be further embedded with an adhesive ingredient on one surface which upon coming in contact with slight moisture can be adhered to body piece. Also placebo body piece and cap piece may be incorporated with active substance based on requirement. Pre-formed cap can also be coated with film coatings containing polymers such as Hydroxypropylmethyl cellulose to provide adhesive properties for attaching it to body piece upon contact with solvents such as water, alcohol etc.

[037] In an embodiment, the powder with active drug substance in the dosage form of invention can be replaced with medicament in the form of pellets or mini tablets or tablets or any other suitable form.

[038] In an embodiment, the diluent may include not limiting to calcium carbonate, calcium phosphate dibasic, calcium phosphate tribasic, calcium sulfate, silicified microcrystalline, cellulose acetate, sugar, dextrates, dextrin, dextrose, fructose, glyceryl palmitostearate,

hydrogenated vegetable oil type I, isomalt, kaolin, lactitol, lactose, mannitol, magnesium carbonate, magnesium oxide, maltodextrin, maltose, mannitol, microcrystalline cellulose, polydextrose, sorbitol, starch, starch pregelatinized, sucrose, xylitol.

[039] In an embodiment, the lubricant may include not limiting to magnesium stearate, Sodium stearyl fumarate, stearic acid, calcium stearate, sodium stearyl fumarate and polyethylene glycols. Further optionally excipients such as binders, glidants, antiadherents, wetting agents may be incorporated into the body piece.

[040] In an embodiment, the placebo blend for body piece may also comprise other ingredients such as a disintegrant to facilitate disintegration of the dosage form such as Crospovidone, Croscarmellose sodium, Sodium starch glycolate, Low substituted hydroxyproyl cellulose, Carboxymethylcellulose calcium, starches, preglatinized starch.

[041] In an embodiment, once the body piece is formed, the capsule shaped body piece is filled with active drug substance blend which may be in the form of powder, granules, immediate release pellets, enteric coated pellets, mini tablets as shown in FIG. 2. Further various forms of active substance blend may comprise of atleast one active drug substance and at least one pharmaceutical excipient.

[042] In an embodiment, various forms of active substance blend such as powders, granules, immediate release pellets, enteric coated pellets, mini tablets used for the preparation of the dosage form of invention may include any of the active ingredients given here not limiting to Anastrozole, Alendronate Sodium, Atorvastatin, Aciclovir, Aspirin, Amitriptyline, Amoxicillin, Amlodipine Besylate, Albuterol, Alprazolam, Atenolol, Azithromycin, Allopurinol, Hydrochlorothiazide, Acyclovir, Amiodarone Hydrochloride, Atomoxetine Hydrochloride, Acetaminophen, Aripiprazole, Amoxicillin, Ambroxol, Atorvastatin, Bisoprolol, Bupropion, Baclofen, Bisoprolol Fumarate, Benztropine Mesylate, Benazepril Hydrochloride, Buspirone Hydrochloride, Cyclobenzaprine, Carvedilol, Clopidogrel Bisulfate, Carbidopa, Chlorthalidone, Carisoprodol, Clonazepam, Clavulanate Potassium, Citalopram, Cefuroxime, Clonidine, Cetirizine Hydrochloride, Chlorthalidone, Chlopromazine, Ciprofloxacin, Cefadroxil, Cefixime, Clarithromycin, Canagliflozin, Carbamazepine, Celecoxib, Ciprofloxacin, Cephalexin, Cefdinir, Codeine Phosphate, Clozapin, Candesartan, Chloroquine, Ceftriaxone, Cefotaxim, Captopril, Cyproheptadine,

Desloratadine, Domperidone, Diclofenac, Diazepam, Duloxetine, Diltiazem Hydrochloride, Dexlansoprazole, Domperidone, Dextroamphetamine, Dexamethasone, Doxycycline, Diphenhydramine Hydrochloride, Donepezil Hydrochloride, Dapagliflozin, Diclofenac salts, Dabigatran Etexilate Mesylate, Desvenlafaxine, Divalproex Sodium, Dextromethorphan, Empagliflozin, Enalapril Maleate, Ergocalciferol, Ezetimibe, Escitalopram Oxalate, Ethinyl Estradiol, Erythromycin, Esomeprazole, Eszopiclone, Epinephrine Hydrochloride, Folic Acid, Ferrous Sulfate, Fluoxetine Hydrochloride, Finasteride, Famotidine, Fentanyl, Furosemide, Fenofibrate, Fluconazole, Fexofenadine, Guaifenesin, Gemfibrozil, Glyburide, Glipizide, Gabapentin, Glimepiride, Guaifenesin, Hydrocodone Bitartrate, Hydrochlorothiazide, Haloperidol, Hydralazine Hydrochloride, Hydroxychloroquine Sulfate, Hydromorphone Hydrochloride, Isoniazid, Itraconazole, Irbesartan, Ibuprofen, Isosorbide Mononitrate, Ketorolac, Levocetirizine, Levothyroxine, Levofloxacin, Lisinopril, Lovastatin, Levodopa, Loperamide, Losartan Potassium, Levetiracetam, Lorazepam, Loratadine, Labetalol, Lamotrigine, Linagliptin, Lansoprazole, Loperamide, Metronidazole, Methylphenidate, Meloxicam, Metoclopramide Hydrochloride, Mirtazapine, Metoprolol, Metformin Hydrochloride, Memantine Hydrochloride, Metformin Hydrochloride, Mesalamine, Methimazole, Minocycline Hydrochloride, Montelukast, Methotrexate, Methylprednisolone, Mometasone, Moxifloxacin, Mefenamic acid, Mebendazole, Metamizole, Miconazole, Meclizine Hydrochloride, Nebivolol, Nifedipine Hydrochloride, Nortriptyline Hydrochloride, Naproxen, Nadolol, Niacin, Nitrofurantoin, Norethindrone, Norgestimate Estradiol, Naphazoline Hydrochloride, Norfloxacin, Omeprazole, Oxcarbazepine, Oxybutynin, Oseltamivir Phosphate, Olmesartan, Ondansetron, Oxycodone, Olanzapine, Oxymetzoline, Ofloxacin, Pantoprazole Sodium, Pravastatin Sodium, Pramipexole Dihydrochloride, Phenytoin, Propranolol Hydrochloride, Prednisolone, Pregabalin, Paroxetine, Prochlorperazine, Pioglitazone, Promethazine Hydrochloride, Pseudoephedrine Hydrochloride, Prazosin Hydrochloride, Prednisone, Piroxicam, Prednisolone, Propranolol, Pyrazinamide, Quetiapine Fumarate, Quinapril, Ropinirole Hydrochloride, Rizatriptan Benzoate, Ranolazine, Rosuvastatin Calcium, Risperidone, Ranitidine, Ramipril, Rabeprazole Sodium, Rivaroxaban, Raloxifene Hydrochloride, Rifampicin, Salbutamol, Sumatriptan, Sitagliptin Phosphate, Spironolactone, Solifenacin Succinate, Sildenafil, Simvastatin, Sulfamethoxazole, Sertraline Hydrochloride, Salmeterol, Sitagliptin Phosphate, Sotalol Hydrochloride, Tizanidine, Timolol, Tolterodine Tartrate, Topiramate, Telmisartan, Trazodone Hydrochloride, Timolol Maleate, Temazepam, Tadalafil, Tramadol Hydrochloride, Tamsulosin Hydrochloride, Testosterone, Tamoxifen Citrate,

Triprolidine, Theophyline, Tranexamic acid, Trimetazidine, Valsartan, Vilazodone, Hydrochloride, Venlafaxine Hydrochloride, Verapamil Hydrochloride, Valacyclovir, Warfarin, Xinafoate, Zolpidem Tartrate.

[043] In an embodiment, pharmaceutical Excipients used for preparation of active substance blend may comprise of a diluent, a binder, a glidant, a disintegrant, lubricant etc.

[044] In an embodiment, a sealing agent may comprise of atleast one adhesive agent and one solvent. A sealing agent may include not limiting to acacia, carbomers, gelatin, guar gum, dextrin, hydroxypropyl starch, liquid glucose, magnesium aluminium silicate, sodium alginate, zein, Povidone, co povidone, Hypromellose, hydroxypropyl cellulose, carboxymethyl cellulose.

[045] In an embodiment, solvents for preparation sealing agent may include not limiting to water or organic solvents such as Iso-propyl alcohol, Ethanol, acetone, Acetic acid, Ethyl acetate, Triethylamine, Dimethyl sulfoxide etc may be used individually or in combination.

[046] In an embodiment, the compressed cap is transported and placed over the body piece filled with active drug substance blend.

[047] In an embodiment, alternatively a pre-formed placebo cap can also be used to seal the body piece which contains at least one pharmaceutical excipient. The pre-formed placebo cap can be further embedded with an adhesive ingredient on one surface which upon coming in contact with slight moisture can be adhered to body piece. Also placebo body piece and cap piece may be incorporated with active substance based on requirement.

[048] In an embodiment, the powder form of active substance blend in the dosage form of invention can be replaced with other forms such as granules, pellets or mini tablets or any other suitable form.

[049] The invention is further illustrated by the following examples which are provided to be exemplary of the invention and do not limit the scope of the invention. While the present invention has been described in terms of its specific embodiments, certain modifications and

equivalents will be apparent to those skilled in the art and are intended to be included within the scope of the present invention

[050] Examples of manufacturing multi-component pharmaceutical single dosage form of invention is provided below:

[051] **Composition – Body piece**

| | |
|---|---|
| Microcrystalline cellulose | 100 mg |
| Lactose Monohydrate | 100 mg |
| Magnesium stearate | 2 mg |

Manufacturing procedure:

Microcrystalline cellulose, lactose monohydrate and magnesium stearate are sifted separately. Microcrystalline cellulose and Lactose monohydrate are mixed. To this Magnesium stearate is added and mixed. Blend is taken for compression in tablet in tablet compression machine.

[052] **Composition – Cap Piece**

| | |
|---|---|
| Microcrystalline cellulose | 50 mg |
| Lactose Monohydrate | 50 mg |
| Magnesium stearate | 1 mg |

[053] Separately sift microcrystalline cellulose, Lactose monohydrate and Magnesium stearate. Microcrystalline cellulose and Lactose monohydrate are mixed. To this Magnesium stearate is added and mixed. Blend is taken for compression in tablet in tablet compression machine.

[054] **Composition - Cap piece with polymer**

| | |
|---|---|
| Microcrystalline cellulose | 50 mg |

| | |
|---|---|
| Lactose Monohydrate | 48.5mg |
| Hydroxypropyl methyl cellulose | 50mg |
| Magnesium stearate | 1.5mg |

[055] Separately sift microcrystalline cellulose, Lactose monohydrate, Hydroxypropyl methyl cellulose and Magnesium stearate. Microcrystalline cellulose, Lactose monohydrate and Hydroxypropyl methyl cellulose are mixed. To this Magnesium stearate is added and mixed. Blend is taken for compression in tablet in tablet compression machine. Cap piece with polymer provide better adhesion on coming in contact with sealing agent.

[056] **Sealing agent**

| | |
|---|---|
| Hydroxypropyl methyl cellulose | 20 gm |
| Ethanol | 50 gm |
| Purified water | 30 gm |

Dissolved Hydroxypropyl methyl cellulose in a mixture of Ethanol and purified water.

[057] **Active ingredient Blend for filling:**

| | |
|---|---|
| Ramipril | 2.5mg |
| Hydroxypropylmethyl cellulose | 0.5mg |
| Purified water (removed during drying) | 0.5mg |
| Amlodipine (as Besilate) | 2.5mg |
| Pregelatinized starch | 50 mg |

[058] **Manufacturing procedure:**

Ramipril and Hydroxypropylmethyl cellulose are sifted and mixed. To this dry mix purified water is added and granulated. Wet mass is dried and sifted.

Ramipril granules are mixed with presifted Amlodipine and Pregelatinized starch. This blend is taken for filling.

[059] **Manufacturing procedure for Capsule like or Cup like Tablet:**

- ✓ For manufacturing dosage form of invention, dual compression machine generally used for tablet in tablet formulations is used with modifications. Optionally cap piece can be prepared separately and used in final compression process.
- ✓ One of the compression machine is fixed with 10 mm Flat, plain upper punches and 10 mm Flat lower punches. In this machine cap piece (lid piece) is compressed.
- ✓ The other compression machine is fixed with special tooling to compress cup like tablet. Upper punch with 10.1 mm outer diameter with 6 mm flat, plain tip with 6 mm deep is used. 10.1mm Flat, plain lower punches are used.
- ✓ Cap piece is compressed in first rotary compression machine. Simultaneously Cup like tablet body piece is compressed in second rotary compression machine. In to this cup like tablet body piece Ramipril and amlodipine granules were filled. Compressed Cap piece is applied with sealing agent and then placed over cup like tablet body piece. Mechanical pressure is applied on to Cap piece to attach it to body piece. After attachment the dosage form of invention is ejected from the compression machine.

[060] The advantage of dosage form of invention is active ingredient blend is not subjected to compression forces of tablet. Also lubricant, binder or disintegrant concentrations required in the blend is lower compared to conventional tablet dosage form. These provide better scale up process with less quality issues. The drawings and examples are provided for understanding the invention and however do not cover all possible examples

[061] In an embodiment, a multi-component pharmaceutical single dosage form may comprise the body piece or cap piece comprising at least one diluent and one lubricant and may not contain active drug substance.

[062] In an embodiment, a multi-component pharmaceutical single dosage form comprising: a plurality of sub-units comprising a body piece and a cap piece, wherein the body piece is a capsule shaped tablet piece filled with an active drug substance blend, and the cap piece compressed in pre-determined dimensions with suitable punches and attached to provide the multi-component pharmaceutical single dosage form.

[063] In an embodiment, the multi-component pharmaceutical single dosage form comprising a compressed cap piece having adhesive properties or applied with binder for

adhesive properties is placed over the capsule shaped tablet piece filled with the active drug substance blend and mechanically attached to form a tablet dosage form.

[064] In an embodiment, the multi-component pharmaceutical single dosage form comprising the active drug substance blend comprise at least one of: an active drug substance and a pharmaceutical excipient.

[065] In an embodiment, the multi-component pharmaceutical single dosage form comprising the body piece or cap piece comprise at least one diluent and one lubricant and optionally contain active drug substance.

[066] In an embodiment, the multi-component pharmaceutical single dosage form comprising the capsule shaped tablet piece is filled with the active drug substance blend is selected from a group comprising at least one of: a powder form; granules form; immediate release pellets; enteric coated pellets; mini tablets and combinations thereof.

[067] In an embodiment, the multi-component pharmaceutical single dosage form comprising the active drug substance blend comprises of a diluent, a binder, a glidant, a disintegrants and a lubricant.

[068] In an embodiment, the multi-component pharmaceutical single dosage form comprising the compressed cap piece and the capsule shaped tablet piece are joined by a sealing agent having adhesive properties applied to the compressed cap piece surface in contact with the capsule shaped tablet piece.

[069] In an embodiment, a process of preparing a multi-component pharmaceutical single dosage form comprising:

Step a) preparing a capsule shaped tablet piece filled with a powder selected from an active drug substance blend;

Step b) compressing a cap piece in pre-determined dimensions with suitable punches; and

Step c) placing the compressed cap piece over the capsule shaped tablet piece filled with the powder selected from the active drug substance blend and compressing the compressed cap piece and the capsule shaped tablet piece filled with the powder selected from the active drug substance blend to provide the multi-component pharmaceutical single dosage form.

[070] Reference throughout this specification to “one embodiment”, “an embodiment”, or similar language means that a particular feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment of the present

disclosure. Thus, appearances of the phrases “in one embodiment”, “in an embodiment” and similar language throughout this specification may, but do not necessarily, all refer to the same embodiment.

[071] The present disclosure has been described in terms of certain preferred embodiments and illustrations thereof, other embodiments and modifications to preferred embodiments may be possible that are within the principles and spirit of the invention. The above descriptions and figures are therefore to be regarded as illustrative and not restrictive. Thus the scope of the present disclosure is defined by the appended claims and includes both combinations and sub combinations of the various features described herein above as well as variations and modifications thereof, which would occur to persons skilled in the art upon reading the foregoing description.

# CLAIMS

I Claim:

1. A multi-component pharmaceutical single dosage form comprising:

a plurality of sub-units comprising a body piece and a cap piece, wherein the body piece is a capsule shaped tablet piece filled with an active drug substance blend, and the cap piece compressed in pre-determined dimensions with suitable punches and attached to provide the multi-component pharmaceutical single dosage form.

2. The multi-component pharmaceutical single dosage form as claimed in claim 1, wherein a compressed cap piece having adhesive properties or applied with binder for adhesive properties is placed over the capsule shaped tablet piece filled with the active drug substance blend and mechanically attached to form a tablet dosage form.

3. The multi-component pharmaceutical single dosage form as claimed in claim 1, wherein the active drug substance blend comprise at least one of: an active drug substance and a pharmaceutical excipient.

4. The multi-component pharmaceutical single dosage form as claimed in claim 1, wherein the body piece or cap piece comprise at least one diluent and one lubricant and optionally contain active drug substance.

5. The multi component pharmaceutical single dosage form as claimed in claim 1, wherein the capsule shaped tablet piece filled with active drug substance blend is selected from a group comprising at least one of: a powder form; granules form; immediate release pellets; enteric coated pellets; mini tablets and combinations thereof.

6. The multi-component pharmaceutical single dosage form as claimed in claim 1, wherein the active drug substance blend comprises of a diluent, a binder, a glidant, a disintegrants and a lubricant.

7. The multi-component pharmaceutical single dosage form as claimed in claim 1, wherein the compressed cap piece and the capsule shaped tablet piece are joined by a sealing agent having adhesive properties applied to the compressed cap piece surface in contact with the capsule shaped tablet piece.

8. A process of preparing a multi-component pharmaceutical single dosage form comprising:

Step a) preparing a capsule shaped tablet piece filled with a powder selected from an active drug substance blend;

Step b) compressing a cap piece in pre-determined dimensions with suitable punches; and

Step c) placing the compressed cap piece over the capsule shaped tablet piece filled with the powder selected from the active drug substance blend and compressing the compressed cap piece and the capsule shaped tablet piece filled with the powder selected from the active drug substance blend to provide the multi-component pharmaceutical single dosage form.

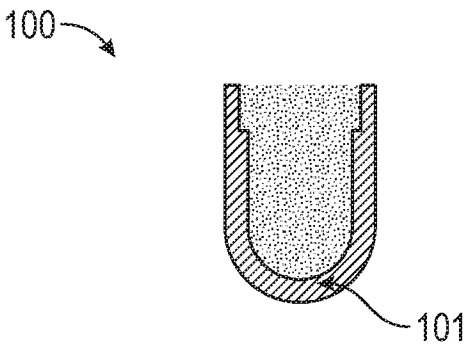


FIG. 1

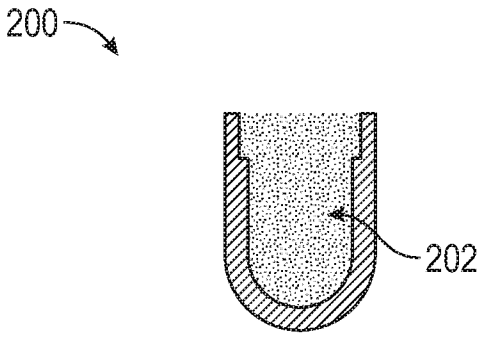


FIG. 2

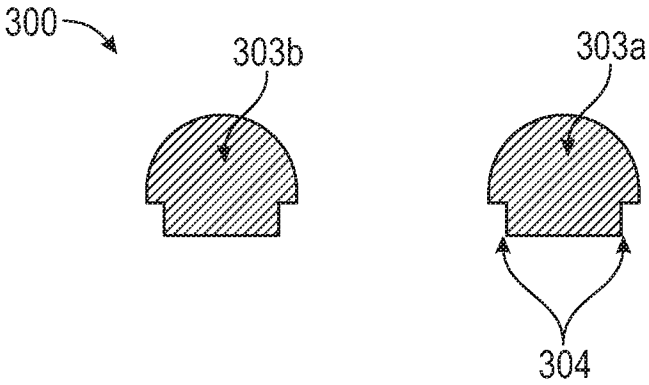


FIG. 3

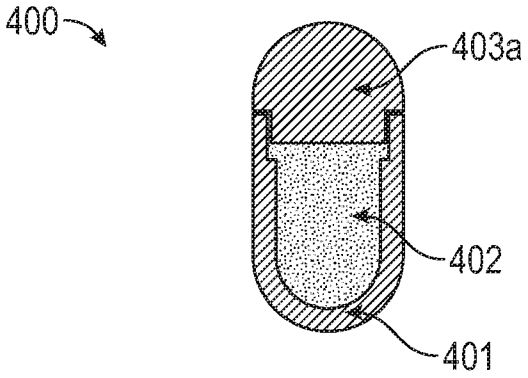


FIG. 4

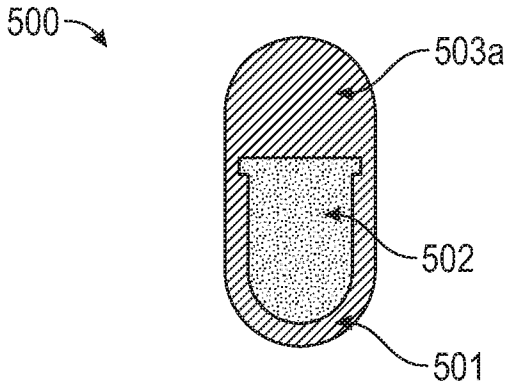


FIG. 5

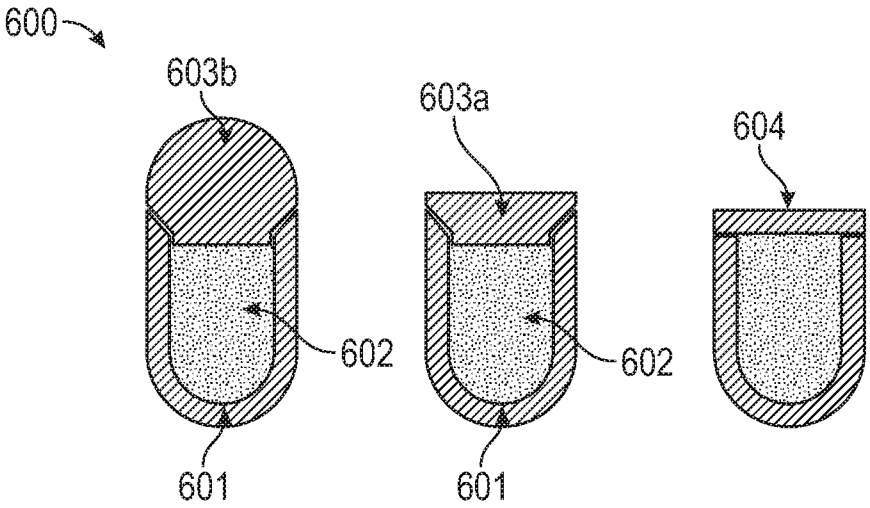


FIG. 6

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2020/053482

A. CLASSIFICATION OF SUBJECT MATTER
A61K9/28,C23C28/00 Version=2020.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K,C23C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

TotalPatent One, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| A | WO 2002060385 A2 SMITHKLINE BEECHAM PLC [GB] 08 AUGUST 2002 (08/08/2002) claims 1-43 | 1-8 |
| A | US 8673350 B2 MCALLISTER STEPHEN MARK [US] 18 MARCH 2014 (18/03/2014) claims 1-26 | 1-8 |
| A | US 20140044784 A1 KIM JE HAK[KR] 13 FEBRUARY 2014 (13/02/2014) claims 1-19 | 1-8 |

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 08-07-2020 | 08-07-2020 |
| Name and mailing address of the ISA/<br>Indian Patent Office<br>Plot No.32, Sector 14,Dwarka,New Delhi-110075<br>Facsimile No. | Authorized officer<br>Donga Naga Raveendra<br>Telephone No. +91-1125300200 |

**INTERNATIONAL SEARCH REPORT**
Information on patent family members

International application No.
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| Citation | Pub.Date | Family | Pub.Date |
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